PUBLIC

UNITED STATES OF AMERICA
FEDERAL TRADE COMMISSION
OFFICE OF ADMINISTRATIVE LAW JUDGES

DOCKET NO. 9344

In the Matter of

POM WONDERFUL LLC and
ROLL GLOBAL LLC,
as successor in interest to
Roll International Corporation,
companies, and

STEWART A. RESNICK,
LYNDA RAE RESNICK, and
MATTHEW TUPPER, individually
and as officers of the companies,

Respondents.

INITIAL DECISION

D. Michael Chappell
Chief Administrative Law Judge

Date: May 17, 2012

TABLE OF CONTENTS

I. INTRODUCTION

A. Summary of Complaint and Answer

The Complaint, issued September 24, 2010, alleges that Respondents POM Wonderful LLC, Roll Global LLC, Stewart A. Resnick, Lynda Rae Resnick, and Matthew Tupper ("Respondents") disseminated advertising and promotional materials representing that the consumption of eight ounces of POM Juice, one POMx Pill, or one teaspoon of POMx Liquid (the "POM Products") daily "prevents or reduces the risk of" or "treats" heart disease, prostate cancer or erectile dysfunction. Complaint ¶¶ 9, 10, 19. Because, according to the Complaint, Respondents represented that they possessed and relied upon, but in fact did not possess or rely upon a reasonable basis substantiating such claims, Respondents' representations were false or misleading. Complaint ¶¶ 19-21.

The Complaint further alleges that Respondents disseminated advertising and promotional materials representing that "clinical studies, research, and/or trials prove" that consuming the POM Products "prevents or reduces the risk of" or "treats" heart disease, prostate cancer or erectile dysfunction. Complaint ¶¶ 9, 10, 12, 14, 16. The Complaint further asserts that these representations are false or misleading because, in fact, clinical studies, research, and/or trials do not prove that consuming the POM Products, "prevents or reduces the risk of" or "treats" heart disease, prostate cancer or erectile dysfunction. Complaint ¶¶ 13, 15, 17, 18.

The Complaint concludes that the foregoing acts and practices of Respondents constitute unfair or deceptive acts or practices, and false advertising, in violation of sections 5(a) and 12 of the Federal Trade Commission Act. Complaint ¶ 22.

Respondents filed their Answer to the Complaint on October 18, 2010. While admitting that they disseminated the advertising and promotional materials attached as exhibits to the Complaint, they denied that such materials make the claims alleged. Answer ¶¶ 9, 10, 12, 14, 16, 19. Respondents also deny making false or misleading claims, and further aver that "there is substantial scientific research indicating the health benefits of [the POM Products] and substantiating their advertising and promotional materials." Answer ¶¶ 13, 15, 17, 18, 21, 22.

B. Procedural History

The administrative hearing (also referred to herein as the "trial" or "administrative trial") in the instant case began on May 24, 2011 and concluded on November 4, 2011. By Order dated November 18, 2011, the hearing record was closed. The hearing record is voluminous. Nearly 2000 exhibits were admitted. Among these exhibits are the advertisements and promotional materials upon which Complaint Counsel relies to prove that Respondents made the representations alleged in the Complaint. These consist of: 27 print advertisements, some of which comprise multiple pages; 2 multi-page newsletters; 7 separate "web captures" of Respondents' 3 websites, recorded at multiple points in time; 2 internet "banner" advertisements; 4 press releases; and 4 television interviews (the "Challenged Advertisements"); *see* Complaint Counsel's Post-Hearing Brief, Appendix A. Also included in the exhibits are more than 46 scientific studies sponsored by Respondents and offered on the issue of substantiation, numerous consumer surveys, and 14 expert reports. In addition, 24 witnesses testified, either live or by deposition, including 14 expert witnesses, and there are 3,273 pages of trial transcript. The parties submitted 3,929 proposed findings of fact (1,130 by Complaint Counsel and 2,799 by Respondents). The parties' proposed findings of fact and conclusions of law, replies to proposed findings of fact and conclusions of law, post-trial briefs, and reply briefs total 3,396 pages.

Commission Rule 3.51(a) states that the Administrative Law Judge ("ALJ") shall file an initial decision within 70 days after the filing of the last filed initial or reply proposed findings of fact, conclusions of law and order pursuant to Commission Rule 3.46 and that the Administrative Law Judge may extend this time period by up to 30 days for good cause. 16 C.F.R. § 3.51(a). The parties filed concurrent post-trial briefs and proposed findings of fact on January 7, 2012. The parties filed replies to the other's proposed findings and briefs on February 7, 2012. Pursuant to Commission Rule 3.41(b)(6), closing arguments were held on March 6, 2012.[1]

[1] Although Commission Rule 3.41(b)(6) states that "[e]ach side shall be permitted to make a closing argument no later than 5 days after the last filed proposed findings," by Order dated January 26, 2012, good cause was found for moving the closing arguments to March 6, 2012.

Seventy days from the last filed reply proposed findings and conclusions and briefs was April 17, 2012 and, absent an order pursuant to Rule 3.51, the Initial Decision was to be filed on or before April 17, 2012. Based on the voluminous and complex record in this matter and other grounds, an Order was issued on April 16, 2012 finding good cause for extending the time period for filing the Initial Decision by 30 days. Accordingly, issuance of this Initial Decision on May 17, 2012 is in compliance with Commission Rule 3.51(a).

C. Evidence

This Initial Decision is based on a consideration of the whole record relevant to the issues, including the exhibits properly admitted into evidence, deposition transcripts, and the transcripts of testimony at trial, and addresses the material issues of fact and law. The briefs and proposed findings of fact and conclusions of law, and the replies thereto, submitted by the parties were thoroughly reviewed. Proposed findings of fact submitted by the parties, but not included in this Initial Decision were rejected, either because they were not supported by the evidence or because they were not dispositive or material to the determination of the allegations of the Complaint or the defenses thereto. The Commission has held that Administrative Law Judges are not required to discuss the testimony of each witness or all exhibits that are presented during the administrative adjudication. *In re Amrep Corp.*, No. 9018, 102 F.T.C. 1362, 1670, 1983 FTC LEXIS 17, *566-67 (Nov. 2, 1983). Further, administrative adjudicators are "not required to make subordinate findings on every collateral contention advanced, but only upon those issues of fact, law, or discretion which are 'material.'" *Minneapolis & St. Louis Ry. Co. v. United States*, 361 U.S. 173, 193-94 (1959); *accord Stauffer Labs., Inc. v. FTC*, 343 F.2d 75, 82 (9th Cir. 1965). *See also Borek Motor Sales, Inc. v. National Labor Relations Bd.*, 425 F.2d 677, 681 (7th Cir. 1970) (holding that it is adequate for the Board to indicate that it had considered each of the company's exceptions, even if only some of the exceptions were discussed, and stating that "[m]ore than that is not demanded by the [Administrative Procedure Act] and would place a severe burden upon the agency").

Under Commission Rule 3.51(c)(1), "[a]n initial decision shall be based on a consideration of the whole record relevant to the issues decided, and shall be supported by reliable and probative evidence." 16 C.F.R. § 3.51(c)(1); *see In re Chicago Bridge & Iron Co.*,

No. 9300, 138 F.T.C. 1024, 1027 n.4, 2005 FTC LEXIS 215, at *3 n.4 (Jan. 6, 2005). Under the Administrative Procedure Act ("APA"), an Administrative Law Judge may not issue an order "except on consideration of the whole record or those parts thereof cited by a party and supported by and in accordance with the reliable, probative, and substantial evidence." 5 U.S.C. § 556(d). All findings of fact in this Initial Decision are supported by reliable, probative, and substantial evidence. Citations to specific numbered findings of fact in this Initial Decision are designated by "F."[2]

Pursuant to Commission Rule 3.45(b), several orders were issued in this case granting *in camera* treatment to material, after finding, in accordance with the Rule, that its public disclosure would likely result in a clearly defined, serious injury to the entity requesting *in camera* treatment. 16 C.F.R. § 3.45(b). Commission Rule 3.45(a) allows the Administrative Law Judge "to grant *in camera* treatment for information at the time it is offered into evidence subject to a later determination by the [administrative] law judge or the Commission that public disclosure is required in the interests of facilitating public understanding of their subsequent decisions." *In re Bristol-Myers Co*., Nos. 8917-19, 90 F.T.C. 455, 457, 1977 FTC LEXIS 25, at *6 (Nov. 11, 1977). As the Commission later reaffirmed in another leading case on *in camera* treatment, since "in some instances the ALJ or Commission cannot know that a certain piece of information may be critical to the public understanding of agency action until the Initial Decision or the Opinion of the Commission is issued, the Commission and the ALJs retain the power to reassess prior *in camera* rulings at the time of publication of decisions." *In*

[2] References to the record are abbreviated as follows:
CX – Complaint Counsel's Exhibit
PX – Respondents' Exhibit
JX – Joint Exhibit
Tr. – Transcript of testimony before the Administrative Law Judge
Dep. – Transcript of Deposition
CCB – Complaint Counsel's Post-Trial Brief
CCRB – Complaint Counsel's Post-Trial Reply Brief
CCFF – Complaint Counsel's Proposed Findings of Fact
CCRRFF – Complaint Counsel's Reply to Respondent's Proposed Findings of Fact
RB – Respondents' Post-Trial Brief
RRB – Respondents' Reply Brief
RTB – Respondent Matthew Tupper's Post-Trial Brief
CCRRTB – Complaint Counsel's Reply to Respondent Matthew Tupper's Reply Brief
RFF – Respondents' Proposed Findings of Fact
RRCCFF – Respondents' Reply to Complaint Counsel's Proposed Findings of Fact

re General Foods Corp., No. 9085, 95 F.T.C. 352, 356 n.7; 1980 FTC LEXIS 99, at *11 n.7 (March 10, 1980). Thus, in instances where a document had been given *in camera* treatment, but the portion of the material cited to in this Initial Decision does not in fact require *in camera* treatment, such material is disclosed in the public version of this Initial Decision, pursuant to Commission Rule 3.45(a) (the ALJ "may disclose such *in camera* material to the extent necessary for the proper disposition of the proceeding"). This Initial Decision does not contain any material that requires *in camera* treatment.

D. Summary of Initial Decision

The preponderance of the evidence shows that some of the Challenged Advertisements disseminated by Respondents would reasonably be interpreted by consumers to contain an implied claim that the POM Products treat, prevent, or reduce the risk of heart disease, prostate cancer, or erectile dysfunction, and further, as to some of these advertisements, that these effects were clinically proven, as alleged in the Complaint. These advertisements are attached to this Initial Decision as an Appendix. As to other Challenged Advertisements disseminated by Respondents, the preponderance of the evidence fails to demonstrate that such advertisements would reasonably be interpreted by consumers as containing such claims.

The evidence further shows that the appropriate level of substantiation for claims that a product treats, prevents, or reduces the risk of a disease is competent and reliable scientific evidence. The evidence also demonstrates that where such claims are made in connection with a food, or food-derived product, that is safe, and that is not being offered as a substitute for medical treatment, double-blind, randomized, placebo-controlled clinical trials, such as those required by the Food and Drug Administration, are not required. However, for claims that a food or food-derived product treats, prevents, or reduces the risk of a disease, experts in the relevant fields would agree that competent and reliable scientific evidence must include clinical studies, although not necessarily double-blind, randomized, placebo-controlled clinical trials, that are adequate to show that the product did treat, prevent, or reduce the risk of disease.

Notwithstanding the fact that double-blind, randomized, placebo-controlled clinical trials are not required to substantiate Respondents' implied claims for the POM Products, the evidence demonstrates that Respondents' substantiation was, nevertheless, inadequate.

Regardless of whether competent and reliable scientific evidence existed to substantiate highly qualified or generalized health claims about the POM Products, the weight of the persuasive expert testimony demonstrates that there was insufficient competent and reliable scientific evidence to support the implied claims in some of the Challenged Advertisements disseminated by Respondents, that the POM Products treat, prevent or reduce the risk of heart disease, prostate cancer, or erectile dysfunction, or were clinically proven to do so. Whether or not Respondents' substantiation was adequate to support the express language of the advertisements is not the material issue. Because Respondents' substantiation was inadequate to support the implied claims, such claims were false or misleading within the meaning of Section 12 of the Federal Trade Commission Act ("FTC Act"), as interpreted by applicable case law. The evidence further shows that such health-related efficacy claims are material to consumers. Accordingly, the preponderance of the evidence supports the conclusion that Respondents violated Sections 5 and 12 of the FTC Act.

Pursuant to Section 5(b) of the FTC Act, a cease and desist order is entered herewith (the "Order"), the provisions of which will serve to prevent Respondents from engaging in deceptive advertising practices in the future, are reasonably related to the unlawful acts or practices found to exist, and are sufficiently clear and precise. The Order is binding upon the corporate Respondents as well as the individual Respondents, and covers any food, drug or dietary supplement that may be advertised by Respondents in the future. Neither applicable law nor the evidence in this case supports Complaint Counsel's proposed provision prohibiting Respondents from making any disease claim in the future, unless the claim has received prior approval from the Food and Drug Administration in accordance with Food and Drug Administration statutes and regulations.

II. FINDINGS OF FACT

A. The Respondents

1. POM Wonderful LLC

1. POM Wonderful ("POM Wonderful" or "POM") is a limited liability company organized under the laws of the State of Delaware. (Complaint ¶ 1; CX1367 at 0002 (S. Resnick, Welch's Dep. at 8); CX1437; Answer ¶ 1).

2. POM Wonderful's principal office or place of business is at 11444 West Olympic Boulevard, Los Angeles, California 90064. (Complaint ¶ 1; Answer ¶ 1).

3. POM Wonderful is wholly owned by the Stewart and Lynda Resnick Revocable Trust, dated December 27, 1988 (the "Resnick Trust"). (Complaint ¶ 1; Answer ¶ 1; CX1384 at 0008).

4. Respondent POM Wonderful is a member-managed company, and the Resnick Trust is the sole member. (Complaint ¶ 1; Answer ¶ 1).

5. In 2002, POM first launched POM Wonderful 100% Pomegranate Juice, a premium, all-natural pomegranate juice made from pomegranates grown from POM's orchards. (L. Resnick, Tr. 145-46).

6. POM Wonderful is currently in the business of selling fresh pomegranates and pomegranate-related products, including 100% pomegranate juice ("POM Juice") and pomegranate extract products known as POMx pills and POMx liquid ("POMx") ("the POM Products"). (S. Resnick, Tr. 1630-31; CX1364 at 0005 (Tupper, Coke Dep. at 20); CX1374 (Tupper, Ocean Spray Dep. at 26); CX1363 at 0012 (S. Resnick, Coke Dep. at 45-46)).

2. Respondent Roll Global LLC

7. Roll International Corporation is a separate corporation organized under the laws of the State of Delaware. (Complaint ¶ 2; Answer ¶ 2).

8. Roll International Corporation was reorganized at the end of 2010 and is currently known as Roll Global ("Roll"). (S. Resnick, Tr. 1629).

9. Roll is wholly owned by the Resnick Trust. (Complaint ¶ 2; Answer ¶ 2).

10. Roll is a privately held corporation. (S. Resnick, Tr. 1630).

11. POM Wonderful, FIJI Water, Suterra, Paramount Farms, Paramount Citrus, Teleflora, Neptune Shipping, Paramount Farming, and Justin Winery are among the separate operating businesses under Roll's ownership umbrella (hereafter "affiliated companies"). (CX1364 at 0004-05 (Tupper, Coke Dep. at 16-17); CX1374 (Tupper, Ocean Spray Dep. at 36); Perdigao, Tr. 593-94).

12. Stewart and Lynda Resnick are the sole owners of Roll and its affiliated companies, including POM Wonderful. (S. Resnick, Tr. 1629; CX1360 (S. Resnick, Dep. at 15); CX1376 (S. Resnick, Ocean Spray Dep. at 13-14)).

13. Roll's affiliated companies pay Roll for certain provided services. (CX1376 (S. Resnick, Ocean Spray Dep. at 24-25); L. Resnick, Tr. 89; CX1359 (L. Resnick, Dep. at 26); Perdigao, Tr. 616-17).

14. Fire Station acts as Roll's in-house advertising agency. Fire Station bills POM and other Roll affiliated companies separately. (CX1376 (S. Resnick, Ocean Spray Dep. at 24-25); L. Resnick, Tr. 88-89; CX1359 (L. Resnick, Dep. at 26); Perdigao, Tr. 616-17).

3. Respondents Stewart and Lynda Resnick

15. POM Wonderful is owned solely by Stewart and Lynda Resnick ("the Resnicks"). (S. Resnick, Tr. 1629; CX1360 (S. Resnick, Dep. at 15).

16. The Resnicks have been, and currently are, the sole trustees and beneficiaries of the Resnick Trust. (Complaint ¶ 1; Answer ¶ 1; CX1421 at 0002-03; CX1384 at 0008).

17. The Resnick Trust had owned Roll International Corporation and POM. (JX0001 ¶¶ 10-11, 18; Complaint ¶¶ 1-2; Answer ¶¶ 1-2).

18. The Resnicks are the sole owners of Roll Global, the successor-in-interest to Roll International Corporation, and its affiliated companies, including POM. (JX0003 ¶ B.2; S. Resnick, Tr. 1629; CX1360 (S. Resnick, Dep. at 15); CX1376 (S. Resnick, Ocean Spray Dep. at 13)).

19. Stewart Resnick ("Mr. Resnick") is, and at all times relevant to this action has been, the Chairman and President of Roll. (JX0001 ¶¶ 12, 18; S. Resnick, Tr. 1629; Complaint ¶ 3; Answer ¶ 3; CX1384 at 0008; CX1363 at 0014 (S. Resnick, Coke Dep. at 54-55)).

20. Mr. Resnick is, and at all times relevant to this action has been, the Chairman of POM Wonderful. (Complaint ¶ 3; Answer ¶ 3).

21. Mr. Resnick is the Chief Executive Officer of POM. (S. Resnick, Tr. 1869).

22. Mr. Resnick's responsibilities include making final decisions about POM's investments and corporate expansion. (S. Resnick, Tr. 1631; CX1360 (S. Resnick, Dep. at 20-21); *see also* CX1357 (Kuyoomjian, Dep. at 154-56) (testifying that Mr. Resnick's participation in POM's business included involvement in strategic planning and financial decisions as well as providing feedback on POM's advertising)).

23. Mr. Resnick spends the second greatest amount of his time on the POM business and, among other activities, sets the overall budgets for POM, including the marketing and advertising and medical research budgets. He has been intimately involved in the development of POM's scientific research program. (S. Resnick, Tr. 1631-32; CX 1363 at 0014 (S. Resnick, Coke Dep. at 56); CX1367 at 0014 (S. Resnick, Welch Dep. at 55)).

24. Mr. Resnick's authority includes "any decisions made with respect to what . . . [POM] talk[s] about, [and] how . . . [POM] talk[s] about it," including "authority for advertising the benefits of POM." (Tupper, Tr. 2975).

25. Mr. Resnick leaves the marketing of POM mostly to Mrs. Lynda Resnick. He considers himself ultimately responsible for whether advertising should or should not go out, although he delegated day-to-day responsibility to Mr. Matthew Tupper. (Tupper, Tr. 2975; S. Resnick, Tr. 1869-70).

26. When Mrs. Lynda Resnick has chosen to involve him, Mr. Resnick has been involved at a high level with POM's advertising and marketing campaigns, including on occasion seeing headlines before advertisements were disseminated. (CX1376 (S. Resnick, Ocean Spray Dep. at 140-42); CX1360 (S. Resnick, Dep. at 50-51)).

27. Lynda Resnick ("Mrs. Resnick") was, at all times relevant to this action, a director and was Vice Chairman of Roll International Corporation. (JX0001 ¶ 18; Complaint ¶ 4; Answer ¶ 4; L. Resnick, Tr. 287; CX1359 (L. Resnick, Dep. at 24-25).

28. Mrs. Resnick is Vice Chairman of Roll Global. (L. Resnick, Tr. 287; CX1359 (L. Resnick, Dep. at 24-25)).

29. Mrs. Resnick is involved in POM's marketing, branding, public relations, and product development. (CX1363 at 0011 (S. Resnick, Coke Dep. at 41); CX1364 at 0007 (Tupper, Coke Dep. at 27); CX1347 (Glovsky, Dep. at 36)).

30. Mrs. Resnick participated in POM's business on almost a daily basis in the company's early years, and on a weekly or biweekly basis thereafter and through 2010, although Mrs. Resnick reduced her day-to-day involvement in POM's business beginning in 2007 (L. Resnick, Tr. 86, 93, 157-58; *see also* CX1375 (L. Resnick, Tropicana Dep. at 19-22, 78); CX1359 (L. Resnick, Dep. at 22, 108)).

31. As of 2011, Mrs. Resnick was still the chief marketing person at POM. (L. Resnick, Tr. 289), and this was also her role in 2010 and 2009. (CX1375 (L. Resnick, Tropicana Dep. at 24); CX1362 (L. Resnick, Coke Dep. at 47, 77-78)).

32. Mrs. Resnick commissioned, helped develop, and used consumer and marketing research for POM's business. (CX1359 (L. Resnick, Dep. at 76-78).

33. Mrs. Resnick has worked with POM's marketing department and Roll's advertising agency, Fire Station, along with scientists and public relations personnel, to implement creative concepts for POM marketing pieces and campaigns. It was a team approach. (L. Resnick, Tr. 87-89; *see also* CX0409; CX0410; CX1359 (S. Resnick, Dep. at 70)).

34. Mrs. Resnick has the "final say" with respect to POM's marketing and advertising content and concepts. (CX1368 at 0003 (L. Resnick, Welch's Dep. at 9); L. Resnick, Tr. 93).

35. According to Mrs. Resnick, when it comes to marketing and creative issues, everyone has a "dotted line" to her, meaning she is in a position of authority even though she may not have day-to-day responsibilities for each employee. (CX1375 (L. Resnick, Tropicana Dep. at 24); L. Resnick, Tr. 287-88).

4. Respondent Matthew Tupper

36. Respondent Matthew Tupper ("Mr. Tupper") joined Roll in May 2001 as Vice President of strategy. (JX0003 ¶ B.5).

37. Mr. Tupper joined POM as a full-time employee in 2003, as Chief Operating Officer. (JX0001 ¶¶ 12, 18; Tupper, Tr. 886-87).

38. In 2005, his title at POM changed to President, but his responsibilities did not change from those in his position as Chief Operating Officer. (JX0001 ¶¶ 12, 18; Tupper, Tr. 886-87).

39. Mrs. Resnick considers Mr. Tupper as having been her "partner at POM since 2003." (CX0001 at 0037; L. Resnick, Tr. 230).

40. Mr. Tupper retired from POM at the end of the 2011. (Tupper, Tr. 2973).

41. Mr. Tupper will not be working for Roll Global or any other company owned by the Resnicks after his retirement from POM. (Tupper, Tr. 2974).

42. In his capacity as an officer of POM, Mr. Tupper, together with others, formulated, directed, or controlled the policies, acts, or practices of POM. (Complaint ¶ 5, Answer ¶ 5).

43. Mr. Tupper reported to the Resnicks. Mr. Tupper reported directly to Mr. Resnick. Mr. Tupper had a "dotted line" reporting to Mrs. Resnick. (CX1367 at 0014 (S. Resnick, Welch Dep. at 53); CX1364 at 0007, 0027 (Tupper, Coke Dep. at 27-28, 107); CX1375 (L. Resnick, Tropicana Dep. at 23-24)).

44. Mr. Tupper was responsible for managing the day-to-day affairs of POM, which employs roughly 350 people worldwide, including management of the day-to-day operations of the POM marketing team. (JX0003 ¶ B.6; Tupper, Tr. 2974; CX1363 at 0011 (S. Resnick, Coke Dep. at 42)).

45. Mr. Tupper oversaw and administered POM's budget for all departments, and had authority to sign checks and contracts on behalf of the company. (Tupper, Tr. 903-04, 912-13; CX0606 at 0003).

46. Mr. Tupper's activities included hiring and firing POM employees, including the head of POM's marketing department, on his own, or, depending on the situation, in

consultation with either Mr. or Mrs. Resnick. (Tupper, Tr. 902-03; *see also* CX1360 (S. Resnick, Dep. at 22-23); CX1359 (L. Resnick, Dep. at 41, 45); CX1353 (Tupper, Dep. at 24-25)).

47. At POM, nine or ten people have directly reported to Mr. Tupper, including the Vice President of Marketing (including former Senior Vice President of Marketing, Diane Kuyoomjian, ("Ms. Kuyoomjian"), the Vice President of Clinical Development (currently Bradley Gillespie ("Dr. Gillespie")), and the head of the Operations Department. (Tupper, Tr. 888-89, 2974; CX1353 (Tupper, Dep. at 24-25); CX1378 at 0008 (Kuyoomjian, Ocean Spray Dep. at 27)).

48. Mark Dreher, Ph.D. ("Dr. Dreher"), POM's former Vice President of Scientific and Regulatory Affairs, reported to Mr. Tupper. (Dreher, Tr. 527, 529; L. Resnick, Tr. 249).

49. Fiona Posell ("Ms. Posell"), former Vice President of Corporate Communications at Roll and POM, reported to Mr. Tupper and Mrs. Resnick. (Posell, Tr. 299, 321, 325).

50. The head of POM's Marketing department reported to Mr. Tupper, as did the departments with sales responsibilities. (Tupper, Tr. 891).

51. Mr. Tupper's responsibilities within POM included implementing POM's direction with regard to health benefit advertising and the use of science in connection with the advertising. With respect to this advertising, Mr. Tupper was the "connecting piece" between the marketing vision and the communication of the science. It was Mr. Tupper's job to work with all parts of the POM team, including marketing, scientists, and lawyers, to make sure that the advertising was done in "the right way." (Tupper, Tr. 2975-76).

52. One of Mr. Tupper's responsibilities was to be a liaison between the marketing staff of POM and the researchers in studies sponsored by POM, to help the marketing team "wade through" the science, of which Mr. Tupper had some understanding. (L. Resnick, Tr. 261; Tupper, Tr. 899, 914).

53. Mr. Tupper had a significant degree of involvement in the research aspects of POM's business, and his responsibilities included discussing which research areas are appropriate for funding, participating in the internal decision-making as to what research to fund, and overseeing for POM the clinical trials on POM's products that were conducted by research institutions. (Tupper, Tr. 895-96, 906; *see also* CX0770; CX0779; CX0800; CX0919; CX0920 (showing Tupper's participation in managing POM's medical and scientific research)).

B. The POM Products

1. Description of the POM Products

54. Respondents have manufactured, advertised, labeled, offered for sale, sold, and distributed products to the public, including POM Juice, POMx Pills, and POMx Liquid. (Answer ¶ 6; Complaint ¶ 6).

55. The Complaint in this case challenges Respondents' advertisements with respect to three products: POM Juice, POMx Pills, and POMx Liquid. (Complaint ¶¶ 6, 9, 10).

56. Respondents also manufacture, advertise, and sell other products containing pomegranate, including various POM Juice blends, Lite POM Juice, POMx bars, POMx iced tea and iced coffee, and a POMx sports recovery beverage. (JX0003 ¶ B.8).

a. POM Juice

57. POM Juice is a 100% juice product derived from whole pomegranate fruits. (PX0353 (Heber, Dep. at 124); CX1362 (L. Resnick, Dep. at 85-86); CX1363 (S. Resnick, Dep. at 46-47)).

58. POM Juice is produced by pressing whole pomegranates, including the arils and peels. (CX0967at 0014, *in camera*). The subsequent cloudy juice is filtered and/or enzyme treated before concentrating. (CX0537 at 0003).

59. The concentrate from POM Juice is stored in 52-gallon drums. (CX1369 (Tupper, Welch Dep. at 22)).

60. To make it ready for sale, the concentrate is reconstituted with water to make "100 percent pomegranate juice," pasteurized, and bottled for sale. (JX0003 ¶ B.9; CX1369 (Tupper, Welch Dep. at 19-23)).

61. The final POM Juice product contains "85.4% water, 10.6% total sugars, 1.4% pectin, 0.2-1.0% polyphenols, and organic acids." (CX0537 at 0003).

62. POM Juice does not contain dietary fiber or vitamin C. (CX0537 at 0014; CX0716 at 0041).

63. POM Juice contains a variety of polyphenols, including 80 to 90% ellagitannins and gallotannins, 8 to 15% anthocyanins and 2 to 5% ellagic acid. (CX0163 at 0007).

64. A single serving of POM Juice is eight ounces. (CX1379 at 0008, *in camera*). A serving of POM Juice provides 140 calories and 34 grams of sugar. (CX1306 (Weidner, Decl. at 0020)).

65. POM Juice is sold in the refrigerated produce section of the grocery store. (CX1367 (S. Resnick, Welch Dep. at 122); CX1374 (Tupper, Ocean Spray Dep. at 56-57)). Consumers must go to the fresh produce aisle of a store to purchase any POM Juice product. (CX1362 (L. Resnick, Coke Dep. at 135-36).

66. POM Juice is not sold in the "drug" or "over the counter" section of any establishment. (CX1362 (L. Resnick, Coke Dep. at 135-36); CX1367 (S. Resnick, Welch Dep. at 122; CX1374 (Tupper, Ocean Spray Dep. at 56-57)).

b. POMx Liquid

67. POMx Liquid "is the product of the pressed whole fruit after most of the juice is extracted and the polyphenols are concentrated by filtering and concentrating using juice processing." (CX0096 at 0014, *in camera*).

68. Consumers can purchase POMx Liquid via the company website or through a telephone call center. (JX0003 ¶ B.14).

69. POM's website states that the company's recommended daily serving of POMx Liquid is one teaspoon and recommends consumers take one teaspoon of POMx Liquid daily. (CX1379 at 0008-09, *in camera*).

c. POMx Pills

70. POMx is an extract from the pomegranate, made through a process by which POMx Liquid is first derived from the whole fruit, and then POMx is extracted from the POMx Liquid. (CX1363 (S. Resnick, Dep. at 46-47)).

71. POMx was created to use up the "tens of thousands of tons of discarded, mashed-up pomegranates left over from the juicing process." (CX0001 at 0013; CX0967 at 0014).

72. Consumers can purchase POMx Pills via the company website or through a telephone call center. POMx Pills also are available through a few U.S. Retail outlets that sell dietary supplement products. (JX0003 ¶ B.14).

73. Pomegranate extracts, because of the production process, contain no anthocyanins. (CX1352 (Heber, Dep. at 358); *see also* CX1258 at 0003 (POMx has only "trace" anthocyanins)).

74. Mrs. Resnick stated "[m]y marketing team and I were eager to learn if we could produce a pomegranate extract that could deliver the power of eight ounces of POM juice in a capsule." (CX0001 at 00013).

75. POMx caters to those consumers who want the benefits of the juice, without the calories or sugar to get, "The Power of POM, in one little pill." (CX0169 at 0001).

76. POM's website recommends consumers take one POMx Pill daily, preferably with eight ounces of water and food. (CX1379 at 0008, *in camera*).

2. Safety of the POM Products

77. Pomegranates have been safely consumed as nutritious food by humans for thousands of years. (PX0192 (Heber Expert Report at 0013, 0018)).

78. Pomegranate juice and pomegranate extract have a "high degree of safety." (PX0192 (Heber Expert Report at 0013)).

79. Pomegranate juice is safe for human consumption if consumed within the nutritional range. (PX0192 (Heber Expert Report at 0018)).

80. POMx is safe for human consumption if consumed within the nutritional range. (PX0192 (Heber Expert Report at 0018)).

81. Unlike some drugs, pomegranate juice has no adverse side effects. (PX0192 (Heber Expert Report at 0042)).

82. The FDA maintains a list of substances that are identified by the FDA as generally regarded as safe ("GRAS"). (Heber, Tr. 2008-09).

83. Before a substance can be GRAS identified, the FDA reviews the scientific literature and the traditional intake of the substance. (Heber, Tr. 2009).

84. Both pomegranate juice and pomegranate extract are GRAS identified. (Heber, Tr. 2009, 2032; 21 C.F.R. § 182.20).

85. There have been no reported cases of persons being harmed by eating a pomegranate or drinking pomegranate juice. (Heber, Tr. 1947-48).

86. There have been no reported cases of toxicity where pomegranates or pomegranate juice have been consumed in nutritional amounts. (Heber, Tr. 1948).

87. In all the studies that have been conducted on pomegranate juice and pomegranate extract, there have never been any reports of any material harm caused to the subjects by consuming the products. (Heber, Tr. 2007-08; PX0353 (Heber, Dep. at 115)).

88. None of the clinical studies conducted on pomegranate juice and pomegranate extract found any serious risk to human health from consuming the products. (PX0192 (Heber Expert Report at 0018)).

89. Pomegranate juice is a food. (PX0192 (Heber Expert Report at 0011)).

90. Pomegranate extract is a food-based dietary supplement that has substances found in pomegranate juice at levels within the nutritional range. (PX0192 (Heber Expert Report at 0011)).

91. In 2007, in a peer-reviewed study titled, "*Pomegranate Juice Does Not Impair Clearance of Oral or Intravenous Midazolam, a Probe for Cytochrome P450-3A Activity: Comparison With Grapefruit Juice*," by Farkas D, Oleson L, Zhao Y, Harmatz, J, Zinny M, Court M, and Greenblatt D (J Clin. Pharmocol 2007; 47:286-294), Dr. Greenblatt and his colleagues examined the effect of POM Juice and grapefruit juice on inhibiting enteric cytocrhome P450-3A activity in healthy human volunteers. The study showed POM Juice did not cause drug interaction in humans. (PX0136 at 0008).

92. In 2007, in a peer-reviewed study titled, "*Safety and Antioxidant Activity of a Pomegranate Ellagitannin-Enriched Polyphenol Dietary Supplement in Overweight Individuals With Increased Waist Size*," by Heber D, Seeram N, Wyatt H, Henning S, Zhang Y, Ogden L, Dreher M, and Hill J (J Agric. Food Chem. 2007; 55:-10050-10054), Dr. Heber and his colleagues examined the safety in humans of consuming POMx Pills. The study reported: Although there were 11 minor adverse events reported by 9 of the 64 subjects, none of these minor adverse effects were deemed to be related to POMx Pills. The study further reported: no adverse events related to the POMx Pill consumption or changes in blood count, serum chemistry, or urinalysis were observed in the subjects. (PX0139 at 0001, 0003, 0004).

93. Complaint Counsel's expert, Dr. Sacks, testified that the issue of the safety of the POM Products was not within the scope of his assignment in this case, that his expert report contains no opinions on the safety of the POM Products, and that he has "no opinion about whether [the POM Products are] safe or not." (PX0361 (Sacks, Dep. at 74, 76); CX1291 (Sacks Expert Report at 0008-09)).

94. Complaint Counsel's expert, Professor Meir Stampfer, admitted that there are no safety concerns with consuming pomegranate juice apart from "the usual harm that comes with fruit juice, sugary beverages . . . but that is not specific to pomegranate juice." (PX0362 (Stampfer, Dep. at 195-96)).

3. Sales of the POM Products

95. Respondents began selling POM Juice in 2002. POM Juice is sold in supermarkets nationally and is a major seller in the premium juice category. (CX0967 at 0014, *in camera*).

96. POM's U.S. Sales of 100% Juice, from September 2002 to November 2010, totaled approximately $247,739,776. (JX0001 ¶ 15).

97. For the 52 weeks ending July 20, 2008, the weighted average base price per unit for POM Juice was $2.93 for an 8-ounce bottle or $4.29 for a 16-ounce bottle. (CX0221 at 0007).

98. In 2007, POM began selling POMx Pills and POMx Liquid. (CX1347 (Glovsky, Dep. at 29-30)).

99. POM's Total POMx Pill Gross Revenue, from May 2007 to November 2010, totaled approximately $4,017,681. (JX0001 ¶ 16).

100. POM's Total POMx Liquid Gross Revenue, from May 2007 to November 2010, totaled approximately $209,820. (JX0001 ¶ 17).

101. If bought directly from POM's website, POM charges $29.95 (excluding shipping) for a 30-count bottle of POMx Pills and $77.85 (excluding shipping) for a 90-count bottle of POMx Pills. (CX1379 at 0009-10, *in camera*).

102. If bought directly from POM's website, POM charges $29.95 (excluding shipping) for a five-ounce bottle of POMx Liquid. (CX1379 at 0010-11, *in camera*).

C. Background Facts

1. History of POM and science program

a. Overview

103. In 1987, the Resnicks acquired farmland containing over 100 acres of mature pomegranate trees. (CX0105 at 0002).

104. Between 1989 and 2001, Paramount Farming Company, one of the Roll affiliated companies (F. 11), continued to acquire and plant additional pomegranate acreage, bringing the total to 6,000 acres by 2001. (CX0105 at 0002-08).

105. In 1998, the Resnicks began collaborating with researchers to determine whether, and to what extent, there was any truth to the folklore surrounding the health properties of the pomegranate. (L. Resnick, Tr. 150; CX1363 at 0016-17 (S. Resnick, Coke Dep. at 61-66); CX0105 at 0003; CX1362 at 0018 (L. Resnick, Coke Dep. at 71-72); S. Resnick, Tr. 1853-56); CX1359 (L. Resnick, Dep. at 82); CX1360 (S. Resnick, Dep. at 84-85); CX1372 (S. Resnick, Tropicana Dep. at 32-33; CX1374 (Tupper, Ocean Spray Dep. at 87); CX1358 (Aviram, Dep. at 4); CX1367 at 0004(S. Resnick, Welch's Dep. at 15); PX0004).

106. In 2000, the Resnicks formed Paramount Juice Company and, shortly thereafter, in 2001, changed the name to POM Wonderful LLC. (CX1418 at 0001-03).

107. By spring 2001, the yield from the Resnicks' 6,000 acres of pomegranates "ha[d] progressed exponentially . . . making it essential to immediately begin a marketing program for the POM Juice product." (CX0004 at 0001).

108. POM began bottling, selling, and marketing POM Juice on a regional basis in the fall of 2002, and in national markets in 2003. (CX1353 (Tupper, Dep. at 41-42); CX1395 at 0003).

109. Currently, the Resnicks own approximately 18,000 acres of pomegranate orchards and are the largest growers of pomegranates in the United States. (CX1374 (Tupper, Ocean Spray Dep. at 29-30)).

110. According to Mrs. Resnick, when Respondents went about creating a market for pomegranate juice, "only about one in ten Americans said they were familiar with pomegranates, and fewer than half of that group said they had eaten one in the past year." (PX0370 at 2).

111. According to Mr. Resnick, a primary part of POM's messaging to consumers is about the health benefits of its products. (S. Resnick, Tr. 1653; CX1372 (S. Resnick, Tropicana Dep. at 31-32)).

112. Mrs. Resnick has stated her belief that POM juice is "health in a bottle" and that this is part of POM Juice's unique selling proposition. (CX0001 at 0006; L. Resnick, Tr. 77-78).

113. POM uses the results of studies it has sponsored for marketing purposes, as part of "[POM's] unique selling proposition." At least part of the reason for sponsoring studies was for marketing and public relations purposes. (CX1375 (L. Resnick, Tropicana Dep. at 87); CX1372 (S. Resnick, Tropicana Dep. at 74-75; CX0003 at 0001)).

b. Early research

114. POM began its pomegranate research under the direction of POM's former Medical Director, and the Resnicks' personal friend and family physician, Dr. Leslie Dornfeld ("Dr. Dornfeld"), a professor of Internal Medicine at the University of California, Los Angeles (UCLA). (L. Resnick, Tr. 150; CX1350 (Liker, Dep. at 29); CX0105 at 0003).

115. In 1998, Respondents and Dr. Dornfeld collaborated with Dr. Michael Aviram, the Head of the Technion Lipid Research Laboratory at the Rambam Medical Center in Haifa, Israel, known for his work exploring the antioxidant properties of red wine, to understand the antioxidant effect and potential cardiovascular benefits of pomegranate juice. (CX1374 (Tupper, Ocean Spray Dep. at 87); CX1358 (Aviram, Dep. at 4); CX1363at 0016-17 (S. Resnick, Coke Dep. at 61-66); CX1367 at 0004 (S. Resnick, Welch Dep. at 15); CX0001 at 0010-11; L. Resnick, Tr. 150; PX0004). Dr. Aviram's initial research paper showed that pomegranates possess antioxidative and antiatherosclerotic properties. (CX1358 (Aviram, Dep. at 7); PX0004).

116. Dr. Dornfeld initially oversaw the development of POM's research program until he was no longer able to do so for health-related reasons. In 2001, Dr. Dornfeld recruited Dr. Harley Liker ("Dr. Liker"), a physician and faculty member at UCLA, to be his

successor as POM's Medical Director. Dr. Dornfeld and Dr. Liker worked together until 2002, when Dr. Liker became POM's Medical Director. (Liker, Tr. 1873, 1877; CX1350 (Liker, Dep. at 15, 27-28); S. Resnick, Tr. 1858).

117. Dr. Liker also became the Resnicks' personal physician and company wellness coordinator and wellness director in 2001. (Liker, Tr. 1876-77).

118. Respondents hired Risa Schulman, who was POM's Director of Research and Development from approximately 2002 to 2005. POM subsequently hired Dr. Mark Dreher ("Dr. Dreher") in 2005 as Vice President of Scientific and Regulatory Affairs. (CX0105 at 0016; Dreher, Tr. 527).

119. After identifying an area of scientific interest, Dr. Liker works with Mr. Tupper and Mr. Resnick to determine the leading experts in that scientific field and contacts them to conduct research for Respondents. (Liker, Tr. 1878-80).

120. Dr. Dreher's duties primarily entailed exploratory research, which was looking at new products such as POMx and developing clinical and basic science for new applications for POM products. "Basic science" refers to test-tube, animal studies, and preclinical research. Dr. Dreher also arranged for contracts and funding of research with universities and contract research organizations, provided the materials for testing, and helped to organize the objectives for the studies and for carrying out the studies. (Dreher, Tr. 528).

121. Dr. Dreher reported to Mr. Tupper and also reported, to a certain extent, to Dr. Liker, to help Dr. Liker manage the logistics associated with some of the larger studies. Dr. Dreher and Dr. Liker met weekly for the first two-and-a-half to three years Dr. Dreher was at POM, and then less frequently in the last year of his employment. (Dreher, Tr. 529-30).

122. After Dr. Dreher left, POM hired Dr. Bradley Gillespie in 2009 as its Vice President of Clinical Development. (CX1349 (Gillespie, Dep. at 10-11); CX1353 (Tupper, Dep. at 28)).

123. POM has also hired scientific consultants, including Dr. Aviram and Dr. David Heber. (CX1380 at 0005; CX1349 (Gillespie, Dep. at 264-65); Heber, Tr. 1941; S. Resnick, Tr. 1637).

c. Relevant studies

124. Respondents' studies have explored the effect of POM products on many different areas of health, including the cardiovascular system, immunity, athletic performance, erectile health, prostate cancer, skin care, cognitive function, dental health, and urinary tract health. (CX1353 (Tupper, Dep. at 48-52); Tupper, Tr. 2979-81).

125. Respondents' research efforts branch in various directions in order to examine the role that oxidation and inflammation play in many seemingly unrelated diseases and conditions. (CX1353 (Tupper, Dep. at 47-49); Tupper, Tr. 2979-81; Heber, Tr. 1957, 2112-13, 2185).

126. The results of five POM-sponsored studies have been referred to in the Challenged Advertisements. The studies are:

a. A study by Dr. Aviram, published in 2001 titled, *Pomegranate Juice Consumption Inhibits Serum Angiotensin Converting Enzyme Activity and Reduces Systolic Blood Pressure* ("Aviram ACE/BP Study"). The Aviram ACE/BP Study, conducted on ten patients, examined the effect of POM Juice consumption on angiotensin converting enzyme ("ACE"). (CX0542; *see e.g.*, CX0013 at 0003; CX0031; CX0473 (Compl. Ex. E-2 at 00:30, 1:25)).

b. A study by Dr. Aviram, published in 2004 titled, *Pomegranate Juice Consumption for 3 Years by Patients with Carotid Artery Stenosis Reduces Common Carotid Intima-Media Thickness, Blood Pressure and LDL Oxidation* ("Aviram CIMT/BP Study"). The Aviram CIMT/BP Study, conducted on 19 patients, examined the effect of POM Juice consumption on carotid intima-media thickness ("CIMT"). (CX0611; *see, e.g.*, CX0029; CX0280 CX0328/CX0331/CX0337; CX0473 (Compl. Ex. E-2 at 00:24)).

c. A study by Dr. Dean Ornish, published in 2005 titled, *Effects of Pomegranate Juice Consumption on Myocardial Perfusion in Patients with Coronary Heart Disease* ("Ornish MP Study"). The Ornish MP Study, examined the effect of POM Juice consumption on 45 patients with coronary heart disease. (CX1198; *see, e.g.*, CX0351; CX0355; CX0473 (Compl. Ex. E-2 at 00:30)).

d. A study by Dr. Allan Pantuck, published in 2006 titled, *Phase II Study of Pomegranate Juice for Men with Rising Prostate-Specific Antigen Following Surgery or Radiation for Prostate Cancer* ("Pantuck Study"). The Pantuck Study examined the effect of POM Juice consumption on 46 men previously treated for prostate cancer by radiation therapy or surgery. (CX0815; *see, e.g.*, CX0351; CX0355; CX0314 at 0004; CX0372 at 0002; CX0379 at 0002; CX0380 at 0002; CX0473 (Compl. Ex. E-2 at 00:24)).

e. A Study by Dr. C.P. Forest and Dr. H. Padma-Nathan, published in 2007 titled, *Efficacy and Safety of Pomegranate Juice on Improvement of Erectile Dysfunction in Male Patients with Mild to Moderate Erectile Dysfunction: A Randomized, Placebo-Controlled, Double-Blind, Crossover Study* ("Forest/Padma Nathan Study"). The

Forest Erectile Dysfunction Study (2007) examined the effect of POM Juice consumption on 53 men with mild to moderate erectile dysfunction. (CX1193; *see, e.g.*, CX0351; CX0355; CX0473 (Compl. Ex. E-2 at 00:24)).

127. POM also sponsored a study by Dr. Michael Davidson titled, *Effects of Consumption of Pomegranate Juice on Carotid Intima-Media Thickness in Men and Women at Moderate Risk for Coronary Heart Disease*, published in 2009 ("Davidson CIMT Study"). The Davidson CIMT Study (2009) tested the effect of POM Juice on CIMT progression rates in 289 subjects at moderate risk for moderate coronary heart disease. (CX1065).

128. In over a decade, Respondents sponsored over 100 studies at 44 different institutions. (Liker, Tr. 1887-88).

129. Of the studies POM had conducted as of 2010, approximately 40 percent were performed at UCLA or by Dr. Aviram at the Technion Faculty of Medicine. (*See* CX1241; CX1360 (S. Resnick, Dep. at 113-17)).

130. More than 70 of the studies sponsored by the Respondents have been published in peer-reviewed scientific journals. Seventeen of these published studies are human clinical trials. (Liker, Tr. 1888; CX0611; CX0908; PX0004; PX0005; PX0014; PX0060; PX0061; PX0020; PX0021; PX0023; PX0073; PX0074; PX0075; PX0127; PX0136; PX0139; PX0146 (Trombold JR, Barnes JN, Critchley L, and Coyle EF, *Ellagitannin Consumption Improves Strength Recovery 2-3 d after Eccentric Exercise*, *Med. Sci. Sports Exerc.*, Vol. 42, No. 3, pp. 493-98, 2010)).

131. Respondents continue to sponsor medical research to determine the benefits of their pomegranate products. Respondents have invested over 35 million dollars in their research program. (S. Resnick, Tr. 1752, 1861-64; CX1363 (S. Resnick, Coke Dep. at 74)).

132. Respondents currently have ongoing research in the areas of cardiovascular health and prostate health. (Tupper, Tr. 984-85, 994; PX0014; PX0023; PX0060; PX0061).

2. Advertising process

a. Overview

133. Roll has a full-service internal advertising agency called Fire Station. (JX0001 ¶ 18; L. Resnick, Tr. 88-89; Leow, Tr. 493; Perdigao, Tr. 593-94).

134. George Michael Perdigao ("Mr. Perdigao") is the president of Roll's advertising agency, Fire Station, and Roll's corporate communications department, and reports to the Resnicks. (CX1376 (S. Resnick, OS Dep. at 145); JX0001 ¶ 18; Perdigao, Tr. 590, 594).

135. Elizabeth Leow Hendry ("Ms. Leow") has been a creative director at Roll since 2005, with POM as one of her clients. Ms. Leow is currently the creative director for Fire Station, one of Roll's companies. She has continued to work on POM's advertising. (Leow, Tr. 415; CX1356 (Leow, Dep. at 16-18, 22)).

136. Prior to Fire Station's creation in approximately January 2008, Roll provided advertising services to its affiliated companies through advertising personnel employed by Teleflora, another Roll affiliate. (F. 11; Perdigao, Tr. 592).

137. This group of advertising professionals at Teleflora and later Fire Station has also been known as "The Agency." (Perdigao, Tr. 592; L. Resnick, Tr. 88-89).

138. POM uses Fire Station for all or virtually all of its domestic advertisement agency needs. (Tupper, Tr. 920-21).

139. Generally, Fire Station would be responsible for coming up with specific creative ideas or media plans, and POM's marketing department would help guide the process and provide input. (CX1357 (Kuyoomjian, Dep. at 88-89)).

140. The creation of POM marketing and advertising was a collaborative effort between Fire Station and POM that entailed coming up with ideas for print, outdoor, or television campaigns, as well as writing copy, creating graphics, and putting the ideas together for a final execution. (Leow, Tr. 420-21; Tupper, Tr. 920).

b. Development of advertising

141. Mrs. Resnick held regular creative meetings with the senior in-house representatives of POM and Roll, including representatives of POM's marketing department ("POM Marketing"), Roll's public relations department, and Roll's advertising agency, Fire Station. Staff members at POM and Roll informally refer to these meetings with Mrs. Resnick as "LRR Meetings." (JX0003 ¶ A.12; L. Resnick, Tr. 87-88, 92)).

142. In addition to Mrs. Resnick, Mr. Tupper and employees from POM's marketing and scientific departments, Fire Station employees and someone from Roll's Corporate Communications department regularly attend LRR meetings. (Rushton, Tr. 1366; Perdigao, Tr. 624-25; Tupper, Tr. 929-30; L. Resnick, Tr. 249; CX1351 (McLaws, Dep. at 33-34).

143. At LRR Meetings and during other interactions with POM Marketing and Fire Station, Mrs. Resnick would approve a general direction for POM's advertising and also approved the lion's share of POM's advertising concepts. (CX1362 at 0008 (L. Resnick, Coke Dep. at 30-31); *see also* Perdigao, Tr. 604, 628 (agreeing that it is fair to say that Mrs. Resnick has final authority on advertising campaigns); Rushton, Tr. 1369-71 L. Resnick, Tr. 99-100, 186-87; Leow, Tr. 470; CX0023 at 0001 (stating that "LRR is going to take a more active role in writing copy[]" and that "[i]f [Mrs. Resnick]

writes it, it will be approved"); CX1351 (McLaws, Dep. at 23-24) (stating that the "decision to either move forward or make adjustments [on marketing on advertising] came from Lynda")).

144. Mr. Tupper attended most of the LRR Meetings, at which the highest-level executives involved in marketing discussed how to better market POM's products. (Perdigao, Tr. 624-25).

c. Creative briefs

145. The first step in the creative process for POM advertising is a "creative brief," prepared by POM's marketing department and provided to Fire Station. (L. Resnick, Tr. 123; Loew, Tr. 451; CX1368 at 0024 (L. Resnick, Welch Dep. at 95)).

146. The creative brief was the document used to formally initiate an advertising project. (Perdigao, Tr. 616-17).

147. A creative brief is an outline of the assignment, with the purpose of providing an overview of the assignment. A creative brief might include information on the key message(s) to be conveyed, a suggested target audience for the advertisement, demographics, and media. (Leow, Tr. 451-52; L. Resnick, Tr. 123; *see* CX0409 (creative briefs ranging from January 2004 to October 2009); *see also* CX0129 to CX0131 (2007 creative briefs for POMx print advertisements)).

148. The creative brief outline addresses matters such as "Objective," "Target Audience," "Insights," "Main Message," "Benefit" or "Benefits," and "Tonality," among other matters. (CX0409).

149. Creative briefs are developed for new marketing campaigns that POM undertakes. (Tupper, Tr. 921).

150. POM's online marketing department prepares creative briefs for online components of POM's marketing initiatives. Such briefs are then submitted to Fire Station. (Rushton, Tr. 1353-54, 1391-92).

151. A creative brief is a concept document, to give the advertising agency (Fire Station) insight on how to start a campaign. The substance of a creative brief may or may not ultimately be reflected in an advertisement. (Tupper, Tr. 921; Leow, Tr. 484-85).

152. By their nature, creative briefs were brief and general, and there would be one or more follow-up meetings to discuss the project. (Rushton, Tr. 1396; Perdigao, Tr. 618).

153. The creative process is a collaborative process in which participants share and mold concepts, thoughts and ideas. "It's not like . . . you get a creative brief, a guy goes in a room, and then comes out with an ad. It's not quite that simple." (Perdigao, Tr. 621-22).

154. Mr. Tupper participated in discussions with the marketing department about individual parts or elements of creative briefs. (Tupper, Tr. 924).

155. Once the creative brief was received by Fire Station, it would be assigned to appropriate personnel at the agency, depending on the project. (Leow, Tr. 452-53).

156. The creative team(s) at Fire Station would then work together to start creating advertisement concepts, which would be reviewed first by Ms. Leow, then by Mr. Perdigao, and finally by POM Marketing. It is a fluid process, including multiple revisions. Depending on the assignment, the concepts were sometimes also reviewed by Mr. Tupper. These reviews at the concept stage involved the general creative direction, look, tone, and idea of the advertising, rather than body copy. (Leow, Tr. 457-60).

157. Advertising concepts would include the graphics and headlines. A headline is the main message of an advertisement and usually appears in larger type. Body copy is the smaller print usually appearing at the bottom of an advertisement. (Leow, Tr. 462-63, 467).

158. After the creative concepts were approved, the creative team at Fire Station would draft body copy with direction from POM Marketing, using the creative brief as an outline and including any additional input marketing might add. (Leow, Tr. 462-64).

159. There are no scientists or technical writers on Fire Station's staff. Therefore, if the body copy of an advertisement were to contain information on studies and POM Marketing wanted specific wording, it would be provided by POM Marketing. (Leow, Tr. 464-65).

160. After the copy of an advertisement was drafted, it would go to the head of marketing for approval, and sometimes, depending on the project, to Mr. Tupper and Mrs. Resnick for approval. (Leow, Tr. 463-64; L. Resnick, Tr. 187-188).

161. Once the concepts for a big advertising campaign were approved, they would ultimately go to Mrs. Resnick for approval. Fire Station presented advertising concepts to Mrs. Resnick during LRR Meetings. (Leow, Tr. 461; Perdigao, Tr. 623-25; Rushton, Tr. 1358).

162. In addition to approving the body copy, POM Marketing would also thereafter provide final review of the completed advertisement, and depending on the project, Mr. Tupper might approve it as well. (Leow, Tr. 464-66).

163. After proofreading by Fire Station personnel, POM's advertisement would be sent to Fire Station's production department to create the "mechanical" – the completed advertisement in final electronic form that is ready to be sent to publications. (Leow, Tr. 466-67).

164. The process POM uses to connect the science to the advertising includes a "checklist of individuals who need to review and sign off on those ads, ultimately culminating in the legal review." (Tupper, Tr. 2977-78).

165. POM approves final executions of advertisements created by Fire Station before dissemination. (Leow, Tr. 466; Perdigao, Tr. 637).

166. Mrs. Resnick would sometimes review finished advertisements. (Leow, Tr. 466).

167. Mrs. Resnick's participation in the creative process included briefing POM Marketing, as well as meeting with POM and Fire Station personnel to review proposed creative pieces developed by Fire Station. (CX1368 at 0003 (L. Resnick, Welch Dep. at 9-10)).

168. Mrs. Resnick has reviewed and provided detailed edits and suggestions for POMx Pill advertisements (CX0126 at 0002) and the POM Wonderful website (CX0024 at 0009-38); approved designs and headlines for advertisements in various media (CX0247 at 0002; CX0248 at 0002); and suggested and reviewed concepts for new advertisements (CX0266 at 0002-03; CX0320 at 0002).

3. Target audience for POM Products advertising

169. The POM Juice print advertisements at issue in this case were disseminated in a wide variety of locally and nationally distributed publications, including but not limited to: the *Chicago Tribune* (CX0016), *Prevention* (CX0029, CX0034, CX0260), *Details* (CX0031), *Rolling Stone* (CX0033, CX0036), *Health* (CX0103, CX0251), I*nStyle* (CX0109), *Town and Country* (CX0109) *Men's Health* (CX0192, CX0260), and *Men's Fitness* (CX0274). *See also* CX0474; CX0371 (declarations describing capture of print advertisements and dissemination information).

170. The POMx Pills print advertisements at issue in this case were disseminated in a wide variety of locally and nationally distributed publications, including but not limited to: *Fortune* (CX0120), the *New York Times* (CX0169, CX0337), *Discover* (CX0122), *Men's Health* (CX0348), *Popular Science* (CX0348), *Time* (CX0350) and *Playboy* (CX0355, CX0470 at 0002; Leow Tr. 496).

171. The POM Products have been advertised in print advertisements in magazines, freestanding inserts ("FSIs") in newspapers, out of home media such as billboards and bus shelters, posters in health clubs and doctors' offices, advertising on prescription drug bags, Internet websites, online banner advertisements, medical outreach, radio, television, and press releases. (L. Resnick, Tr. 81-82 (radio), 186 (FSIs); Leow, Tr. 426-28, 457 (out of home, health clubs, banner ads, television); Perdigao, Tr. 597-98 (press releases), 608-09 (prescription drug bags); Tupper, Tr. 927 (magazine wraps); CX1375 (L. Resnick, Trop. Dep. at 167 (medical outreach)); CX1357 (Kuyoomjian, Dep. at 85-86 (posters in doctors' offices)), 122 (radio)).

172. POM placed advertising in such magazines as *Health Magazine*, *Men's Health*, and *Men's Fitness*, because these publications are geared toward the health-conscious consumer. (Leow, Tr. 425-26).

173. POM has purchased online banner advertisements on websites, including specific websites with audiences interested in personal health, fitness, and physical well-being such as *Men's Health*, *ESPN*, *Livestrong*, and *WebMD*. (Rushton, Tr. 1397-98; CX0463; CX0466; CX0468; Leow, Tr. 428-29).

174. Current POM Juice buyers tend to be in their forties, possibly older, and are sophisticated to some extent about their health. (L. Resnick, Tr. 127-28).

175. For purposes of a creative brief (*see* F. 145-151) "target audience" refers to the audience to whom the advertisement would appeal. (Leow, Tr. 451-52).

176. Seven creative briefs for POM Juice advertising projects, dating between January 2004 and July 2006, described the "target audience" for the subject advertisement as: "Hip Gen X 25-39. Skews female (60/40) likely to be affluent, professional, college grads who are very health-conscious (hypochondriacs) and live in urban areas. Either single or married without kids." (CX409 at 0001; *see also* CX0409 at 0003, 0005, 0006, 0008, 0010, and 0022). In July 2006, this description was prefaced with the comment, "same as general POM consumer." (CX409 at 0022)

177. Two creative briefs dated June 28, 2006 and July 13, 2006, which stated that they were to be used for all future POMx Pill projects, identified the target audience for POMx Pills as "Age and Gender: 25-64 year old men and women (50/50 split) Psychographic: (1) Core POM Consumer, (2) Consumer who won't drink the juice or tea but who is seeking a natural cure for current ailments or to maintain health and prevent future ailments[.]" These creative briefs further noted, under "tonality," in part, "catchy headlines but serious copy that reflects the fact that antioxidants are important for health. The pill form is more medicinal by nature and attracts consumers that are looking for health benefits but won't drink the juice or tea." (CX0409 at 0016, 0018).

178. A creative brief for POMx Pills, dated September 1, 2006, referred to "a handful of different creative approaches targeting different consumers that include men, seniors and young health conscious females." Under target consumer audience," this creative brief stated: "Age & Gender: Start with men 40+, HH income $75K+, primarily men who are scared to get prostate cancer . . . Two other targets based on this plan include seniors 55+ who are heavy supplement users (AARP & Readers' Digest) and young health conscious women (Oprah, More, Health) – both of whom will benefit from the antioxidants (cardiovascular, anti-aging, etc.)." (CX0409 at 0023).

179. In a creative brief for the "Health Benefits" section of the POM Wonderful website, from June 2008, the "target audience" was described as "General population (35+, 60% Female): Consumers . . . Who are looking for general information about Pomegranate Health, Antioxidant, Polyphenol or related topics and want to learn more . . . or find out

the truth about Pomegranates[,] Who have seen articles about pomegranates or antioxidants[,] With an ailment that pomegranates have been rumored to help[.]" The "target audience" for the website was also identified to include "Health Care Professionals" including "Primary care physicians[,] Urologists[,] Dieticians[,] Nutritionalists[,] Other healthcare industry professionals." (CX0200 at 0002).

180. Ms. Leow, a creative director for Roll, expressed her opinion that scientific information in advertising and marketing material helps sell the products, because the scientific information provides the consumer with a "reason to believe." (Leow, Tr. 512-13).

181. A creative brief attached to an email from Michael Perdigao to Lynda Resnick dated June 25, 2008, noted that the "primary target consumer" for an unidentified referenced POM Juice campaign "should be the 30-something health conscious (hypochondriac?) who is educated and affluent." (CX0211 at 0002).

D. Testifying Experts

1. Complaint Counsel's experts

a. Dr. Meir Stampfer

182. Dr. Meir J. Stampfer is a Professor of Epidemiology and Nutrition, Harvard School of Public Health; Faculty Member, Division of Biological Sciences, Harvard School of Public Health; Professor of Medicine, Harvard Medical School; and Faculty Member, Dana Farber Harvard Cancer Center. (Stampfer, Tr. 689-91; CX1293 (Stampfer Expert Report at 0001)). He teaches epidemiology, advanced epidemiology, and preventive medicine. (CX1293 (Stampfer Expert Report at 0001)). Epidemiology is the study of the determination and distribution of disease in humans. (Stampfer, Tr. 691).

183. Dr. Stampfer has been an investigator in several large studies focused on the relationship between nutrition and cancer and cardiovascular disease ("CVD"), and their precursors. (CX1293 (Stampfer Expert Report at 0003-04)). These include: Nurses' Health Study (started 1976, 121,700 women, cancer prevention, CVD, diabetes, and other health issues); Nurses' Health Study II (started 1989, 116,800 women, same as Nurses' Health Study); Physicians' Health Study (started 1982, 29,000 men, multivitamin supplements, and aspirin, and beta carotene for prevention of CVD and cancer); and Health Professionals Follow-up Study (started 1986, 51,529 men, nutritional factors as related to cancer, including prostate cancer, and heart disease). (CX1293 (Stampfer Expert Report at 0003-04); Stampfer, Tr. 692-94). Additionally, he has participated in research investigating risk factors (including food intake and dietary factors) associated with prostate cancer and conducted randomized clinical trials involving nutrition and health, including dietary interventions to reverse atherosclerosis. (Stampfer, Tr. 698-700).

184. Dr. Stampfer has published more than 850 articles in medical journals, including the *New England Journal of Medicine, American Journal of Epidemiology, Epidemiology,*

and *Journal of American Medical Association*. (CX1293 (Stampfer Expert Report at 0002)). Over 300 of these articles relate to the relationship between nutrition and the prevention or treatment of CVD or prostate cancer. (Stampfer, Tr. 701; *see also* CX1293 (Stampfer Expert Report at 0002)).

185. In 2003, the Institute for Scientific Information identified Dr. Stampfer as the most cited researcher in clinical medicine and epidemiology in the world during the past 20 years. (CX1293 (Stampfer Expert Report at 0002)). In 2005, the Institute for Scientific Information identified him as the most cited researcher in clinical medicine over the previous decade. (CX1293 (Stampfer Expert Report at 0002)).

186. Dr. Stampfer currently is an editor for leading medical journals, including the Journal of the *American College of Nutrition, American Journal of Epidemiology, American Journal of Medicine*, and *Clinical Chemistry*. Dr. Stampfer also had editorial positions on the *American Journal of Clinical Nutrition*, *New England Journal of Medicine*, and *American Journal of Medicine*. (Stampfer, Tr. 701; CX1293 (Stampfer Expert Report at 0001-02)). Dr. Stampfer is a member of professional organizations relating to epidemiology, cancer, and CVD, including the Society of Epidemiological Research, the American College of Nutrition, the American Heart Association, and the American Association for Cancer Research. (Stampfer, Tr. 701-03). He also has consulted for the government on the U.S. Dietary Guidelines. (Stampfer, Tr. 703).

187. Dr. Stampfer was accepted as an expert on: 1) epidemiology; 2) nutrition, including its relation to the prevention and treatment of CVD and prostate cancer; and 3) clinical testing related to the prevention of prostate cancer and CVD. (Stampfer, Tr. 704-05; *see also* CX1293 (Stampfer Expert Report at 0005)).

188. Dr. Stampfer was asked to evaluate, from his perspective as an expert in the fields of epidemiology, nutrition, and clinical testing, whether the following claims were supported by the materials submitted by the Respondents:

- drinking eight ounces of POM Juice, or taking one POMx Pill or one teaspoon of POMx Liquid, daily, treats, prevents, or reduces the risk of heart disease, including by decreasing arterial plaque, lowering blood pressure, and/or improving blood flow to the heart;

- tests prove that drinking eight ounces of POM Juice or taking one POMx Pill or one teaspoon of POMx Liquid, daily, treats, prevents, or reduces the risk of heart disease, including by decreasing arterial plaque, lowering blood pressure, and/or improving blood flow to the heart;

- drinking eight ounces of POM Juice, or taking one POMx Pill or one teaspoon of POMx Liquid, daily, treats, prevents, or reduces the risk of prostate cancer, including by prolonging prostate-specific antigen doubling time ("PSADT"); and

- tests prove that drinking eight ounces of POM Juice, or taking one POMx Pill or one teaspoon of POMx Liquid, daily, treats, prevents, or reduces the risk of prostate cancer, including by prolonging "PSADT."

(CX1293 (Stampfer Expert Report at 0005-06)).

189. To form his opinions, in addition to drawing upon his own expertise, Dr. Stampfer reviewed materials submitted by Respondents and affiliated researchers, including published and unpublished study reports, protocols, data and data analyses from Respondents' sponsored research, information about ingredients contained in the POM Products, and deposition transcripts of researchers who conducted studies for Respondents and related deposition exhibits and reports. Dr. Stampfer also reviewed materials he found through his independent literature search. (CX1293 (Stampfer Expert Report at 0006-07); Stampfer, Tr. 734-36; CX1294).

190. Dr. Stampfer opined that the materials relied upon by Respondents do not provide competent and reliable scientific evidence to support claims that: (1) drinking eight ounces of POM Juice or taking a daily serving of POMx is clinically proven to treat, prevent, or reduce the risk of heart disease or prostate cancer; (2) a daily eight ounce serving of POM Juice or a serving of POMx treats, prevents, or reduces the risk of heart diseases, including by prolonging PSADT (defined *infra* F.1042); or (3) a daily eight ounce serving of POM Juice or a serving of POMx treats, prevents, or reduces the risk of heart disease, including by decreasing arterial plaque, lowering blood pressure, and/or improving blood flow to the heart. (CX1293 (Stampfer Expert Report at 0007)).

b. Dr. Frank Sacks

191. Dr. Frank M. Sacks is a Professor of Cardiovascular Disease Prevention, Department of Nutrition, Harvard School of Public Health, and Professor of Medicine, Harvard Medical School. (Sacks, Tr. 1411-12; CX1291 (Sacks Expert Report at 0001)). He has taught pharmacology, epidemiology, and nutrition courses related to human disease, CVD, biochemistry, or preventative medicine. (Sacks, Tr. 1412-13; CX1291 (Sacks Expert Report at 0002)).

192. Dr. Sacks has researched CVD and coronary heart disease ("CHD") and their risk factors, including lipid profiles, hypertension, obesity, and diabetes, and the effects of potential risk-modifying diets, foods, food components, and drugs. (CX1291 (Sacks Expert Report at 0002); Sacks, Tr. 1415-18). He is the principal investigator of several National Institute of Health studies focusing on dietary nutrients and weight loss, carbohydrate amount and type affecting risk of CVD and diabetes, and dietary fat and high-density lipoprotein ("HDL") metabolism in humans. (CX1291 (Sacks Expert Report at 0005-06)).

193. Dr. Sacks has published more than 160 articles in peer-reviewed scientific journals relating to CVD, CHD, and the relationship between nutrition and these diseases. (Sacks, Tr. 1412-13, 1424-25; CX1291 (Sacks Expert Report at 0002-04)). Dr. Sacks

has also written over 60 reviews, reports, editorials, and book chapters, addressing CVD, CHD, and the relationship between nutrition and these diseases or their risk factors. (CX1291 (Sacks Expert Report at 0004)).

194. Through his professional memberships and activities, Dr. Sacks keeps current on new developments and research in the areas of nutrition, CVD, cholesterol disorders, and hypertension. (Sacks, Tr. 1424). He served as an editor for the *American Journal of Clinical Nutrition*, *Journal of Clinical Lipidology*, a *Nutrition Journal (BioMed Central)*, and *The Journal of Lipid Research.* (CX1291 (Sacks Expert Report at 0006)). In these positions, he reviewed the adequacy of the design, the conduct of clinical research, and the appropriateness and accuracy of the statistical methodology in hundreds of papers submitted for publication. (Sacks, Tr. 1424-25; CX1291 (Sacks Expert Report at 0006)).

195. Dr. Sacks serves as a chair of the Nutrition Committee of the American Heart Association (AHA), which advises the AHA on matters of science and public policy and devises guidelines and advisory statements to the government, health professionals, and the public on nutrition. (Sacks, Tr. 1426; CX1291 (Sacks Expert Report at 0006-07)). Dr. Sacks is also a member of the National Cholesterol Education Program of the National Heart, Lung and Blood Institute of NIH, which revises national guidelines on prevention and treatment of CVD. (CX1291 (Sacks Expert Report at 0007); Sacks, Tr. 1426).

196. Dr. Sacks was accepted as an expert in the areas of nutrition, CVD, CHD, cholesterol disorders, hypertension, and analysis of clinical studies. (Sacks, Tr. 1429-30; CX1291 (Sacks Expert Report at 0008)).

197. Dr. Sacks was asked to determine whether the materials he reviewed were sufficient to support claims that: (1) drinking eight ounces of POM Juice, or taking one POMx Pill, or one teaspoon of POMx Liquid, daily, treats, prevents, or reduces the risk of heart disease, including by decreasing arterial plaque, lowering blood pressure, and/or improving blood flow to the heart; and (2) clinical studies, trials, and/or tests prove that drinking eight ounces of POM Juice, or taking one POMx Pill, or one teaspoon of POMx Liquid, daily, treats, prevents, or reduces the risk of heart disease. (CX1291 (Sacks Expert Report 0008-09)).

198. To form his opinions, in addition to drawing upon his own expertise in nutrition and CVD treatment, Dr. Sacks reviewed materials submitted by Respondents and affiliated researchers, including published and unpublished study reports, protocols, data, and data analysis from Respondents' sponsored research, information about ingredients contained in the POM Products, and deposition transcripts of researchers who conducted studies for Respondents and related deposition exhibits. Dr. Sacks also reviewed materials he found through an independent literature search. (Sacks, Tr. 1447-49; CX1291 (Sacks Expert Report at 0008-09); CX1292, Apps. 2, 3, 4).

199. Dr. Sacks opined that: (1) the materials relied upon by Respondents do not support claims that drinking eight ounces of POM Juice or taking one POMx Pill or one teaspoon of POMx Liquid, daily, prevents, reduces the risk of, or treats heart disease, including by decreasing arterial plaque, lowering blood pressure and/or improving blood flow to the heart; and (2) clinical studies, research, and/or trials do not prove that drinking eight ounces of POM Juice or taking one POMx Pill or one teaspoon of POMx liquid, daily, prevents or reduces the risk of or treats heart disease, including by, decreasing arterial plaque, lowering blood pressure and/or improving blood flow to the heart. (CX1291 (Sacks Expert Report at 0010)).

c. Dr. James Eastham

200. Dr. James A. Eastham is the Chief of Urology in the Department of Surgery at Memorial Sloan-Kettering Cancer Center in New York. He serves as the Director of Clinical Research, Urology and chairs the protocol review committee for clinical trials in the Department of Surgery. (CX1287 (Eastham Expert Report at 0001); Eastham, Tr. 1207-08). He is a board-certified urological surgeon who has treated more than 2,000 patients with prostate cancer, including some who experienced a rise in prostate-specific antigen ("PSA") after receiving initial therapy. (CX1287 (Eastham Expert Report at 0002); Eastham, Tr. 1206, 1225-28, 1233).

201. Dr. Eastham has extensive experience, including as an investigator, in the design and conduct of clinical trials studying prostate cancer. (Eastham, Tr. 1215-17). As a member of the Data Safety Monitoring Board for the Selenium and Vitamin E Cancer Prevention Trial, he is familiar with the design and performance of the largest prevention trials studying antioxidants and prostate cancer. (CX1287 (Eastham Expert Report at 0002-03); Eastham, Tr. 1210-11).

202. Dr. Eastham is a member of several professional associations, including the American Urological Association, the Society of Urologic Oncology, and the National Comprehensive Cancer Network ("NCCN") Prostate Cancer Guidelines Committee. He regularly attends and speaks at national and international meetings of professional societies that specialize in urology and prostate cancer. (CX1287 (Eastham Expert Report at 0003); Eastham, Tr. 1211-13).

203. Dr. Eastham has peer-reviewed numerous papers involving randomized, double-blinded, controlled human clinical studies that were submitted to medical journals, such as *Urology*, *Journal of Urology*, and *Journal of Clinical Oncology*. (CX1287 (Eastham Expert Report at 0003); Eastham, Tr. 1224-25). Dr. Eastham has published over 200 peer-reviewed articles in scientific journals, as well as dozens of book chapters or reviews pertaining to urology and the treatment of prostate cancer. (CX1287 (Eastham Expert Report at 0003-04); CX1288, Ex. A; Eastham, Tr. 1214-15).

204. Dr. Eastham was accepted as an expert in the areas of: (1) urology specializing in prostate cancer, including the prevention and treatment of prostate cancer; and (2)

clinical testing related to the prevention and treatment of prostate cancer. (Eastham, Tr. 1234; CX1287 (Eastham Expert Report at 0004)).

205. Dr. Eastham was asked to determine whether the materials he reviewed were sufficient to support claims that: (1) drinking eight ounces of POM Juice, or taking one POMx Pill, or one teaspoon of POMx Liquid, daily, treats, prevents, or reduces the risk of prostate cancer, including by prolonging prostate-specific antigen doubling time ("PSADT"); and (2) tests prove that drinking eight ounces of POM Juice, or taking one POMx Pill, or one teaspoon of POMx Liquid, daily, treats or prevents prostate cancer, including by prolonging PSADT. (CX1287 (Eastham Expert Report at 0004-05)).

206. To form his opinions in addition to drawing upon his own expertise in the field of urology, specializing in prostate cancer, including the prevention and treatment of prostate cancer, and clinical testing relating to the treatment and prevention of prostate cancer, Dr. Eastham reviewed the materials submitted by Respondents and affiliated researchers, including published and unpublished study reports, protocols, data and data analysis from Respondents' sponsored research, and information about ingredients contained in the POM Products. Dr. Eastham also reviewed materials he found through an independent literature search. (CX1287 (Eastham Expert Report at 005); Eastham, Tr. 1287-88; CX1288, Ex. B).

207. Dr. Eastham provided the following opinion: the materials relied upon by Respondents do not provide reliable scientific evidence that POM Juice, POMx Pills, or POMx Liquid effectively prevents, reduces the risk of, or treats prostate cancer or are clinically proven to do so. (CX1287 (Eastham Expert Report at 006, 012)).

d. Dr. Arnold Melman

208. Dr. Arnold Melman is a Professor and Chairman of the Department of Urology at Albert Einstein College of Medicine and Montefiore Medical Center in New York. (Melman, Tr. 1072-73). Dr. Melman is a board-certified, practicing clinical urologist at Montefiore Medical Center and has treated thousands of patients with erectile dysfunction. (Melman, Tr. 1071-73).

209. Dr. Melman has extensive experience in designing and reviewing protocols for well-designed clinical trials. As an editor of *Sexuality and Disability*, the *Journal of Urology*, and the *International Journal of Impotence Research*, Dr. Melman reviewed hundreds of articles involving erectile dysfunction by evaluating, among other factors, the design, data collection and reporting, and statistical analysis of clinical studies. (Melman, Tr. 1075-77; CX1289 (Melman Expert Report at 0002)). Furthermore, Dr. Melman was a principal investigator on two National Institutes of Health research grants relating to erectile dysfunction. (Melman, Tr. 1079-80; CX1289 (Melman Expert Report at 0002-03)).

210. Dr. Melman was chairman of the U.S. Food and Drug Administration's Gastroenterology and Urology Devices Panel of the Medical Devices Advisory

Committee, and was a member of the National Institutes of Health's Urology Special Emphasis Panel. (Melman, Tr. 1077-78; CX1289 (Melman Expert Report at 0001-02)). Dr. Melman is a member of several professional organizations, including the American Federation for Clinical Research, Society of University Urologists, American Urological Association, American Association of Clinical Urologists, International Society of Urology, and International Academy of Sex Research; and has spoken at national and international meetings of professional societies that specialize in urology and erectile dysfunction. (Melman, Tr. 1077-79; CX1289 (Melman Expert Report at 0001-02)). Dr. Melman has published more than 200 peer-reviewed articles relating to urology in scientific journals. Many of these published articles relate to erectile dysfunction. (Melman, Tr. 1076-77; CX1289 (Melman Expert Report at 0002)).

211. Dr. Melman was accepted as an expert in: (1) urology as it relates to the treatment, prevention, and reduction of risk of erectile dysfunction; and (2) clinical testing involving erectile dysfunction. (Melman, Tr. 1080-81).

212. Dr. Melman was asked to determine whether the materials he reviewed were sufficient to support claims that: (1) drinking eight ounces of POM Juice, daily, prevents, reduces the risk of, or treats erectile dysfunction; and (2) clinical studies, research, and/or trials prove that drinking eight ounces of POM Juice, daily, prevents, reduces the risk of, or treats erectile dysfunction. (CX1289 (Melman Expert Report at 0003)).

213. To form his opinions, in addition to relying on his expertise in urology as it relates to the treatment, prevention, and reduction of risk of erectile dysfunction, and clinical testing involving erectile dysfunction, Dr. Melman reviewed materials submitted by Respondents and affiliated researchers, including published and unpublished study reports, protocols, and data and data analyses from Respondents' sponsored research. (CX1289 (Melman Expert Report at 0003); Melman, Tr. 1083). Dr. Melman also reviewed articles he found through his independent research of peer-reviewed journals. (Melman, Tr. 1083; CX1289 (Melman Expert Report at 0003)).

214. Dr. Melman opined that POM Wonderful pomegranate juice has not been proven to prevent, reduce the risk of, or treat erectile dysfunction. (CX1289 (Melman Expert Report at 0005)).

2. Respondents' experts

a. Dr. Denis Miller

215. Dr. Denis R. Miller is a board certified pediatrician and pediatric hematologist and oncologist licensed to practice medicine in the state of New Jersey. (PX0206 (Miller Expert Report at 1); PX0354 (Miller, Dep. at 16)). He directs one of the largest pediatric oncology/ hematology programs in the world and holds an endowed chair. (PX0206 (Miller Expert Report at 3)).

216. Dr. Miller has, for over 40 years, directed clinical care, education, laboratory and clinical research, and administration, and led departments at some of the most prestigious hospitals in the world. (PX0206 (Miller Expert Report at 2); Miller, Tr. 2190). Dr. Miller has designed, managed, and directed many different research studies calculated to develop new anti-cancer agents. (PX0206 (Miller Expert Report at 2-3)).

217. Dr. Miller has authored or co-authored over 300 book chapters, peer-reviewed articles, and abstracts mostly on cancer and blood disorders. (PX0206 (Miller Expert Report at 4); Miller, Tr. 2191).

218. Complaint Counsel has retained Dr. Miller on several matters, and he testified for Complaint Counsel previously in the matter of *Daniel Chapter One*. (PX0206 (Miller Expert Report at 5, 18)).

219. Dr. Miller was accepted as an expert in the design of clinical research protocols and asked to testify on the areas of the applicable standards of substantiating evidence for fruit and fruit juice or food products in general as opposed to the standard that is applicable to drugs. (Miller, Tr. 2192, 2218).

220. Dr. Miller provided the following opinions: pomegranates are a food that have been eaten for thousands of years and its consumption as a food is without known risks; the appropriate level of scientific substantiation regarding the health benefit claims of pomegranates should be flexible and consider several factors (including risk of harm) with the desirability of getting information to the public; the standard for substantiating foods that are clearly safe need not be as rigorous as that for a new drug or anticancer agent, but should be based on reliable and competent scientific data; and POM Wonderful is not being put forth as a substitute or alternative to conventional and approved drug therapies and medical care. (PX0206 (Miller Expert Report at 15)).

b. Dr. David Heber

221. Dr. David Heber received his Ph.D. in Physiology from UCLA, an MD from Harvard Medical School, and a B.S. in Chemistry from UCLA. (PX0192 (Heber Expert Report at 0005)). Dr. Heber is the founding director of the UCLA Center for Human Nutrition, which is a center for clinical research, education, and public health endeavors. (Heber, Tr. 1937).

222. Dr. Heber is a treating physician with patients, and has been a member of the faculty of UCLA Medical School for 33 years. He is currently a Professor of Medicine in Public Health. (Heber, Tr. 1937; CX1407 (Heber, Tropicana Tr. 76)).

223. Dr. Heber has co-authored over 200 peer-reviewed publications in the field of nutrition and its relation to various diseases and written 25 chapters in other scientific texts. (Heber, Tr. 1939-40). He was the editor-in-chief of the leading text on nutritional oncology and has written a book on the importance of diet in maintaining health and resisting diseases. (Heber, Tr. 1939).

224. Dr. Heber was accepted as an expert in the relationship between nutrition and various diseases, including coronary heart disease and prostate cancer, as well as other diseases. (Heber, Tr. 1941).

225. Dr. Heber was asked to testify on Dr. Stampfer's expert report and provide opinions on issues related to pomegranate juice and extract, including: (1) antioxidants found in pomegranates, their potency, and how they act in the body (their mechanisms of action); (2) the health and safety effects; and (3) nutritional research methodology relating to the evaluation of scientific research on health benefits. (PX0192 (Heber Expert Report at 0004)).

226. Dr. Heber provided the following opinions: it is not appropriate to require the use of double-blind placebo-controlled studies for evaluating the health benefits of foods; translational nutritional science looks at the best available evidence, as a totality, rather than just one type of clinical study; and the body of research on pomegranate juice and extract, revealing how they act in the body, provides support for potential benefits for heart disease and prostate cancer. (PX0192 (Heber Expert Report at 0013-15)).

c. Dr. Dean Ornish

227. Dr. Dean Ornish is a medical doctor and Clinical Professor of Medicine at the University of California at San Francisco. (Ornish, Tr. 2314).

228. Dr. Dean Ornish is the Founder and President of the Preventative Medicine Research Institute ("PMRI") in Sausalito, CA. (PX0025 (Ornish Expert Report at 0001)).

229. For over 34 years, Dr. Ornish directed clinical research on the relationship between diet and lifestyle and coronary heart disease. He was the first to prove by a series of RCTs that heart disease could be reversed by making changes in diet and lifestyle. (Ornish, Tr. 2316-17).

230. Dr. Ornish has written six published books on the subject of the effect of diet and lifestyle on heart disease and other diseases. (Ornish, Tr. 2318). Dr. Ornish's research has been reported in many prestigious journals, and he has written numerous articles for distinguished peer-reviewed journals. (Ornish, Tr. 2318-19).

231. Dr. Ornish was accepted as an expert in the relationship between the heart and nutrition and in cardiovascular disease and its relationship to nutrition and nutrients. (Ornish, Tr. 2321-22).

232. Dr. Ornish was asked to evaluate: (1) whether drinking eight ounces of POM Juice or taking one POMx Pill or one teaspoon of POMx Liquid may be beneficial in maintaining cardiovascular health and lessening the risk of cardiovascular disease; and (2) whether basic science, clinical studies, research, and/or trials show that the consumption of POM Juice, POMx Pill, or POMx Liquid may be beneficial in

maintaining cardiovascular health and lessening the risk of cardiovascular disease. Dr. Ornish was further asked to review the report titled, "Expert Report of Frank M. Sacks" and to evaluate the claims and statements made in that document. (PX0025 (Ornish Expert Report at 0004-05)).

233. Dr. Ornish provided the following opinion: the scientific evidence from basic science studies, animal research, and clinical trials in humans indicates that pomegranate juice in its various forms (including POM Wonderful 100% Pomegranate Juice, POMx Pill, or POMx Liquid) is likely to be beneficial in maintaining cardiovascular health and is likely to reduce the risk of cardiovascular disease. (PX0025 (Ornish Expert Report at 0005)).

d. Dr. Arthur Burnett

234. Dr. Arthur Burnett is a Professor of Urology serving on the faculty of the Department of Urology at the Johns Hopkins University School of Medicine/Johns Hopkins Hospital. (PX0149 (Burnett Expert Report at 0001); Burnett, Tr. 2241). Dr. Burnett holds a faculty appointment in the Cellular and Molecular Medicine Training Program of the Johns Hopkins University School of Medicine and is the Director of the Basic Science Laboratory in Neuro-urology of the James Buchanan Brady Urological Institute and Director of the Male Consultation Clinic/Sexual Medicine Division of the Department of Urology at Johns Hopkins. (PX0149 (Burnett Expert Report at 0001); Burnett, Tr. 2241).

235. Dr. Burnett obtained his medical degree from the Johns Hopkins University School of Medicine in Baltimore, Maryland and completed his internship, residency and fellowship at the Johns Hopkins Hospital. (PX0149 (Burnett Expert Report at 0001); Burnett, Tr. 2240-41).

236. Dr. Burnett has authored and published over 180 original peer-reviewed articles and 40 book chapters. (PX0149 (Burnett Expert Report at 0003)).

237. Dr. Burnett has treated between 10,000 and 15,000 patients for erectile dysfunction. (Burnett, Tr. 2244).

238. Dr. Burnett has conducted world renowned research on nitric oxide ("NO"). (PX0149 (Burnett Expert Report at 0003)).

239. Dr. Burnett was accepted as an expert in the field of urology and sexual medicine to offer opinions on: (1) the science of nitric oxide biology; (2) the mechanisms by which nitric oxide is formed and acts in penile erection and in the promotion of erectile health, erectile function and treatment of erectile dysfunction; (3) the impact of pomegranate juice and antioxidants and nitric oxide on erectile health, erectile function and erectile dysfunction; and (4) scientific studies involving erectile function and dysfunction. (PX0149 (Burnett Expert Report at 0001-07); Burnett, Tr. 2243-44, 2249-51, 2255-56, 2270-74; PX0349 (Burnett, Dep. at 23-25, 103, 112, 116-118, 137)).

240. Dr. Burnett was asked to provide expert testimony regarding POM's basic science and clinical study, as well as pomegranate juice's effect on the nitric oxide regulatory mechanism, the vascular system/function, and on erectile health, erectile function and erectile dysfunction. (PX0149 (Burnett Expert Report at 0004-07); PX0349 (Burnett, Dep. at 103, 112, 116-118); Burnett, Tr. 2243-44, 2255-56, 2270-74).

241. To form his opinions, Dr. Burnett reviewed studies on erectile function and nitric oxide, including POM-sponsored studies such as the Forest Erectile Dysfunction Study (2007) and a few *in vitro* and animal studies. (PX0149 (Burnett Expert Report at 0004)). Dr. Burnett relied upon his "education, experience, and knowledge of developments in the fields of urology and sexual medicine, including the promotion of erectile health and treatment of erectile dysfunction." (PX0149 (Burnett Expert Report at 0004)).

242. Dr. Burnett provided the following opinion: pomegranate juice possesses potent anti-oxidative endothelial NO mechanisms in vasculature. These mechanisms serve potential beneficial effects on vascular blood flow and promote vascular biologic health. Basic scientific and clinical evidence supports the probable benefit of pomegranate juice on the vascular structures involved in penile erection. (PX0149 (Burnett Expert Report at 0005-06)).

e. Dr. Irwin Goldstein

243. Dr. Irwin Goldstein is a sexual medicine physician who has been practicing medicine since 1976 and has been involved in sexual medicine clinical practice, clinical research and basic science research since 1980. (PX0189 (Goldstein Expert Report at 0001-02); PX0352 (Goldstein, Dep. at 14)).

244. Dr. Goldstein has been certified by the American Board of Urology since 1982. He was a Professor of Urology and Professor of Gynecology at the Boston University School of Medicine from 1990 to 2005 and 2002 to 2005, respectively. (PX0189 (Goldstein Expert Report at 0001-03)).

245. Dr. Goldstein has published over 250 original peer-reviewed manuscripts in male and female sexual medicine. (PX0189 (Goldstein Expert Report at 0002-03)).

246. Dr. Goldstein was part of the original advisory board to Pfizer that engaged in an extensive drug development plan that developed sildenafil (Viagra), and was also on the advisory boards of Bayer and Eli Lilly for the development of vardenafil (Levitra) and tadalafil (Cialis). (Goldstein, Tr. 2590-91).

247. Dr. Goldstein was accepted as an expert in the field of sexual medicine, the studies that have been done on sexual medicine and the impact of pomegranate juice and antioxidants and nitric oxide on erectile function and dysfunction. (Goldstein, Tr. 2592). Dr. Goldstein was asked to provide testimony on: (1) sexual medicine; (2) the study, design, and treatment of men with sexual health problems; (3) the studies that

have been done on sexual medicine particularly regarding the promotion of erectile health and treatment of erectile dysfunction; (4) the mechanisms by which nitric oxide is formed and acts in penile erection and in the promotion of erectile health and treatment of erectile dysfunction; (5) urology as it relates to the treatment, prevention, and reduction of risk of erectile dysfunction; (6) the impact of pomegranate juice and antioxidants and nitric oxide on erectile health, erectile function and erectile dysfunction; and (7) scientific testing involving erectile health, erectile function and erectile dysfunction. (PX0352 (Goldstein, Dep. at 19-22, 37-42); PX0189 (Goldstein Expert Report at 0003-15); Goldstein, Tr. 2592, 2600-05, 2611, 2620).

248. To form his opinions, Dr. Goldstein reviewed studies on erectile function, nitric oxide, and the Mediterranean diet, including POM-sponsored studies such as the Forest Erectile Dysfunction Study (2007), an article titled, *Recreational Use of Phsphodiesterase Type 5 Inhibitors by Healthy Young Men* (2010), and several *in vitro* and animal studies. (PX0189 (Goldstein Expert Report at 0005); PX0352 (Goldstein, Dep. at 125)).

249. Dr. Goldstein offered the following opinions: (1) the available body of scientific literature, including *in vitro*, and preliminary clinical trials, strongly suggests that consuming pomegranate juice promotes erectile health; and (2) the use of pomegranate juice to promote erectile health is a separate and distinct concept from the use of a neutraceutical as a safe and effective treatment for the medical condition of erectile dysfunction such as with a PDE5 inhibitor. (PX0189 (Goldstein Expert Report at 0004-05)). Dr. Goldstein concluded that reasonable and competent scientific evidence shows that pomegranate produced a definite benefit to proper and effective erectile function. (Goldstein, Tr. 2605).

f. Dr. Jean deKernion

250. Dr. Jean deKernion is a practicing urologist certified by both the American Board of Surgery and the American Board of Urology. He obtained his medical degree in 1965 from Louisiana State University School of Medicine in New Orleans, Louisiana and did his residencies in surgery and urology at the university hospitals of Cleveland and the National Cancer Institute. (deKernion, Tr. 3039-40, 3127; PX0161 (deKernion Expert Report)).

251. Dr. deKernion was, from 1981 until his retirement in 2011, Chairman of the Department of Urology and Senior Associate Dean for Clinical Affairs (2001-2011) at the David Geffen UCLA School of Medicine. Dr. deKernion's responsibilities included the urological clinical and research education of students, residents, and fellows at all levels; a busy practice in urologic oncology, primarily related to prostate cancer but also bladder and kidney cancer; growth and oversight of large and diverse research programs; and administration of programs for the Dean's office and hospital. (deKernion, Tr. 3039; PX0161 (deKernion Expert Report at 0001)).

252. During Dr. deKernion's tenure as Chair of the Department of Urology at UCLA, he built a multidisciplinary research portfolio, which ranks among the largest and best in the United States. (PX0161 (deKernion Expert Report at 0003)).

253. Dr. deKernion's career in urologic oncology has involved both clinical and basic/translational research. (PX0161 deKernion Expert Report at 0001)).

254. Dr. deKernion co-authored the first book on urologic oncology and has co-authored 133 chapters since. His research has involved both basic laboratory research and clinical research publishing 228 papers to date in peer-reviewed journals and many other invited manuscripts. For six years, Dr. deKernion was the associate editor of the Journal of Urology and has been a reviewer for approximately 20 other peer-reviewed journals. (PX0161 (deKernion Expert Report at 0002); deKernion, Tr. 3041-43).

255. Dr. deKernion has served on a number of national committees and was a founding member of the Society of Urologic Oncology, was elected as a trustee of the American Board of Urology, and numerous committees of national urological societies and was appointed to the National Cancer Advisory board by President Bush. (deKernion, Tr. 3040; PX0161 (deKernion Expert Report at 0002)).

256. Dr. DeKernion was accepted as an expert in the field of urology and prostate health to offer opinions on research done on pomegranate juice and POM Products as they relate to the prostrate. He was also asked to provide expert opinions on the validity of PSA doubling time in assessing response to POM Products and on the strength of the science supporting the role of POM in prostate health and prostate cancer. In addition, Respondents asked Dr. DeKernion to rebut the opinions in Dr. Eastham's expert report. (deKernion, Tr. 3043-44; 3108-09; PX0161 (deKernion Expert Report at 0003)).

257. To form his opinions, Dr. deKernion reviewed the expert reports of Dr. Eastham and Dr. Miller, the FTC depositions of Dr. Pantuck and Dr. Carducci, protocols for the Pantuck Phase II Prostate Cancer Study (2006), the Carducci Dose Study, and the Pantuck Phase III Study, articles cited in Dr. Eastham's report, scientific articles found by conducting a literature search, and marketing materials. (PX0351 (deKernion, Dep. at 6-8, 27-29); PX0351a04; PX0351a05).

258. Dr. de Kernion provided the following opinions: (1) based on the data available, it is reasonable to state that POM products have shown an effect on prostate cancer with little or minimal toxicity; (2) given the current evidence, Dr. deKernion would suggest to patients and friends who have early prostate cancer that they consider taking POM, among other measures such as exercise, restrict intake of fatty foods, and weight control, to improve their probability for prevention or control of a tumor. (PX0161 (deKernion Expert Report at 0011-12)).

g. Dr. Ronald Butters

259. Dr. Ronald Butters is Professor Emeritus at Duke University and has been on faculty at Duke for over 40 years. He served as the Chairman of the Linguistics Department at Duke and Chairman of Duke University's English Department. (Butters, Tr. 2812).

260. Dr. Butters is a member of the advisory board of the New Oxford American Dictionary and has served as editor and co-editor of multiple prestigious scientific and academic publications. He participates in numerous professional associations and is the past president of the International Association of Forensic Linguistics. (Butters, Tr. 2812-13).

261. Dr. Butters has written textbooks and other books on the subjects of linguistics, which is the study of all forms of human language: semantics and semiotics. (Butters, Tr. 2814-15).

262. Dr. Butters was accepted as an expert in linguistics, including the meaning of language and symbols and the context in which they appear. (Butters, Tr. 2816, 2954-55).

263. Dr. Butters offered his opinions as a linguistics expert on the meanings of Respondents' advertisements. (Butters, Tr. 2816-17).

264. Dr. Butters concluded that Respondents' advertisements do not convey, either expressly or by implication: that scientific research proves that the use of certain recommended amounts, in recommended frequencies, of Pom Wonderful products successfully treats, prevents, or reduces: (1) the risk of heart disease, including decreasing arterial plaque, lowering blood pressure, and/ or improving blood flow to the heart; (2) the risk of prostate cancer, including by prolonging prostate-specific antigen doubling time ("PSADT"); and (3) the risk of erectile dysfunction. (PX0158 (Butters Expert Report at 0002-03)).

265. Dr. Butters also opined that Respondents' advertisements convey that (1) pomegranate juice is a healthy beverage and (2) Pom Wonderful products contain "antioxidants," for which there has been preliminary scientific research regarding their potential beneficial properties, and (3) readers and hearers are generally encouraged to investigate scientific research and draw their own conclusions. (PX0158 (Butters Expert Report at 0002-03)).

h. Dr. David Reibstein

266. Dr. David Reibstein is a tenured Professor of Marketing at the University of Pennsylvania in The Wharton School. Dr. Reibstein has taught courses in marketing management, marketing strategy and marketing metrics to MBA Program and Executive MBA Program students; marketing research courses to MBA Program students; and other marketing courses to undergraduate students. Many of these courses involve the use and design of surveys. (Reibstein, Tr. 2482; PX0356a01 at 0002-03).

267. Dr. Reibstein has been a visiting professor at Stanford Business School, Harvard Business School and Purdue University where he taught marketing courses. Dr. Reibstein has taught courses in marketing strategy and advanced industrial marketing strategy at INSEAD, a top business school in Europe. (Reibstein, Tr. 2483; PX0356a01 at 0002, 0003).

268. Dr. Reibstein received his Doctor of Industrial Administration from the Herman C. Krannert Graduate School of Industrial Administration at Purdue University with a major in marketing and a minor in behavioral science. (Reibstein, Tr. 2481). Dr. Reibstein's doctoral dissertation was titled, "*An Empirical Study of Brand Choice and Switching Behavior*." (PX0356a01 at 0001). Dr. Reibstein attended the Master of Business Administration Program at the Graduate Business School at Tulane University. (Reibstein, Tr. 2480-81; PX0356a01 at 0001). Dr. David Reibstein received a B.S. in Business Administration and a B.S. in Statistics and Political Science from the University of Kansas. (Reibstein, Tr. 2480; PX0356a01 at 0001). Dr. Reibstein has been awarded an Honorary Master of Science by The Wharton School at the University of Pennsylvania. (PX0356a01 at 0001).

269. Dr. Reibstein was the Executive Director for the Marketing Science Institute, an organization of 72 company-members. The Marketing Science Institute works closely with its members to identify the major marketing issues confronting them. The Marketing Science Institute prepares reports on various marketing issues which are disseminated to its members and the general business community. The Marketing Science Institute sets the research agenda for marketing academia globally. (Reibstein, Tr. 2483-84; PX0356a01 at 0002).

270. Dr. Reibstein has published extensively in prestigious peer-reviewed marketing journals, including many articles on marketing and marketing research. Those journals include, among others, the Journal of Consumer Research, Journal of Marketing Research, Marketing Science and the Harvard Business Review. (Reibstein, Tr. 2484; PX0356a01 at 0004-07).

271. Dr. Reibstein has written over seven books and numerous chapters in books on marketing and marketing research. (Reibstein, Tr. 2484; PX0356 (Reibstein, Dep. at 14; (PX0356a01 at 0007, 0008)). Dr. Reibstein authored the book "Marketing Metrics: 50+ Metrics Every Executive Should Master (2006)" which was named as the "Best Business Book: Marketing" by Strategy & Business in 2007. (PX0356a01 at 0004).

272. Dr. Reibstein has provided management education in the field of marketing to more than 300 companies. He has designed, executed, and supervised hundreds of market research studies for over 30 years, including surveys concerning consumer behavior. (Reibstein, Tr. 2485-86).

273. Dr. Reibstein has performed consulting research for a variety of companies where his work focuses on understanding the reasons that customers buy, what motivates

customers to buy, and the interface with customer behavior and a company's marketing activities, price, product, place, and promotion. (Reibstein, Tr. 2484-85; PX0356 (Reibstein, Dep. at 14-15)). Dr. Reibstein's consulting work for companies involves collecting and processing information to better inform the company about what has or might influence customers to make the purchase decisions they do, and in the manner they do to reduce uncertainty in the decisions they make. Dr. Reibstein's consulting work also involves determining the messages consumers take from certain advertising. (PX0356 (Reibstein, Dep. at 16)). Dr. Reibstein has also provided extensive management education in the field of marketing to more than 300 companies over his career. (Reibstein, Tr. 2485).

274. Dr. Reibstein serves on the board of the Marketing Accountability Standards Board. This board sets the standards on what are the most important marketing metrics and how to measure them both in the United States and globally. (Reibstein, Tr. 2485).

275. Dr. Reibstein was accepted as an expert witness in marketing and marketing research. (Reibstein, Tr. 2485).

276. Dr. Reibstein prepared for Respondents a survey analysis titled, Survey of POM Wonderful 100% Pomegranate Juice Users ("Reibstein Survey") to understand the underlying motivations that consumers had for purchasing pomegranate juice and what those motivations might have been. (PX0356 (Reibstein, Dep. at 11, 39); Reibstein, Tr. 2487).

277. As stated in the Reibstein Survey, the primary objective of the survey was to evaluate the main factors driving the purchasing decision for POM Wonderful 100% Pomegranate juice buyers, including whether and to what extent POM Wonderful 100% Pomegranate juice buyers purchase the product based on their belief that the product cures or prevents a particular disease. Dr. Reibstein's finding and opinion is that there is a very small percentage of people that bought, would buy again, or would recommend to a friend POM Wonderful Pomegranate Juice because they believed it was beneficial to any disease. (PX0223 at 0003).

278. Dr. Reibstein also reviewed the Bovitz Survey and the OTX Attitudes & Usages ("A&U") Study. (*See* Section II.J, *infra*). Dr. Reibstein opined that these studies have methodological flaws, cannot be relied on, and do not invalidate the results of the Reibstein Survey. (Reibstein, Tr. 2517; PX0223 at 0003).

3. Complaint Counsel's rebuttal experts

a. Dr. Michael Mazis

279. Dr. Michael Mazis is a Professor Emeritus of Marketing at the Kogod School of Business, American University. (PX0296 (Mazis Expert Report at 0002); Mazis Tr. 2653). He was a Professor of Marketing at American University from 1981 to 2008,

serving ten years as chair of the Department of Marketing. (PX0296 (Mazis Expert Report at 0002); Mazis, Tr. 2653).

280. Dr. Mazis has served as a paid consultant for numerous federal government agencies, including the FTC, FDA, Consumer Product Safety Commission, Department of Justice, Federal Deposit Insurance Corporation, Bureau of Alcohol, Tobacco and Firearms and U.S. Mint. (Mazis, Tr. 2656, 2697).

281. Dr. Mazis was employed by the FTC from July 1977 through August 1979. During that time, he was Chief of Marketing and Consumer Research in the Office of Policy and Planning. In addition, Dr. Mazis was employed by the FTC one day per week for a period of five or six years, beginning in the mid-1990's. He has also served as the FTC's principal marketing witness in several cases. Dr. Mazis has been a testifying expert witness in at least 24 legal proceedings during the last four years. (PX096a001 at 0001; Mazis, Tr. 2653, 2696-98; PX0296 (Mazis Expert Report at 0002-03, 0012); PX0359 (Mazis, Dep. at 22-24)).

282. Dr. Mazis is a former director of the Association for Consumer Research. He was Editor of the Journal of Public Policy & Marketing from 1992 to 1995 and Associate Editor of The Journal of Consumer Affairs from 1998 to 2001. (PX0296 (Mazis Expert Report at 0002); Mazis, Tr. 2654). Among his duties as an editor and associate editor, Dr. Mazis would review and critique survey research. (Mazis, Tr. 2655-56). Dr. Mazis has conducted hundreds of surveys and research studies, including over one hundred surveys for use in legal proceedings. (Mazis, Tr. 2657).

283. Dr. Mazis was called as an expert rebuttal witness in marketing and marketing research to rebut the expert testimony of Dr. Reibstein. (Mazis, Tr. 2659; CX1297 (Mazis Expert Report at 0002)).

284. Dr. Mazis opinioned that the Reibstein Survey contains substantial defects in its design and interpretation and that, as a result of these flaws, no reliable conclusions can be drawn from the Reibstein Survey, with regard either to the materiality of any of the challenged claims or to whether any of the challenged advertisements communicate any of the challenged claims. (CX1297 (Mazis Expert Report at 0004)).

b. Dr. David Stewart

285. Dr. David W. Stewart is a full Professor of Marketing in the A. Gary Anderson Graduate School of Management, University of California at Riverside, where he served as dean of the business school for four years before being asked to step down. (PX0295a01 at 0002, 0041; Stewart, Tr. 3161, 3224-25; CX1295 (Stewart Expert Report at 0002)). During his academic career, Dr. Stewart has taught a variety of graduate and undergraduate level courses related to advertising, consumer behavior, marketing research, and marketing strategy. (PX0295a01 at 0050-51; Stewart, Tr. 3160-61; CX1295 (Stewart Expert Report at 0003-04)).

286. Dr. Stewart has authored or co-authored eight books on advertising related issues and has written over 125 articles which have been accepted in peer-reviewed academic journals. (Stewart, Tr. 3162-63; PX0295a01 at 0002, 0005, 0008-17; CX1295 (Stewart Expert Report at 0002)). Dr. Stewart has served as the editor, associate editor, or member of the editorial board of numerous academic journals. (PX0295a01 at 0043-47; CX1295 (Stewart Expert Report at 0002); Stewart, Tr. 3161). Dr. Stewart has served as the President of the Academic Council of the American Marketing Association and chairman of the Section on Statistics in Marketing of the American Statistical Association. (Stewart, Tr. 3161-62; PX0295a01 at 0002, 0043). He is a past president of the Society of Consumer Psychology of the American Psychological Association. (Stewart, Tr. 3162; PX0295a01 at 0002, 0045; CX1295 (Stewart Expert Report at 0003)).

287. Dr. Stewart was accepted as an expert in advertising, marketing, consumer behavior, and survey methodology. (Stewart, Tr. 3168).

288. Dr. Stewart was called as a rebuttal witness to respond to Respondents' expert, Dr. Butters. (Stewart, Tr. 3168).

289. Dr. Stewart opined that Dr. Butters' conclusions are inconsistent with the extant literature on consumer response to advertising, POM Wonderful's own internal planning documents, and empirical evidence, and thus Dr. Butters' conclusions have no merit with regard to the determination of what claims are communicated by any challenged POM Wonderful advertisement. (CX1295 (Stewart Expert Report at 0017-18)).

E. Alleged Advertising Claims

1. Facial analysis

a. Alleged "clinically proven" claims

i. Print advertisements

(a) CX0016 ("Drink and be healthy" print advertisement)

290. CX0016 is a POM Juice advertisement with a headline "Drink and be healthy." CX0016 is reprinted in the Appendix to this Initial Decision. (Appendix at 1). (CX0016 at 0001).

291. CX0016 ran once in the Chicago Tribune on October 12, 2003. (CX0016 at 0002).

292. CX0016 ran in 2003 as part of the original launch of the POM Juice product and has not been disseminated since 2003. It was one of the first advertisements Respondents ever ran. (Tupper, Tr. 2995; L. Resnick, Tr. 157).

293. Based on the overall, common-sense, net impression of the advertisement, including the statements and representations set forth below, a significant minority of consumers, acting reasonably under the circumstances, would interpret CX0016 to contain the message that it is clinically proven that drinking eight ounces of POM Juice daily prevents or reduces the risk of heart disease, by reducing arterial plaque. (CX0016 at 0002; F. 294-296).

294. CX0016 draws a clear and direct connection between consumption of POM Juice and prevention or reduction of risk for heart disease by juxtaposing statements and representations that (a) POM Juice has more antioxidants than other drinks, (b) antioxidants protect against free radicals, (c) free radicals can cause "heart disease," (d) "medical studies have shown" that consumption of POM Juice "minimizes factors that lead to atherosclerosis," which the advertisement defines for the reader as "plaque buildup in the arteries," and (e) such plaque buildup is "a major cause of heart disease." (CX0016 at 0001).

295. The statement in the advertisement that "[m]edical studies have shown that drinking 8 oz. of POM Wonderful pomegranate juice daily minimizes factors that lead to atherosclerosis (plaque buildup in the arteries), a major cause of heart disease" uses definitive and unambiguous language. This language draws a clear and direct connection between the referenced proof and the claimed effect on heart disease. (CX0016 at 0001 (emphasis added)).

296. In the context of CX0016, the elements of the advertisement communicating that POM is a food product, including the large image of the pomegranate fruit, the reference to POM Juice as "delicious" and "refreshing," and the reference to POM being "[i]n the refrigerated produce section of your grocer[,]" do not materially alter the message conveyed, described in F. 293. (CX0016 at 0001).

(b) CX0029 ("10 OUT OF 10 PEOPLE DON'T WANT TO DIE" print advertisement)

297. The advertisement for POM Juice identified as CX0029 is a POM Juice advertisement with a headline "10 OUT OF 10 PEOPLE DON'T WANT TO DIE" that ran in *Prevention* magazine in or about November 2004 and January 2005. The advertisement also ran in *Martha Stewart Living* magazine in or about May 2005. (CX0029 at 0001-03).

298. CX0029 is reprinted in the Appendix to this Initial Decision. (Appendix at 2-3).

299. Based on the overall, common-sense, net impression of the advertisement, including the statements and representations set forth below, a significant minority of consumers, acting reasonably under the circumstances, would interpret CX0029 to contain the message that drinking eight ounces of POM Juice daily treats, prevents, or reduces the

risk of heart disease, and is clinically proven to do so, by reducing arterial plaque. (CX0029 at 0001-02; F. 300-305).

300. There are elements in CX0029 that weigh against the interpretation described in F. 299. These include an irreverent and/or humorous headline, "10 OUT OF 10 PEOPLE DON'T WANT TO DIE," the bold notation on the first page indicating that POM Juice is found "in the refrigerated produce section of your grocer," the image of the pomegranate, the reference to a study as a "pilot" study, and the language in the last paragraph which refers to keeping "your heart healthy" with regular exercise and a healthy diet, in addition to drinking POM Juice. (CX0029 at 0001-02).

301. Notwithstanding the elements described in F. 300, other elements in CX0029 dominate the communication, and result in the overall net impression that consuming POM Juice prevents, reduces the risk of, or treats heart disease, and is clinically proven to do so by reducing arterial plaque. These elements include statements and representations that: (1) free radicals "lead to" "heart disease"; (2) antioxidants "neutralize" free radicals; (3) "scientific research shows" that POM Juice has a superior ability to prevent LDL oxidation and a "clinical pilot study shows that" consuming an "8 oz. glass" of POM Juice "daily" "reduces plaque in the arteries up to 30%" with a footnoted citation to a study by Dr. Aviram published in *Clinical Nutrition* in 2004; (4) "heart attacks are due to . . . plaque in the arteries"; and (5) "heart disease" is America's number one killer. The language used is affirmative and non-qualified. (CX0029 at 0001-02).

302. Interspersed with the language described in F. 301 are an image of a human heart and an image of a graph asserting POM Juice's superior abilities to prevent oxidation of LDL, which the advertisement defines as "bad cholesterol" that "clogs arteries." In the context of this advertisement, these images reinforce the message conveyed by the language described in F. 301. (CX0029 at 0001-02).

303. Through the language and images described in F. 301 and F. 302, the advertisement draws a clear connection between the consumption of POM Juice and prevention, treatment or reduction of the risk of heart disease. The advertisement also draws a clear connection for the reader between reduced arterial plaque, as shown by the referenced study, and prevention of heart disease. (CX0029 at 0001-02).

304. Notwithstanding the irreverent or humorous headline, "10 OUT OF 10 PEOPLE DON'T WANT TO DIE," the overall tone of the advertisement is serious. In addition, the advertisement resembles a news article. (CX0029 at 0001-02).

305. In the context of the language and images described in F. 301 and F. 302, the fact that the advertisement pertains to a food product does not materially alter the message conveyed. (CX0029 at 0001-02).

(c) CX0314; CX0372; CX0379; CX0380 ("Magazine Wrap" Advertisements)

306. A "magazine wrap" is a type of advertisement that covers, or wraps, the actual magazine cover. (CX1357 at 87 (Kuyoomjian, Dep. at 86)).

307. POM disseminated a *New York Times* "magazine wrap" advertisement, identified as CX0314, in fall 2008, which included the headline, "Drink to prostate health[]" with an image of the POM Juice bottle on the cover. (CX0314 at 0003).

308. CX0372, CX0379, and CX0380 are *Time* magazine wraps, disseminated in August 2009 (CX0379) and September 2009 (CX0372 and CX0380). The cover of each of these magazine wraps uses the image of the POM bottle "speaking" the headline, "Lucky I have super Health Powers!" The body copy of each advertisement, CX0372, CX0379, and CX0380, is virtually identical to the body copy of CX0314. (CX0372 at 0001-04; CX0379 at 0001-04; CX0380 at 0001-06).

309. CX0314, CX0372, CX0379 and CX0380 are reprinted in the Appendix to this Initial Decision. (Appendix at 4-26).

310. Based on the overall, common-sense, net impression of these advertisements, including the statements and representations set forth below, a significant minority of consumers, acting reasonably under the circumstances, would interpret CX0314, CX0372, CX0379, and CX0380 to contain the message that drinking eight ounces of POM Juice daily treats, prevents, or reduces the risk of prostate cancer, by slowing PSA doubling times, and that these effects have been demonstrated in clinical testing. (CX0314; CX0372; CX0379; CX0380; F. 307-308, 311-319).

311. The text on the inside front cover of each of these magazine wrap advertisements describes the results of a published study involving POM Juice, which "followed 46 men previously treated for prostate cancer . . . ." "After drinking eight ounces of POM Wonderful 100% Pomegranate Juice daily for at least two years, these men experienced significantly slower" "PSA doubling times." The text then draws for the viewer a clear link between PSA levels and prostate cancer by immediately informing the viewer that "PSA (Prostate-Specific Antigen) is a biomarker that indicates the presence of prostate cancer. 'PSA doubling time' is a measure of how long it takes for PSA levels to double. A longer doubling time may indicate slower progression of the disease." (CX0314 at 0004; CX0372 at 0002; CX0379 at 0002; CX0380 at 0002).

312. CX0314 further states: "In addition, in-vitro testing using blood serum from the patients who drank pomegranate juice showed a 17% increase in prostate cancer cell death and a 12% decrease in cancer cell growth." This language does not materially detract from the overall net impression that the efficacy of POM Juice has been demonstrated in clinical testing; however, the language does represent that the degree of clinical proof is not fully conclusive. (CX0314 at 0004).

313. The magazine wrap further states: "Backed by Science. Only POM is backed by $25 million in medical research conducted at the world's leading universities." The page on which these claims appeared was titled, "The proof is in the POM." In the context of this advertisement, these statements contribute to and reinforce an overall net impression that efficacy for prostate cancer has been demonstrated by clinical testing. (CX0314 at 0005).

314. The text on the inside front cover of each of these magazine wrap advertisements quotes Dr. Allan Pantuck, "lead author" of the study referenced in F. 311, as stating: "This is a big increase." This language bolsters the strength and authoritative nature of the study referenced in the advertisements. (CX0314 at 0004; CX0372 at 0002; CX0379 at 0002; CX0380 at 0002).

315. The inside front cover of each of the magazine wraps states in part, "Results from this study were so promising that many of the original patients continued to drink pomegranate juice daily, and their PSA doubling times remained suppressed." This statement further bolsters the strength of the referenced PSA study. Moreover, the additional statements in this paragraph that the "[r]esearch [c]ontinues" and that "[t]hree more clinical studies are now underway to further investigate the effects of POM on prostate health" do not materially detract from the overall net impression that the claimed efficacy of POM Juice for prostate cancer is based upon clinically testing. (CX0314 at 0004; CX0372 at 0002; CX0379 at 0002; CX0380 at 0002).

316. Amid the text on the inside front cover of each of these magazine wrap advertisements is the "caduceus" symbol, showing snakes curling around a staff. In the context of this advertisement, the symbol, considered to be a symbol of medicine or medical practice, creates a "medical" tone and contributes to the overall net impression described in F. 310. (CX0314 at 0004; CX0372 at 0002; CX0379 at 0002; CX0380 at 0002; *see also* F. 541).

317. The overall tone of each of the magazine wraps is serious. With respect to the relationship between POM Juice and prostate cancer, the language of the advertisements is clear and affirmative, and not meaningfully qualified. (CX0314; CX0372; CX0379; CX0380).

318. The italicized statements in the middle of the inside front cover of each magazine wrap, that "[p]rostate cancer is the most commonly diagnosed cancer in men in the United States. After lung cancer, it's the second leading cause of cancer death in men," further reinforce the already serious tone of the advertisement. (CX0314 at 0004; CX0372 at 0002; CX0379 at 0002; CX0380 at 0002).

319. There are elements of these magazine wraps which, in a different context, could militate against the message described in F. 310. These include: (1) generalized references to "health," "prostate health," and (2) general descriptions of POM's antioxidant characteristics and relationship to free radicals. In the context of these advertisements, however, these elements do not materially detract from the message described in F. 310.

Similarly, in the context of these advertisements, the reference to POM Juice being "available in your supermarket produce section" does not materially alter the overall net impression described in F. 310. (CX0314 at 0004-05; CX0372 at 0002-03; CX0379 at 0002-03; CX0380 at 0002-03).

320. In the context of these advertisements, the use of humor and/or hyperbole, such as (1) the image of the POM bottle dressed as a caped superhero (CX0314 at 0006); and (2) the POM bottle announcing "Lucky I have super HEALTH POWERS!" "HOLY HEALTH" and "100% PURE pomegranate juice to the rescue!" (CX0372 at 0001-02, 0004; CX0379 at 0001- 02; CX0380 at 0001-02, 0005-06) does not materially detract from the message described in F. 310.

(d) CX0351/CX0355 ("The Only Antioxidant Supplement Rated X" print advertisement)

321. The advertisements identified as CX0351 and CX0355, with the headline, "The Only Antioxidant Supplement Rated X," were disseminated, respectively, in the publication the *Advocate* on or about June 1, 2010, and in *Playboy* magazine on or about July 1, 2010. (CX0351 at 0001-02; CX0355 at 0001-02). These advertisements are reprinted in the Appendix to this Initial Decision. (Appendix at 27-28).

322. The imagery and advertisements in CX0351 and CX0355 are substantially identical to each other. (CX0351 at 0001; CX0355 at 0001).

323. These advertisements state and represent (1) antioxidants keep you healthy by protecting against free radicals, which "emerging science suggests" can damage the body; (2) POMx Pills give you in supplement form "super-potent," and the best available, antioxidants, that are the same antioxidants contained in POM Juice; (3) POMx is "backed by" millions of dollars in research, showing unique and superior antioxidant power and also revealing "promising results for" "prostate, cardiovascular and erectile health." (CX0351 at 0001; CX0355 at 0001).

324. These advertisements further state that "[i]n a preliminary study on erectile function, men who consumed POM Juice reported a 50% greater likelihood of improved erections as compared to placebo. 'As a powerful antioxidant, enhancing the actions of nitric oxide in vascular endothelial cells, POM has potential in the management of ED . . . further studies are warranted'. *International Journal of Impotence Research*, '07." (CX0351 at 0001; CX0355 at 0001).

325. Based on the overall, common-sense net impression of CX0351 and CX0355, a significant minority of consumers, acting reasonably under the circumstances, would interpret these advertisements as claiming that a clinical study has shown that taking one POMx Pill daily treats, prevents or reduces the risk of, erectile dysfunction. The advertisements specifically reference "improved erections" and "ED" and draw a direct connection between taking POMx Pills and "improved erections" and "managing" "ED." (CX0351 at 0001; CX0355 at 0001; F. 323-324).

326. In the context of these advertisements, the use of the phrase "erectile health" or "erectile function," rather than the express term, "erectile dysfunction" is insufficient to alter the overall net impression that the advertisement is conveying a message about erectile dysfunction. (CX0351 at 0001; CX0355 at 0001; *see also* F. 537).

327. The headline (F. 321), and the sub-headlines "[a]lways use protection," "[s]uper-potent just like you" and "[w]e're not just playing doctor," although humorous or irreverent, in the context of these advertisements, fail to detract from the overall, net impression described in F. 325. (CX0351 at 0001; CX0355 at 0001).

(e) CX1426 at 00038-42/Compl. Ex. I (POMx "Antioxidant Superpill" Package Insert)

328. CX1426 at 0038-0042 (POMx "Antioxidant Superpill" package insert), which is attached to the Complaint in this matter as Exhibit I, is a brochure that was disseminated by Respondents as a package insert for shipment with POMx Pills, in or about June 2007. (CX1426 at 0038-42 (Compl. Ex. I); Answer ¶ 10; L. Resnick, Tr. 177-78: CX1356 at 180 (Leow, Dep. at 179)).

329. The package insert consists of five pages of text and images. (CX1426 at 0038-42 (Compl. Ex. I)).

330. The package insert is reprinted in the Appendix to this Initial Decision. (Appendix at 29-33).

331. Based on the overall, common-sense, net impression of CX1426 at 0038-42, including the statements and representations set forth below, a significant minority of consumers, acting reasonably under the circumstances, would interpret the package insert to contain a claim that drinking eight ounces of POM Juice or taking one POMx Pill daily treats, prevents, or reduces the risk of prostate cancer, by slowing PSA doubling times, and that these effects have been demonstrated in clinical testing. (CX1426 at 0041 (Compl. Ex. I); F. 332, 334-336).

332. The first page of the package insert features the POMx bottle, with the headline "Antioxidant Superpill" and the sub-headline, "POM in a Pill." The second page of the package insert represents that POMx is safe, has been reviewed for safety by the FDA, and that POMx has the same "polyphenol antioxidants" contained in POM Juice. The third page of the package insert then clearly represents a link between consuming the antioxidants provided by the POM products and prevention or reduction of the risk of disease, specifically including heart disease and cancer, by stating or representing: (1) POMx contains the same antioxidant power as POM Juice; (2) antioxidants fight free radicals, which "emerging science tells us" destroy healthy cells and "may be linked to . . . serious health threats like cancer and heart disease"; and (3) antioxidants "neutralize" free radicals, thereby "helping to prevent the damage that can lead to disease." (CX1426 at 0038-40 (Compl. Ex. I)).

333. The fourth page of this package insert begins with a headlined quotation attributed to the July 4, 2006 *New York Times* that findings from a small study suggest that pomegranate juice "may one day prove" an effective weapon against prostate cancer and statements that "new studies are under way to further investigate." This headline does not materially detract from the overall net impression that the efficacy of POMx has been demonstrated in clinical testing; however, the headline does indicate that the degree of clinical proof is not fully conclusive. (CX1426 at 0041 (Compl. Ex. I)).

334. The fourth page of the package insert states or represents that (1) "Prostate cancer is the most commonly diagnosed cancer . . . and the second-leading cause of cancer death" among men in the United States; (2) POMx is a "time pill" because "stable levels of PSA," which is defined for the reader as "prostate-specific antigens," are "critical for men with prostate cancer," "[p]atients with quick PSA doubling times are more likely to die from their cancer," and "[a]ccording to a UCLA study of 46 men age 65 to 70 with advanced prostate cancer, drinking an 8oz glass of POM Wonderful 100% Pomegranate Juice every day slowed their PSA doubling time by nearly 350%. 83% of those who participated in the study showed a significant decrease in their cancer regrowth rate"; and (3) "basic studies" indicate POMx may have the same effects as POM Juice with respect to "prostate health." (CX1426 at 0041 (Compl. Ex. I)).

335. The package insert expressly refers to "prostate cancer." Moreover, the representations in F. 334, especially in the context of previous representations regarding the effect of POM antioxidants on cancer (F. 332), represent a connection between the consumption of POMx, a slowing of PSA doubling times, and a beneficial effect on the progress of prostate cancer, including avoiding death from prostate cancer. (CX1426 at 0041 (Compl. Ex. I)).

336. In addition, references on the final page of the advertisement to "backed by $20 Million in medical research" and "clinically tested on adults" tend to bolster the nature and amount of clinical research or testing supporting the efficacy of the POM products for prostate cancer. (CX1426 at 0042 (Compl. Ex. I)).

337. In the context of this advertisement, use of the phrase "promote prostate health" is insufficient to alter the overall net impression that the advertisement is conveying a message about prostate cancer. (CX1426 at 0041 (Compl. Ex. I)).

338. Based on the overall, common-sense, net impression of CX1426 at 0038-42, including the statements and representations set forth below, a significant minority of consumers, acting reasonably under the circumstances, would interpret this package insert to contain a claim that drinking eight ounces of POM Juice or taking one POMx Pill daily treats, prevents or reduces the risk, of heart disease, by reducing arterial plaque or improving blood flow to the heart, and that these effects have been demonstrated by clinical testing. (CX1426 at 0038-42 (Compl. Ex. I); F. 339-342).

339. The final page of the package insert begins with a headline, which represents that POMx may have the same "cardiovascular health benefits" as POM Juice, which has been "proven" to "promote cardiovascular health." This page further represents: (1) "groundbreaking" "preliminary studies" showed that "patients" who drank POM Juice "experienced impressive cardiovascular results"; including (2) a "pilot" study on 19 "patients" with "atherosclerosis," which the text defines for the reader as "clogged arteries," showed that "arterial plaque decreased 30%" for those that consumed 8 oz. of POM Juice daily"; (3) an "additional study" of 45 "patients" with "impaired blood flow to the heart" who drank POM Juice daily "experienced a 17% improvement in blood flow"; (4) POMx has "similar promise" for heart health; (5) POMx is high in antioxidants; and (6) "backed by $20 Million in medical research" and "clinically tested on adults." Depicted within these representations is an image captioned as "the heart." (CX1426 at 0042 (Compl. Ex. I)).

340. The representations regarding "impressive cardiovascular results," a decrease in "clogged arteries" and "improvement in blood flow to the heart" in "patients," appear in the context of preceding representations regarding the effect of POM antioxidants on heart disease. Moreover, the representations of "proven" heart health benefits in the headline are juxtaposed to the descriptions of these study results. (CX1426 at 0042 (Compl. Ex. I); F. 339).

341. The package insert represents a link between consumption of POM-provided antioxidants, the referenced study results, and effectiveness for heart disease. (F. 339-340).

342. In the context of this advertisement, describing studies as "preliminary," (particularly when described as "groundbreaking"), "initial" or "pilot" is insufficient to modify the overall net impression that the claimed efficacy is based upon clinical testing; however, such language does indicate that the nature of the referenced clinical testing is not fully conclusive. (CX1426 at 0038-42 (Compl. Ex. I); F. 338-341).

ii. Newsletters

343. The advertisements identified as CX1426 at 0046-48, which comprises Exhibit M to the Complaint in this matter, and CX1426 at 0049-51, which comprises Exhibit N to the Complaint, were disseminated by Respondents. (CX1426 at 0046-51; Complaint ¶ 10; Answer ¶ 10). These advertisements are reprinted in the Appendix to this Initial Decision. (Appendix at 34-39).

344. Exhibit M to the Complaint contains a notation, "POMx Heart Newsletter, Pills and Liquid, Monthly, 2nd Continuity Shipment, Summer '07-present (ongoing)" (hereafter, "Heart Newsletter"). Exhibit N to the Complaint contains the notation, "POMx Prostate Newsletter, Pills and Liquid, Monthly, 3rd Continuity Shipment, Fall '07-present (ongoing)" (hereafter, "Prostate Newsletter") (collectively, the "Newsletters"). (CX1426 at 0046, 0049 (Compl. Exs. M, N)).

345. Each Newsletter consists of two pages, and is dense with text. (CX1426 at 0047-48, 0050-51(Compl. Exs. M, N)).

(a) Heart Newsletter

346. Based on the overall, common-sense, net impression of the Heart Newsletter, including the statements and representations in F. 347-349, a significant minority of consumers, acting reasonably in the circumstances, would interpret the Heart Newsletter as claiming that that drinking eight ounces of POM Juice or one POMx Pill taken daily, prevents, treats, or reduces the risk of heart disease, by decreasing arterial plaque, or by improving blood flow to the heart, and that these effects are based upon clinical testing. (CX1426 at 0047-48 (Compl. Ex. M); F. 347-350).

347. The Heart Newsletter begins with the heading "What's New in the Lab by Dr. Mark Dreher" followed by a photograph of Dr. Dreher next to his title: Mark Dreher, PhD, Chief Science Officer, POM Wonderful, LLC. The introductory text, by Dr. Dreher, represents that the purpose of the Heart Newsletter is to advise readers of POM Wonderful's "latest research." This beginning to the Heart Newsletter implies a scientific or medical message. (CX1426 at 0047 (Compl. Ex. M)).

348. The Heart Newsletter states or represents that (1) "58.8 million Americans suffer from some form of heart disease" and that reducing the risk of "cardiovascular disease" is a core part of lifelong wellness; (2) that diet and exercise are the best weapons against "heart disease", but may not be enough, and that supplementation with antioxidants is "your ally" in fighting "heart disease"; (3) antioxidants fight free radicals and help prevent cell and tissue damage that lead to "disease"; (4) POM Juice and POMx have polyphenol antioxidants, which are unique and superior; and (5) POMx provides antioxidant supplementation without adding the calories of POM Juice. These representations draw a connection for the reader between POM antioxidants and prevention or reduction of the risk of heart disease. (CX1426 at 0047-48 (Compl. Ex. M)).

349. The Heart Newsletter further states that POM's "scientists have found" that POM Juice "may help counteract factors leading to arterial plaque build up, as well as inhibit a number of factors associated with heart disease." The text then proceeds to describe these findings, from "new research," including (1) a "pilot" study involving 19 "patients" with "clogged arteries" which found a "30% decrease in arterial plaque," among those drinking eight ounces of POM Juice daily; and (2) a study involving 45 "patients" with "impaired blood flow to the heart," showing "17% improved blood flow" among those who consumed eight ounces of POM Juice daily. The Heart Newsletter further states that "the antioxidants in POMx are supported by $20 million in initial scientific research." (CX1426 at 0048 (Compl. Ex. M)).

350. The representations set forth in F. 349, in the context of the representations in F. 348, draw a connection between reducing arterial plaque and treating, preventing, or reducing the risk of heart disease. (CX1426 at 0048 (Compl. Ex. M)).

(b) Prostate Newsletter

351. Based on the overall, common-sense, net impression of the Prostate Newsletter, including the statements and representations described in F. 352 and F. 353, below, a significant minority of consumers, acting reasonably in the circumstances, would interpret the Prostate Newsletter as claiming that drinking eight ounces of POM Juice or one POMx Pill taken daily, prevents, treats, or reduces the risk of prostate cancer, by prolonging PSA doubling time, and that these effects are clinically proven. (CX1426 at 0050-51 (Compl. Ex. N); F. 352-354).

352. The Prostate Newsletter draws a clear link for the reader between antioxidants and reduction of the risk of prostate cancer, including through the following statements or representations: The Prostate Newsletter states prominently "Prostate Cancer Affects 1 Out of Every 6 Men," and that "Prostate cancer is the second leading cause of cancer related death in men in the United States . . . " The associated text discusses "risk factors" for prostate cancer, including "diet," and advises a diet that includes, among other things, "fruits rich in antioxidants." (CX1426 at 0050-51 (Compl. Ex. N)).

353. The Prostate Newsletter draws a connection for the reader between research results showing prolonged PSA doubling time and effectiveness for prostate cancer, including through statements or representations that: early detection, including through a PSA test, increases prostate cancer survival rates; a "preliminary UCLA medical study" on 46 men treated for prostate cancer, showed that a majority of those consuming eight ounces of POM Juice daily "experienced a significantly extended PSA doubling time. Doubling time is an indicator of prostate cancer progression – extended doubling time may indicate slower disease progression"; testing on "patient" blood serum showed a decrease in "cancer cell proliferation," and "increase in cancer cell death"; in another study, "in vitro laboratory testing at UCLA showed that POMx significantly decreased human prostate cancer cell growth and increased cancer cell death" and that POMx has the same active ingredients in POM Juice. (CX1426 at 0050-51 (Compl. Ex. N)).

354. In the context of the Prostate Newsletter, reference to research as "preliminary" or "*in vitro*" is insufficient to modify the claim described in F. 351 that the claimed efficacy is based upon clinical testing, particularly in light of other statements and representations promoting the strength and credibility of the research, as part of $25 million in "world-class research" including "clinical studies published in top peer-reviewed medical journals." Such language does, however, indicate that the degree of proof provided by the referenced studies is not fully conclusive. (CX1426 at 0050-51 (Compl. Ex. N)).

iii. Website advertising

(a) Website background facts

355. POM's websites include pomwonderful.com, pomegranatetruth.com, and pompills.com (collectively, the "websites"). (JX0003 ¶ B.11; Rushton, Tr. 1354-55; Leow, Tr. 433).

356. POM has maintained the pomwonderful.com website since approximately January 2003. (CX0013 at 0004). It has maintained the pomegranatetruth.com website since approximately January 2008. (CX0170 at 0002). POM launched pompills.com in early 2007. (CX1347 (Glovsky, Dep. at 135-36)).

357. Since at least September 2007, POM has had an online department. The online department is part of POM's marketing department and handles anything related to the Internet, including marketing, engagement, interaction, and development. (Rushton, Tr. 1353-54).

358. Jeffrey Rushton was the Director of Marketing for Online for POM Wonderful, from September 2007 through March 2010. (Rushton, Tr. 1353).

359. In approximately 2008, POM converted pomwonderful.com from a traditional static format to a blog format that sought engagement from external sources. (Rushton, Tr. 1354). POM launched this "Community" version of pomwonderful.com in approximately December 2009. (CX0473 (Dec. 2009, pomwonderful.com)).

360. In October 2009, one of the rotating frames on the pomwonderful.com homepage welcomed consumers to its "new community site." (CX0473 (Oct. 2009, pomwonderful.com at 00:25)). The "community" design encouraged website visitors to "participate," including by "Tell[ing] Us Your Health Story." (CX0473 (Oct. 2009, pomwonderful.com at 00:25)).

361. Testimonials appeared on the POM Wonderful website briefly, for much less than a year. (L. Resnick, Tr. 134).

362. The "Community" section of the pomwonderful.com site also featured blog posts and videos by "POM Experts" like Dr. Aviram, Dr. Heber, and Susan Bowerman, Assistant Director at the UCLA Center for Human Nutrition. (CX0473 (Oct. 2009, pomwonderful.com at 06:52)). POM paid Susan Bowerman to, among other things, write blog posts for pomwonderful.com. (CX0203 at 0001; CX1346 (Rushton, Dep. at 145)).

363. To direct traffic to its website, POM used keyword advertising with search engines. With keyword advertising, marketers can pay for their advertisements to appear on the search results pages of search engines such as Google, Yahoo, Bing, among others, by purchasing keywords that consumers may search for. (Rushton, Tr. 1357-58).

364. Examples of keywords POM has used in its search engine advertising include: "prostate cancer prevention," "prostate cancer info," "prostate cancer research," and "cancer prostate." (CX0427 at 0004-05, 0007-08; Rushton, Tr. 1387-89).

(b) Website claims

365. CX0473 consists of electronically recorded "captures" of Respondents' websites on particular dates, as follows:

> Pomwonderful.com – April, October, December, 2009 and January 2010;
> Pompills.com – April 2009 and January 2010; and
> Pomegranatetruth.com – April 2009

(CX0473).

366. Each website capture reflects an electronic recording of navigation through the pages of the subject website, "clicking" on various hyperlinks to other pages. The web captures total approximately 95 minutes of material, with each capture totaling approximately 15 minutes in length, except for CX0473 Ex. E-1 (pomegranatetruth.com), which is approximately 5 minutes in length. (CX0473).

367. Printouts of those pages referred to in the following findings are reprinted in the Appendix to this Initial Decision. (Appendix at 40-93).

(i) Pomwonderful.com

368. Based on the overall, common-sense, net impression of the pomwonderful.com website, including the "health benefits" or "health" pages and links therefrom, a significant minority of consumers, acting reasonably in the circumstances, would interpret the pomwonderful.com website as claiming that drinking eight ounces of POM Juice daily treats, prevents, or reduces the risk of heart disease, prostate cancer, and/or erectile dysfunction, and that these effects are shown in clinical testing, as more fully explained below. (CX0473 (pomwonderful.com website: April 2009 (Compl. Ex. E-2); October 2009, December 2009, January 2010); F. 369-381).

369. In April 2009, the pomwonderful.com homepage included a link to a "health benefits" page. (CX0473 (Compl. Ex. E-2 at 00:04 and 00:15)).

370. In April 2009, the linked "health benefits" webpage displayed a large graphic depicting the POM Juice bottle hanging upside down on a pole, with the juice running through a tube at the bottom of the bottle, in the manner of a hospital intravenous line, while the juxtaposed text refers to POM Juice being "backed by" $25 million in "medical research" and "clinically tested." The page then introduces the "medical results" in separate areas designated "cardiovascular health," "prostate health," and "erectile function" sections. Introductory text in each such section summarizes research, with the cardiovascular section providing a further link to "read more." (CX0473 (Compl. Ex. E-2 at 00:17)).

371. In April 2009, the "Prostate Health" section of the health benefits webpage described "[a] preliminary UCLA medical study" on "46 men previously treated for prostate cancer," published by "The American Association for Cancer Research," showing that after drinking eight ounces of POM Juice daily for two years, "these men experienced significantly slower PSA doubling times." The description clearly links the significance of this research finding to prostate cancer, stating "PSA is a biomarker for prostate cancer, and slower PSA doubling time may indicate slower disease progression." (CX0473 (Compl. Ex. E-2 at 00:24)).

372. In April 2009, the "Erectile Function" section of the health benefits webpage reported a 2007 "pilot" study, published in the *International Journal of Impotence Research*, involving 61 male subjects with "mild to moderate erectile dysfunction," showing that those men drinking eight ounces of POM Juice daily for four weeks "were 50% more likely to experience improved erections." (CX0473 (Compl. Ex. E-2 at 00:24)).

373. In April 2009, the "Cardiovascular" section of the health benefits webpage described the results of studies as follows: (1) a 2005 study published in the *American Journal of Cardiology*, involving 45 "patients" with "coronary heart disease who had reduced blood flow to the heart," showed that "patients" who drank eight ounces of POM Juice daily had "improved blood flow to the heart," while those who did not drink POM Juice got worse; and (2) a "pilot" study on 19 "patients" with "atherosclerosis," which the text defines for the reader as "clogged arteries," showing that those "patients" who drank eight ounces of POM Juice daily for one year showed a decrease in arterial plaque, while those who did not drink POM Juice got worse. Each of these study descriptions offered a "read more" link. (CX0473 (Compl. Ex. E-2 at 00:24)).

374. In April 2009, the "read more" link from the "Cardiovascular" section of the health benefits webpage took the viewer to a page titled, "Heart Health-Emerging Science." The text advises the reader that "heart disease" is a leading killer of men and women in the United States, that "atherosclerosis," which is defined for the readers as too much "plaque," is a leading factor in "heart attacks" and further describes the role of antioxidants in reducing LDL (defined as "bad" cholesterol) oxidation. The text then invites the reader who wants to learn more about consumption of POM Juice and cardiovascular health, to "click on" the links to a 2005 study on effect of pomegranate on myocardial perfusion published in the *American Journal of Cardiology*; a 2004 study on reduction of carotid intima-media thickness, blood pressure and LDL oxidation, published in the journal, *Clinical Nutrition*; and a 2001 study on reduction of systolic blood pressure, published in the journal, *Atherosclerosis*. This page draws a clear connection for the reader between "heart health" and "heart disease," and between the effects referenced in the studies and effectiveness for heart disease. (CX0473 (Compl. Ex. E-2 at 00:30)).

375. While the link to the 2005 myocardial perfusion study (F. 374) took the viewer to a reprint of a copy of the actual published study, (CX0473 (Compl. Ex. E-2 at 00:45)), the link to the 2004 study on reduction of carotid intima-media thickness, blood pressure and LDL oxidation (F. 374)) took the viewer to a further description of the study with

highlighted commentary by Dr. Aviram and graphs emphasizing the reduced plaque and "anti-atherosclerotic" effects of POM Juice. At the top of this page was a quote attributed to Dr. Aviram that "[t]he present study clearly demonstrates for the first time that pomegranate juice consumption by patients with carotid artery stenosis possesses anti-atherosclerotic properties." (CX0473 (Compl. Ex. E-2 at 01:00, 01:06)).

376. The link to the 2001 study on reduction of systolic blood pressure (F. 374) took the viewer to a further description of the study. The description begins: "This pilot study demonstrates that pomegranate juice lowers blood pressure in patients with hypertension." A quote attributed to Dr. Aviram states that the "potent inhibitory effect on lipid peroxidation" and the "inhibitory effect of pomegranate juice on serum ACE activity" "suggest[] that pomegranate juice consumption may offer wide protection against cardiovascular diseases." The decreased ACE (angiotensin converting enzyme) activity is illustrated by a graph. (CX0473 (Compl. Ex. E-2 at 01:25)).

377. In April 2009, the "Health Benefits" section of pomwonderful.com also included links to other pages, including one titled, "Cancer." (CX0473 (Compl. Ex. E-2 at 01:44)).

378. In April 2009, the linked "Cancer" page stated: "Emerging science has shown that diets rich in fruits and vegetables that contain antioxidants, along with regular exercise, might slow or help prevent the development of cancer. Two great sources of antioxidants are POM Wonderful Pomegranate Juice and POM Tea." The page featured a link to the "Clinical Cancer Research." (CX0473 (Compl. Ex. E-2 at 03:45)).

379. In April 2009, pomwonderful.com included a "Glossary," which was linked to the "Health Benefits" page. A number of definitions reasserted and reinforced the study results referred to F. 374-376. For example, the definitions of "Atherosclerosis," "ACE" (*i.e.*, angiotensin-converting enzyme), and "plaque" provided in the glossary explain for the reader the purported connection between the effects shown by the study results and effects for heart disease. (CX0473 (Compl. Ex. E-2 at 01:44, 04:15-07:08)).

380. Having fully reviewed later versions of the pomwonderful website, captured in October and December in 2009, and January 2010, they are not materially different with respect to linking viewers to text summarizing research results, under the categories of cardiovascular, prostate cancer, and erectile "function," and drawing a connection for the reader between consumption of POM antioxidants, the research results summarized, and the prevention, treatment, or reduction of the risk of diseases associated with the conditions addressed in the research results. Thus, these later versions of the pomwonderful website also convey the claims described in F. 368 as to the April 2009 website. (CX0473; F. 381).

381. As an example that later versions of the pomwonderful website also convey the claims described in F. 368 as to the April 2009 website, in October 2009, links from the "health" page directed the viewer to a "research study synopses," link, which page further stated *inter alia*: (1) under "cardiovascular," the rate of "CIMT progression" slowed in nearly one-third of the "patients" having "cardiovascular risk factors,"

(CX0473 (Oct. 2009, pomwonderful.com at 02:43)); (2) under "prostate cancer," that "PSA doubling time increased" among the POM Juice drinkers, and that "PSA doubling time is an indicator of prostate cancer progression, (*Id.*); and (3) under "Erectile Function," that POM Juice drinkers "reported 50% greater likelihood of experiencing improved erections." (*Id.* at 02:52; *see also* CX0473 (January 2010, pomwonderful.com at 00:26; 00:50, "Featured Scientific Studies" page)); CX0473 (December 2009, pomwonderful.com, "Let's Talk about Prostate Cancer" video, in which Dr. Heber states, *inter alia*, that "pomegranate inhibits inflammation in the prostate gland, that it also inhibits prostate cancer growth in animals, both in early prostate cancer and advanced prostate cancer. And in humans, we were able to reduce the rate of rise of PSA in men with prostate cancer"); CX0473 (Dec. 2009, pomwonderful.com at 08:06; CX0473 (Jan. 2010, pomwonderful.com at 00:54, and CX0473 (October 2009 pomwonderful.com at 7:25 (Dr. Aviram stating, regarding "The Unique Antioxidants of Pomegranates," that pomegranates inhibit "atherosclerosis development, . . . as well as its consequent cardiovascular events")).

382. The "POM Community" section of pomwonderful.com in December 2009 included consumer testimonials. (CX0336 at 0011-19).

383. Testimonials were in the "POM Community" section of pomwonderful.com for much less than a year. (L. Resnick, Tr. 134).

384. Attached to the expert report of Respondents' linguistic expert, Dr. Butters, is a copy of what Dr. Butters identified as printouts from the pomwonderful.com website in 2011, taken on or before March 25, 2011, the date of Dr. Butters' report. As of that date, the "health" page omits reference to "protective effects," does not refer to any diseases, and does not summarize research results. The linked "glossary" omits the references described in F. 379. (PX0158 (Butters Expert Report at 0042); PX0160 at 0029-36, 0038-53, attachment 3) ("2011 website")).

385. The health page of the 2011 website (F. 384) does provide a link to "view studies" on the POM products, which when activated brings up a disclaimer that the studies are not "intended to make express or implied health or disease claims, . . . do not constitute . . . advertising for any POM Wonderful product. . . . Instead they are intended solely for general educational and informational purposes." The linked website is titled "wonderfulpomegranateresearch.com." (PX0158 (Butters Expert Report); PX0160 at 0036-37, attachment 3)).

(ii) Pompills.com

386. The pompills.com website is an e-commerce site that contains everything from learning about the product to ordering the product. (CX1347 (Glovsky, Dep. at 135)).

387. Based on the overall, common-sense, net impression of the pompills.com website, including the "health benefits" or "medical research" sections and the links to other information included therein, a significant minority of consumers, acting reasonably in

the circumstances, would interpret the pompills.com website to be claiming that taking one POMx Pill, or one teaspoon of POMx Liquid, daily, treats, prevents, or reduces the risk of heart disease, prostate cancer, and/or erectile dysfunction, and that these effects are shown in clinical testing, as explained more fully below. (CX0473 (Pompills.com website: April 2009 (Compl. Ex. E-8)), January 2010 (Compl. Ex. E-9); F. 388-410).

388. In April 2009, the menu bar on the home page of pompills.com contained links, *inter alia*, to "POMx Pills," "POMx Liquid," "health benefits" and "Buy Now." In January 2010, the menu bar was the same but the "health benefits" link is replaced by a link to "medical research." (CX0473 (Compl. Ex E-8 at 00:10); CX0473 (Compl. Ex E-9 at 00:04)).

389. A review of the April 2009 and January 2010 web captures show that the pompills.com website made substantially the same representations as those contained in POMx Pill print advertising, described in F. 323 and F. 332, including that POMx Pills provide the same antioxidant "power" as POM Juice, without the calories (CX0473 (Compl. Ex. E-8 at 00:15-00:25); CX0473 (Compl. Ex. E-9 at 00:16)); that POMx Pills have the best available, polyphenol antioxidants (CX0473 (Compl. Ex. E-8 at 00:25); CX0473 (Compl. Ex. E-9 at 00:16, 00:30)); and that antioxidants "fight" free radicals which are linked to, among other things, "cancer and heart disease." (CX0473 (Compl. Ex. E-8 at 04:37); CX0473 (Compl. Ex. E-9 at 01:01); *see also* CX0351; CX0355; CX1426 at 0040 (Compl. Ex. I) (POMx package insert)).

390. In April 2009, the POMx Liquid page on pompills.com stated that POMx Liquid is "the most concentrated source of pomegranate antioxidants available," and that "POMx Liquid is a highly concentrated, incredibly powerful blend of all-natural polyphenol antioxidants made from the very same pomegranates in POM Wonderful 100% Pomegranate Juice." The page also depicted the POMx Liquid bottle and teaspoon with the caption, "One teaspoon = the antioxidant power of 8oz. of POM Wonderful 100% Pomegranate Juice" and a link to "BUY NOW." The menu bar on the POMx Liquid webpage also included a link to "health benefits." (CX0473 (Compl. Ex. E-8 at 01:00 1:38)).

391. In April 2009, under the subheading "Science, Not Fiction," the POMx Pills page represented, *inter alia*, that POMx is "backed by $25 million in medical research," and is "[c]linically tested." (CX0473 (Compl. Ex. E-8 at 00:35); *see also* January 2010 pompills.com (CX0473 (Compl. Ex. E-9 at 00:16 ($32 million); CX1426 at 0040 (Compl. Ex. I) (POMx package insert ($20 Million in research)).

392. In April 2009 and January 2010, the POMx Liquid page on pompills.com contained the same language as set forth in F. 392 that appeared on the POMx Pills page. (*Compare* CX0473 (Compl. Ex. E-8 at 00:35) *with* CX0473 (Compl. Ex. E-8 at 01:15); *see also* January 2010 pompills.com (CX0473 (Compl. Ex. E-9 at 00:30)($32 million in research)).

393. In April 2009, and in January 2010, the "Health Benefits" section of pompills.com offered further links to web pages titled, "Research," "Antioxidant Benefits," "Heart Health," and "Prostate Health." (CX0473 (Compl. Ex. E-8 at 01:38); CX0473 (Compl. Ex. E-9 at 00:36)).

394. In April 2009, and in January 2010, the "Heart Health" section advised the reader that arterial plaque buildup is one of a number of factors "associated with heart disease" that POM Juice consumption may help "counteract." In the context of this webpage, the term, "heart health" implies "heart disease." (CX0473 (Compl. Ex. E-8 at 05:05); CX0473 (Compl. Ex. E-9 at 00:36).

395. In April 2009, the "Learn more" link on the "Heart Health" webpage took the consumer to a page titled "The Heart of The Matter." This page, in April 2009 and in January 2010, noted that atherosclerosis, defined for the reader as "too much plaque in the arteries[]is a leading cause of heart disease" and that "pomegranate antioxidants neutralize free radicals," which "can oxidize LDL (also known as 'bad' cholesterol – turning it into plaque that clogs up arteries." This page then summarizes results of the Aviram Carotid Intima-media Thickness/Blood Pressure ("CIIMT/BP") Study and the Ornish Myocardial Perfusion (MP) Study in a manner that is substantially similar to the summaries on pomwonderful.com. (CX0473 (Compl. Ex. E-8 at 05:09-05:10); CX0473 (Compl. Ex. E-9 at 01:22); *see* F. 373-374).

396. In April 2009, and in January 2010, the linked "Heart of The Matter" page on pompills.com displayed a large image of the caduceus symbol, juxtaposed to a subheading "Amaze your cardiologist. Take POMx." This language and imagery convey a medical message. (CX0473 (Compl. Ex. E-8 at 05:09-05:10); CX0473 (Compl. Ex. E-9 at 01:22)).

397. The language on the "Heart of The Matter" page of the pompills.com website that POMx is made from pomegranates "supported by $25 million of initial scientific research" reinforces the message that the efficacy of POMx for heart disease is demonstrated by the results of clinical research. (CX0473 (Compl. Ex. E-8 at 05:09-05:10); *see also* CX0473 (Compl. Ex. E-9 at 01:22 ("supported by $32 million")).

398. In April 2009, the "Antioxidant Benefits" page of the pompills.com website advised the reader that "antioxidants neutralize free radicals," which are "linked to [among other things] cancer and heart disease," and that POMx is made from pomegranates having "$25 million in medical research behind them." This language, which also appears in the January 2010 version of pompills.com ("$32 million"), draws a connection for the viewer between antioxidants and disease, and conveys the message of scientific support for the website's claims. (CX0473 (Compl. Ex. E-8 at 04:37, 04:50); CX0473 (Compl. Ex. E-9 at 01:01)).

399. In April 2009, the "Research" link on the "Health Benefits" section of pompills.com took the viewer to a list of linked studies, including "Cardiovascular" studies and "Cancer" studies. The text of the links include: "Pomegranate juice improves

myocardial perfusion in coronary heart patients," "Pomegranate juice pilot research suggests anti-atherosclerosis benefits," "Pomegranate juice helps promote normal systolic blood pressure." The "Research" page of the January 2010 version of pompills.com contains the same text. (CX0473 (Compl. Ex. E-8 at 01:38); CX0473 (Compl. Ex. E-8 at 01:43-04:23); CX0473 (Compl. Ex. E-9 at 00:55))

400. Some of the linked study titles referred to in F. 399 appear to be paraphrases of the studies' actual titles. (CX0473 (Compl. Ex. E-8 at 01:43-04:23); *see, e.g.*, CX0473 (Compl. Ex. E-8 at 02:10) (study listed as "Pomegranate juice improves myocardial perfusion in coronary heart patients," was published with the title, "*Effects of Pomegranate Juice Consumption on Myocardial Perfusion in Patients with Coronary Heart Disease*"); CX0473 (Compl. Ex. E-8 at 02:45) (study listed as "Pomegranate juice delays PSA doubling time in humans," was published with the title "*Phase II Study of Pomegranate Juice for Men with Rising Prostate-Specific Antigen following Surgery or Radiation for Prostate Cancer*")).

401. In April 2009, and in January 2010, the "Prostate Health" section of the "Health Benefits" page on pompills.com stated: "A preliminary UCLA medical study on POM Wonderful 100% Pomegranate Juice showed hopeful results for men with prostate cancer who drank an 8oz. glass of pomegranate juice daily. And every POMx capsule provides the antioxidant power of an 8oz. glass of POM Wonderful 100% Pomegranate Juice. Learn more." (CX0473 (Compl. Ex. E-8 at 05:50); CX0473 (Compl. Ex. E-9 at 00:36) (underlined hyperlink in original)). The "Learn more" link took the consumer to a page titled "Pomegranates and Prostate Health." (CX0473 (Compl. Ex. E-8 at 05:55)).

402. Like "The Heart of the Matter" page (F. 397), in April 2009, the "Pomegranates and Prostate Health" page displayed the caduceus symbol. (CX0473 (Compl. Ex. E-8 at 05:55)).

403. In April 2009, on the "Pomegranates and Prostate Health" page of the pompills.com website, the explanatory text under the subheading "Prostate Health" states or represents: "Prostate cancer is the most commonly diagnosed cancer among men in the United States, and the second leading cause of cancer death in men, after lung cancer." In the context of this webpage, the reference to "prostate health" clearly implies "prostate cancer." The text then describes a study in which "A majority of the 46 men participating in the study experienced a significantly extended PSA doubling time. . . . Before the study of pomegranate juice, the average PSA doubling time for the participants was 15 months. After drinking 8oz. of juice daily, the average PSA doubling time increased to 54 months. That's a 350% increase." (CX0473 (Compl. Ex. E-8 at 05:55)).

404. The April 2009 the "Pomegranates and Prostate Health" page of the pompills.com website further linked the study results showing prolongation of PSA doubling time to the progress of prostate cancer, explaining "PSA (prostate-specific antigen) is a marker that is thought to be associated with the progression of prostate cancer; a slower PSA

doubling time may reflect slower progression of the disease." Placing the mouse over the hyperlinked word "doubling time" produced a pop-up text box that reiterated: "The amount of time it takes for the prostate-specific antigen[s] (also called PSA levels) to double in men with prostate cancer may reflect the progression of the disease. A longer doubling time may indicate a slower growing cancer." (CX0473 (Compl. Ex. E-8 at 05:55-05:59, underlined hyperlink in original)).

405. The April 2009 the "Pomegranates and Prostate Health" page further represented that study results for POM Juice should apply to POMx by quoting Dr. Heber, identified as "Director of UCLA's Center for Human Nutrition," as stating: "The most abundant and most active ingredients in Pomegranate Juice are also found in POMx. Basic studies in our laboratory so far indicate that POMx and Pomegranate Juice have the same effect on prostate health." The foregoing text was printed in bold font and was italicized. (CX0473 (Compl. Ex. E-8 at 05:59)).

406. In April 2009, the pompills.com website also featured a "FAQs" page. (CX0473 (Compl. Ex. E-8 at 07:51)).

407. In April 2009, the response to the FAQ "Heart Disease: How does drinking pomegranate juice help the fight against cardiovascular disease?" stated: (1) "Improved Cardiac Blood flow," juxtaposed to the representation that a "published human study . . . [on] 45 patients with impaired blood flow to the heart" showed that "[p]atients" who drank eight ounces of POM Juice "daily" experienced "improved blood flow" while the blood flow of the placebo group declined; and (2) "Decrease in Arterial Plaque" juxtaposed to the representation that "[a]nother published human study . . . [on] 19 patients with atherosclerosis (clogged arteries) showed that, for those who drank eight ounces of POM Juice "daily," "artery plaque decreased 30%" while the placebo group experienced a worsening of arterial plaque buildup. This page further represented that results for POM Juice are applicable to POMx by quoting Dr. Aviram, identified as "one of the world's preeminent cardiovascular researchers," as commenting: "The results of our pre-clinical studies showed that POMx is as potent an antioxidant as pomegranate juice, and just like pomegranate juice may promote cardiovascular health." The foregoing quotation was italicized. (CX0473 (Compl. Ex. E-8 at 09:05)).

408. In April 2009, the response to the FAQ "Erectile Dysfunction" stated: "Can pomegranate juice benefit men with erectile dysfunction?" stated: "Initial results linking POM Wonderful 100% Pomegranate Juice and erectile performance are promising. In a soon-to-be-published clinical study on men with erectile dysfunction, the group who consumed 8oz. of POM Juice daily experienced better erectile performance than the group who drank a placebo." (CX0473 (Compl. Ex. E-8 at 9:05)).

409. In April 2009, the response to the FAQ "Prostate Cancer" stated: "There has been promising news on the benefits of pomegranate juice in the fight against prostate cancer. Is this really true?" summarized study results showing the effect of POM Juice on extending PSA doubling times (the Pantuck Phase II Prostate Cancer Study (2006)). (CX0473 (Compl. Ex. E-8 at 09:05)). The answer went on to state that "[a] new study

is underway to more fully investigate the potential of POMx to extend PSA doubling time" and quoted Dr. Heber, identified as "Director of UCLA's Center for Human Nutrition," as commenting, "The most abundant and most active ingredients in pomegranate juice are also found in POMx. Basic studies in our laboratory so far indicate that POMx and pomegranate juice may have the same effects." The foregoing quotation was italicized. (CX0473 (Compl. Ex. E-8 at 09:05)).

410. In April 2009, the response to the FAQ, "Dosage: How much POMx should I take?" stated: "Whether you choose pills or liquid, it is important to remember that to reap POMx's full health benefits: you must take it every day." (CX0473 (Compl. Ex. E-8 at 11:03)).

(iii) Pomegranatetruth.com

411. Based on the overall, common-sense, net impression of the pomegranatetruth.com website, including the "backed by science" and "heart health-emerging science" sections and links therefrom, a significant minority of consumers, acting reasonably in the circumstances, would interpret the pomegranatetruth.com website as claiming that drinking eight ounces of POM Juice daily treats, prevents, or reduces the risk of heart disease, and that these effects are clinically proven, as explained more fully below. (CX0473 pomegranatetruth.com (Compl. Ex. E-1); F. 412-414)).

412. In April 2009, the home page of pomegranatetruth.com stated or represented that POM is 100% authentic pomegranate juice, obtained through a unique process, and is the only pomegranate juice "backed by $25 million in medical research" including "clinical studies" documenting its benefits, including heart benefits, prostate health, and "better erectile function." Each subsection contained a "read more" link. This page displayed the caduceus symbol next to the "backed by science" reference. (CX0473 (Compl. Ex. E-1 at 00:10)).

413. The linked "Backed By Science" page on the pomegranatetruth.com website proceeded to introduce the "medical results" on POM Juice, dividing into subsections on "Heart Health," "Prostate Health" and "Erectile Dysfunction." The "Heart Health" section provided a "read more" link. (CX0473 (Compl. Ex. E-1 at 01:15)).

414. The linked "heart health" page on the pomegranatetruth.com website contained the headline "Heart Health – Emerging Science." The text advises the reader that "heart disease" is a leading killer of men and women in the United States, that "atherosclerosis," which is defined for the reader as too much "plaque," is a leading factor in "heart attacks" and the role of antioxidants in reducing LDL (defined as "bad" cholesterol) oxidation. The text then invites the reader who wants to learn more about consumption of POM and cardiovascular health to review research studies on the effects of pomegranate on myocardial perfusion, reduction of carotid intima-media thickness, blood pressure, and LDL oxidation; and reducing systolic blood pressure. This page draws a clear connection for the reader between "heart health" and "heart disease," and

between the effects shown by the studies and the prevention, treatment or reduction of the risk of heart disease. (CX0473 (Compl. Ex. E-1 at 01:45)).

415. CX0473 Compl. Ex. E-1 does not show the content of the "prostate" page or the "erectile health" page, referred to in F. 413.

iv. Press releases

(a) January 2003 Press Release (CX0013)

416. POM issued a press release in January 2003 titled "Consumer Demand for POM Wonderful's Refrigerated All-Natural Pomegranate Juice Grows as the Health Benefits of Pomegranate Juice Become Recognized." (CX0013 at 0002-05). A copy of this press release is reprinted in the Appendix to this Initial Decision. (Appendix at 94-97).

417. Based on the overall, common-sense, net impression of CX0013, a significant minority of reasonable consumers would interpret this press release as claiming that drinking eight ounces of POM Juice daily treats, prevents, or reduces the risk of heart disease, by reducing arterial plaque, and that the effects have been clinically proven. (CX0013 at 0002-05; F. 418-420).

418. This press release had the subtitle, "Scientific support indicates that drinking pomegranate juice provides the body with an active source of antioxidants and shows promise against cardiovascular disease." (CX0013 at 0002).

419. This press release further states or represents that "cardiovascular diseases rank as America's No. 1 killer," and that 61.8 million Americans have some form of "cardiovascular disease such as diseases of the heart, high blood pressure, and hardening of the arteries." This release further states that "[m]edical research shows that daily consumption" of eight ounces of POM Juice "confers heart health benefits by lessening factors that contribute to atherosclerosis," which is defined for the reader as "plaque in the arteries." (CX0013 at 0002).

420. A paragraph titled "Effects on Heart Health" asserts that "[n]ew research is showing that antioxidants can play a highly beneficial role in reducing one of the major risk factors in heart disease: atherosclerosis (plaque in the arteries)," and explains the connection between "progression of atherosclerosis," "oxidation of LDL cholesterol" and "adhesion of LDL molecules" to the blood vessel. The paragraph further explains that (1) "one human study" showed that drinking eight ounces of POM Juice for two weeks "lowered" LDC oxidation, "clumping and adhesion" and (2) an "additional human study showed that consuming pomegranate juice reduces . . . ACE (angiotensin converting enzyme)" which "lessens the progression of atherosclerosis." "Pomegranate juice inhibited ACE by 36% after two weeks of juice consumption" and a "5% decrease in systolic blood pressure . . . a known risk factor for atherosclerosis." (CX0013 at 0003).

(b) September 2005 Press Release (CX0044)

421. POM issued a press release in September 2005 titled, "Pomegranate Juice May Affect the Progression of Coronary Heart Disease," which highlighted the results of the Ornish MP Study (2005). (CX0044 at 0001). A copy of this press release is reprinted in the Appendix to this Initial Decision. (Appendix at 98-99).

422. Based on the overall, common-sense, net impression of CX0044, a significant minority of reasonable consumers would interpret this press release as claiming that drinking eight ounces of POM Juice daily treats, prevents, or reduces the risk of heart disease, by improving blood flow to the heart, and that clinical studies prove these effects. (CX0044 at 0001; F. 423-427).

423. This press release stated that "Men and women with coronary heart disease who drink one glass of pomegranate juice daily may improve blood flow to their heart, according to a new study." (CX0044 at 0001).

424. This press release described "the first randomized, double-blind, placebo-controlled trial showing that pomegranate juice may affect the progression of coronary heart disease, which is the #1 cause of death in the U.S. and in most of the world" and that "results . . . [would] be published in . . . the American Journal of Cardiology, one of the leading peer-reviewed cardiology journals." (CX0044 at 0001).

425. This press release described the study as involving 45 "patients" with "coronary heart disease" having "reduced blood flow to the heart" and reported that the results showed "blood flow to the heart improved" in those drinking a daily glass of pomegranate juice, but showed worsening in the comparison group. (CX0044 at 0001).

426. The press release explained that "[p]omegranate juice from POM Wonderful was used in this study." (CX0044 at 0002).

427. Dr. Ornish, identified as senior author of the referenced study (F. 424), founder of the Preventive Medicine Research Institute, and clinical professor of medicine at UCSF, is quoted as stating that although the study sample was "relatively small," "the strength of the design and the significant improvements in blood flow to the heart observed after only three months suggest that pomegranate juice may have important clinical benefits in those with coronary heart disease" and that "[a]lso, it may help to prevent it." In the context of Dr. Ornish's entire statement, and in the context of the press release as a whole, the reference to a small sample, and use of words "suggest" and "may have" do not materially modify the overall net impression from the press release described in F. 422. (CX0044 at 0002).

(c) July 2006 Press Release (CX0065)

428. POM issued a press release in July 2006 titled, "POMx, a Highly Concentrated Form of Healthy Pomegranate Antioxidants, Becomes Available to Consumers for the First

Time." (CX0065 at 0001-02). A copy of this press release is reprinted in the Appendix to this Initial Decision. (Appendix at 100-101).

429. Based on the overall, common-sense, net impression of CX0065, a significant minority of reasonable consumers would interpret this press release as claiming that that drinking eight ounces of POM Juice or taking one POMx Pill daily, treats prostate cancer by prolonging PSADT and that these effects have been demonstrated by clinical studies. (CX0065 at 0001-02; F. 430-431).

430. This press release discussed research published by the American Association for Cancer Research "indicat[ing] that a daily pomegranate regimen has a positive effect for men with prostate cancer" and that "[s]pecifically, drinking 8 ounces of POM Wonderful pomegranate juice daily prolonged post-prostate surgery PSA doubling time from 15 to 54 months (*Clinical Cancer Research*, July 1, 2006). PSA is a protein marker for prostate cancer and the faster PSA levels increase in the blood of men after treatment, the greater their potential for dying of prostate cancer." (CX0065 at 0002).

431. This press release represented that study results using POM Juice are applicable to POMx, by quoting Dr. Heber, identified as "Professor of Medicine and Director, UCLA Center for Human Nutrition," as stating, "[b]asic studies indicate that the effects of POMx and POM Wonderful pomegranate juice on prostate cancer are the same. The most abundant and most active ingredients in pomegranate juice are also found in POMx." (CX0065 at 0002).

(d) June 2007 Press Release (CX0128)

432. POM issued a press release in June 2007 titled, "POM Wonderful 100% Pomegranate Juice May Improve Mild to Moderate Cases of Erectile Dysfunction, Study Finds." (CX0128 at 0002-04). A copy of this press release is reprinted in the Appendix to this Initial Decision. (Appendix at 102-104).

433. Based on the overall, common-sense, net impression of CX0128, a significant minority of reasonable consumers would interpret this press release as claiming that drinking eight ounces of POM Juice treats erectile dysfunction, and that this effect has been demonstrated by clinical studies. (CX0128 at 0002-04; F. 434-439).

434. This press release stated, "[r]esearch shows 8 ounces a day of POM Wonderful 100% Pomegranate Juice may help the management of erectile dysfunction" and "[a]ccording to a pilot study released in the *International Journal of Impotence Research* (http://www.nature.com/ijir), POM Wonderful 100% Pomegranate Juice was found to have beneficial effects on erectile dysfunction (ED), a disorder that affects 1 in 10 men worldwide and 10 to 30 million men in the United States alone." (CX0128 at 0002).

435. This press release describes the study as a "randomized, placebo-controlled, double-blind, crossover pilot study" on the "efficacy of pomegranate juice," and notes that "to qualify" for the study, among other things, the "participants had to experience mild to

moderate ED for at least 3 months." The press release defined "mild" and "moderate" ED in relation to the extent of the "decreased ability to get and keep an erection." (CX0128 at 0002).

436. This press release reported the results as showing that "[f]orty-seven percent of the subjects reported that their erections improved with POM Wonderful Pomegranate Juice." (CX0128 at 0003).

437. The press release attributed the study results of improved erections to "enhance[d] blood flow," which is an effect of "potent pomegranate antioxidants," noting that in "previously published medical studies, pomegranate juice has been shown to enhance blood flow." (CX0128 at 0003).

438. The press release disclosed that the "study did not achieve overall statistical significance"; however, in the context of the press release as a whole, this disclosure does not materially modify the overall net impression described in F. 433. (CX0128 at 0002-04).

439. Use of the phrase, "may help," in the overall context of this press release, is insufficient to modify the net impression of the press release as a whole, described in F. 433. (CX0128 at 0002-04).

b. Alleged efficacy claims

(a) CX0031 ("Floss your arteries. Daily")

440. The advertisement identified as CX0031 (Floss your arteries. Daily) was disseminated on or about December 1, 2004. (CX0031at 0001-02).

441. CX0031 is reprinted in the Appendix to this Initial Decision. (Appendix at 105).

442. POM first ran this advertisement in 2004 and stopped running it that same year. The "Floss your arteries" headline, image and body copy have not run as part of any advertisement since 2004. (Tupper, Tr. 2995-96).

443. Based on the overall, common-sense, net impression of the advertisement, a significant minority of consumers, acting reasonably under the circumstances, would interpret CX0031 to contain the message that drinking eight ounces of POM Juice daily treats, prevents or reduces the risk of heart disease, by reducing arterial plaque. (CX0031 at 0001; F. 444-445).

444. This advertisement draws a connection between the consumption of POM Juice and the prevention, treatment or reduction of the risk of heart disease, through statements and/or representations that (1) POM Juice has more antioxidants than other drinks; (2) antioxidants fight free radicals; (3) free radicals cause "artery clogging plaque"; (4) consumption of POM Juice "can reduce plaque by up to 30%!"; and (5) "Clogged

arteries lead to heart trouble. It's that simple. That's where we come in." (CX0031 at 0001).

445. The headline, "Floss your arteries. Daily," is clearly an exaggeration which would not be taken literally; however, in the context of this advertisement, the headline contributes to the overall net impression described in F. 433. (CX0031 at 0001).

446. An implied claim that consuming POM Juice is "clinically proven" to prevent, treat, or reduce the risk of heart disease is not reasonably clear or conspicuous on the face of the advertisement. A review of the advertisement alone, considering all its elements, does not lead to a confident conclusion that a significant minority of reasonable consumers would interpret CX0031 as claiming that POM Juice is "clinically proven" to prevent, treat or reduce the risk of "heart disease." (CX0031 at 0001).

447. Among other things, in the context of this advertisement, the language that POM Juice "can" reduce plaque by "up to 30%" is qualified and non-definitive, and the citation to a study appears in a small print footnote, which states: "Aviram, M. Clinical Nutrition, 2004. Based on a clinical pilot study." (CX0031 at 0001).

448. Having fully examined CX0031 in its totality, and having further considered any extrinsic evidence in the record pertaining thereto (*see* Section II. E. 2, *infra*), the preponderance of the evidence fails to demonstrate that CX0031 conveys a claim that drinking eight ounces of POM Juice daily is "clinically proven" to prevent, treat, or reduce the risk of heart disease. (CX0031 at 0001; F. 446-447).

(b) CX0033 ("Life Support")

449. CX0033("Life Support") is an advertisement for POM Juice that was disseminated on or about December 30, 2004 in *Rolling Stone* magazine, and on or about February 1, 2005 in *Details* magazine. (CX0033 at 0001-02).

450. CX0033 is reprinted in the Appendix to this Initial Decision. (Appendix at 106).

451. The advertisement's headline is "Life Support," next to a large image of a POM Juice bottle hanging upside down on a pole, with the juice running through a tube at the bottom of the bottle, in a manner reminiscent of an intravenous line. (CX0033 at 0001).

452. The body copy of this advertisement juxtaposes the statements and representations that (a) POM Juice possesses "more . . . antioxidants" than other drinks; (b) antioxidants "fight hard" against free radicals that "can cause heart disease"; and (c) if you drink POM Juice daily, "you'll be on life support – in a good way." (CX0033 at 0001).

453. Through the language and images described in F. 451 and F. 452, CX0033 draws a connection for the reader between consuming POM Juice and efficacy for heart disease. (CX0033 at 0001).

454. In the context of this advertisement, the reference to POM Juice as "refreshing" and "delicious" does not materially alter the overall message conveyed. (CX0033 at 0001; F. 453, 455).

455. Based on the overall, common-sense, net impression of CX033, a significant minority of reasonable consumers, would interpret CX0033 to be claiming that drinking eight ounces of POM Juice daily prevents or reduces the risk of heart disease. (CX0033 at 0001; F. 451-454).

(c) CX0034 ("Amaze your cardiologist")

456. The POM Juice advertisement identified as CX0034 ("Amaze your cardiologist") was disseminated in *Prevention* magazine in February 2005. (CX0034 at 0001-02).

457. CX0034 is reprinted in the Appendix to this Initial Decision. (Appendix at 107).

458. This advertisement stopped running in 2005. (Tupper, Tr. 2996-97).

459. The headline of the advertisement is "Amaze your cardiologist." The headline is juxtaposed to an image of a POM Juice bottle with electrocardiogram (EKG) leads attached to it, in the manner of a patient having a heart exam. (CX0034 at 0001).

460. The body copy of CX0034 includes the statements or representations: (a) "Ace your EKG: just drink 8 ounces of delicious POM Wonderful Pomegranate Juice a day"; (b) POM Juice has more "antioxidants" than other drinks; (c) antioxidants fight free radicals that "can cause . . . artery clogging plaque"; (d) a glass of POM Juice a day "can reduce plaque by up to 30%!"; and (e) "your cardiologist will be amazed." (CX0034 at 0001).

461. The advertisement draws a clear connection between consumption of POM Juice and reduction of arterial plaque. (CX0034 at 0001).

462. The advertisement draws a further connection between reduction of arterial plaque and effectiveness for heart disease through the juxtaposition of (1) the dressed bottle image undergoing an EKG (F. 459) and (2) the references to pleasing "your cardiologist" with positive EKG results. (CX0034 at 0001).

463. Based on the overall, common-sense, net impression of this advertisement, a significant minority of consumers, acting reasonably under the circumstances, would interpret CX0034 to contain the message that drinking eight ounces of POM Juice daily treats, prevents, or reduces the risk of heart disease, by reducing arterial plaque. (CX0034 at 0001; F. 459-462).

464. The depiction of the POM Juice bottle with an EKG, even if itself humorous or not to be taken literally, does not materially alter the message conveyed by the advertisement. (CX0034 at 0001; F. 463).

465. An implied claim that consuming POM Juice is "clinically proven" to prevent, treat, or reduce the risk of heart disease is not reasonably clear or conspicuous on the face of the advertisement. A review of the advertisement alone, considering all its elements, does not lead to a confident conclusion that a significant minority of reasonable consumers, would interpret CX0034 as claiming that POM Juice is "clinically proven" to prevent, treat or reduce the risk of "heart disease." (CX0034 at 0001).

466. Among other things, in the context of this advertisement, the language that POM Juice "can" reduce plaque by "up to 30%" is qualified and non-definitive, and the citation to a study is appears in a small print footnote, which states: "Aviram, M. Clinical Nutrition, 2004. Based on a clinical pilot study." (CX0034 at 0001).

467. In the context of this advertisement, the fact that the advertisement cites studies in connection with the arterial plaque representation is not enough to conclude, based on the face of the advertisement alone, that the advertisement claims POM Juice is clinically proven to prevent, treat, or reduce the risk of heart disease, including by reducing arterial plaque. (CX0034 at 0001).

468. Having fully examined CX0034 in its totality, and having further considered any extrinsic evidence in the record pertaining thereto (*see* Section II.E.2, *infra*), the preponderance of the evidence fails to demonstrate that CX0034 conveys a claim that POM Juice is "clinically proven" to prevent, treat, or reduce the risk of heart disease, including by reducing arterial plaque. (CX0034 at 0001; F. 465-467).

(d) CX0036 ("Cheat Death")

469. In 2005 and 2006, POM disseminated a POM Juice advertisement with the headline, "Cheat Death." The advertisement ran in *Rolling Stone* magazine in March, June, and July 2005; in *Prevention* magazine in May 2005; and in *Fitness* magazine in January 2006. (CX0036 at 0001-02).

470. CX0036 is reprinted in the Appendix to this Initial Decision. (Appendix at 108).

471. The headline, "Cheat Death," is juxtaposed to a large image of the POM Juice bottle with a noose around the bottle's neck. (CX0036 at 0001).

472. The text of CX0036, which is brief, includes the statement that POM Juice "can help prevent" "heart disease." (CX0036 at 0001).

473. This "Cheat death" advertisement, with the above-quoted body copy that POM "can help prevent" certain diseases stopped running in or around 2005. (Tupper, Tr. 2987-90).

474. Based upon the overall, common-sense, net impression of CX0036, particularly the statement that consumption of POM Juice "can help prevent . . . heart disease," CX0036

would convey to a significant minority of reasonable consumers, a claim that that drinking eight ounces of POM Juice daily reduces the risk of heart disease. (CX0036 at 0001; F. 471-473).

475. In the context of this advertisement, use of the qualifying phrase "can help" does not alter the overall, common sense, net impression of CX0036 set forth in F. 474.

476. The headline and noose imagery, even if constituting humor or hyperbole, does not, in the context of the entirety of the advertisement, materially detract from the overall net impression of the advertisement, as described in F. 474.

2. Extrinsic evidence regarding advertisement interpretation

a. Summary of expert opinions

i. Respondents' expert Dr. Butters

477. Dr. Butters offered his opinion as a linguistics expert on the meanings of Respondents' advertisements. (Butters, Tr. 2816-17).

478. Linguistics is the study of human language in all its forms and manifestations. (Butters, Tr. 2813). Linguistics encompasses a number of often intersecting scientific subfields, including semantics, the study of word and sentence meanings; pragmatics, the study of how such meaning is affected by nonlinguistic contexts; and semiotics, the study of extra-linguistic and paralinguistic meaning systems that individuals assign to nonlinguistic signs, such as pictures, colors, visual patterns, and icons. (PX0158 (Butters Expert Report at 0006-07)).

479. To draw his conclusions in this case, Dr. Butters applied all the subdivisions of linguistics, including semantics, pragmatics, and semiotics, and considered the nature of the product advertised, as part of the overall context for the advertisement. (Butters, Tr. 2814-15, 2817-18).

480. Dr. Butters reviewed an extensive number of POM advertisements, including the advertisements included as exhibits to the Complaint and representative samples of other advertisements admitted into evidence. (PX0158 (Butters Expert Report at 0008); Butters, Tr. 2817, 2847).

481. Dr. Butters offered opinions on Respondents' advertising in general, and also offered opinions on the meanings of many of the Challenged Advertisements in this case. (PX0158 (Butters Expert Report)).

482. In summary, Dr. Butters opined that the Challenged Advertisements do not expressly convey or convey by implication that the Challenged Products prevent, reduce the risk of, or treat heart disease, prostate cancer or erectile dysfunction, or that such alleged

medical effects or benefits are scientifically established facts. (PX0158 (Butters Expert Report at 0003, 0042)).

483. In Dr. Butters' opinion, none of Respondents' advertisements that he reviewed stated or implied that POM products treated any disease. (Butters, Tr. 2822, 2825).

484. In linguistic terms, an advertisement "implies" a message if it is the meaning that a reasonable consumer "takes away," or infers, from the words and context of the advertisement. (Butters, Tr. 2826-2829).

485. Dr. Butters further opined, among other things, that the POM advertisements and POM communications he reviewed, make no definitive health claims, beyond the general accepted notion that consuming fruit products as part of an overall healthy diet is a healthy thing to do, including in order to reduce the risk of various diseases. (PX0158 (Butters Expert Report at 0042)).

486. Dr. Butters expressed his opinion that, at most, Respondents' advertising conveys that pomegranate juice is a healthy beverage; that POM products are high in antioxidants; that antioxidants are believed to fight free radicals and promote health; and that preliminary research performed on POM products indicates potential beneficial properties. (PX0158 (Butters Expert Report at 0003-04, 0043)).

487. In Dr. Butters' opinion, the POM advertisements he reviewed depend upon parody, exaggeration, and humor to bring their message to the potential purchaser. (PX0158 (Butters Expert Report at 0033)).

488. In Dr. Butters' opinion, the use of humor and parody in the advertisements work to "block" any inference that the advertisements are "intended to make definitive health claims" with respect to disease. (PX0158 (Butters Expert Report at 0004)).

489. Dr. Butters opined that hyperbole and humor block literal interpretation of such headings as "I'm off to save prostates" because these are absurd terms which would not be viewed as making disease claims. (Butters, Tr. 2958; PX0158 (Butters Expert Report at 0004)).

490. In drawing his conclusions, Dr. Butters relied, in part, on the use of such words as "promising," "pilot studies," or "preliminary results" and that the advertisements generally encourage those reading and hearing the advertisements to investigate the research and draw their own conclusions. (PX0158 (Butters Expert Report at 0003-04, 0043)).

491. In Dr. Butters' opinion, what people might infer with respect to a food product might be different than what they might infer with respect to a drug. (Butters, Tr. 2818).

492. In Dr. Butters' opinion, an advertisement promoting the consumption of food is far less likely to be interpreted by a reasonable consumer as conveying a treatment claim, than an advertisement promoting a drug. (Butters, Tr. 2825; *see also* Butters, Tr. 2818).

493. Dr. Butters analyzed the Challenged Advertisements from the perspective of the ordinary adult user of the English language in America. (Butters, Tr. 2816-17, 2831-32).

494. Dr. Butters did not take into account education or income level of the viewer of an advertisement, or whether the advertisement viewer was concerned about health issues. (Butters, Tr. 2832-34).

495. Dr. Butters stated that his conclusions about the Challenged Advertisements would be no different if analyzed from the perspective of more educated, affluent people, who are concerned about their health. (Butters, Tr. 2829-30).

496. In Dr. Butters' opinion, the phrase, "I'm off to save prostates" could be interpreted by outliers (*i.e.*, viewers that are not ordinary or reasonable) to mean protect or rescue from disease but that interpretation is unlikely. (Butters, Tr. 2898; PX0350 (Butters, Dep. at 125)).

497. Dr. Butters stated that use of the term "may" would not cause a reasonable person to believe that the product will produce that result. (Butters, Tr. 2822-23).

498. In Dr. Butters' opinion the representation that POM Juice will "fight for" "cardiovascular, prostate, erectile health" does not imply that the product will "treat cardiovascular, prostate, and erectile disease, or even give you cardiovascular, prostate, and erectile health." Dr. Butters further opined that a closer possible inference is that pomegranate juice "improves your odds of maintaining" health in those areas, in a general way like any other food that is good for you, and to this extent, the language implies some kind of health benefit. (Butters, Tr. 2885-86, 2888; *see also* Butters, Tr. 2893 (phrase "fight for" "doesn't necessarily mean that you are going to win it").

499. Dr. Butters acknowledged that a reasonable viewer could take away from CX0016 ("Drink and be healthy") that pomegranate juice, in general, and POM Wonderful, in particular, can help to reduce the risk of heart disease. (Butters, Tr. 2929-30).

500. According to Dr. Butters, a reasonable viewer could not take away from the entire advertisement comprising CX0016 "Drink and be healthy" that pomegranate juice, in general, and POM Wonderful in particular, will treat atherosclerosis. (Butters, Tr. 2930).

501. In Dr. Butters' opinion, CX0274/1426 Ex. C ("I'm off to save PROSTATES"), could communicate to viewers, among other things, that POM Juice is protecting or defending prostates from disease. (Butters, Tr. 2899-2901).

502. Regarding CX0274/1426 Ex. C ("I'm off to save PROSTATES"), Dr. Butters opined that "the parodic method of presentation [use of parody] is so frivolous that no definite or clear claims will be understood, beyond the general notion that pomegranate juice is a good source of [anti]oxidants, and a healthy drink to include in one's diet." Dr. Butters has the same opinion with respect to CX0034 ("Amaze Your Cardiologist"); CX0031 ("Floss Your Arteries") and CX0351/CX0355 ("The Only Antioxidant supplement Rated X"). (PX0158 (Butters Expert Report at 0019-22)).

503. Regarding CX0034 Dr. Butters opined that the headline, "Amaze Your Cardiologist" is hyperbolic and cannot be taken literally. According to Dr. Butters, this language serves to "make explicit the theme of the importance of heart health using advertising-cliché language." (CX0034; PX0158 (Butters Expert Report at 0019-20)).

504. Dr. Butters opined that CX0351 and CX0355 (both having the title, "The Only Antioxidant Supplement Rated X"), convey the message that preliminary initial studies suggest that pomegranate extract, a strong source of antioxidants, could help alleviate erectile dysfunction. (Butters, Tr. 2943).

505. Regarding CX0351 and CX0355 ("The Only Antioxidant Supplement Rated X"), Dr. Butters opined that the advertisement only suggests that emerging science suggests that antioxidants are "critically important," and that "preliminary . . . initial studies" suggest that pomegranate extract, a strong source of antioxidants, could help alleviate erectile dysfunction. (Butters, Tr. 2943).

506. Regarding CX0260 ("Drink to Prostate Health"), Dr. Butters acknowledged that one inference that would be drawn is that POM Juice might be beneficial for people who have had prostate cancer, because this is what has been found in the preliminary medical study referenced in the advertisement.. (Butters, Tr. 2943-44; PX0158 (Butters Expert Report at 0024); PX0350 (Butters, Dep. at 121-22)).

507. Regarding CX0260 ("Drink to Prostate Health"), Dr. Butters expressed the opinion that ordinary consumers would not find that the advertisement communicates that POM Juice could treat, prevent, or reduce the risk of disease. Dr. Butters further testified that there may be some outliers who may interpret the advertisement to make such claims, but those outliers would, by definition, not be ordinary or normal. (PX0350 (Butters, Dep. at 121-25)).

508. Regarding CX0036 ("Cheat Death"), Dr. Butters opined that based on use of the words and phrases "can" and "help" with respect to heart disease, which words have intrinsic meaning in the English language, reasonable consumers would not interpret this advertisement to communicate that drinking eight ounces of POM Juice prevents or reduces the risk of heart disease. (PX0350 (Butters, Dep. at 102-05)).

509. Regarding CX0103 ("Decompress"), Dr. Butters testified that it would be a gross exaggeration for anybody to think that the image of a blood pressure cuff around the POM Juice bottle and the headline "Decompress" could literally mean drink a glass of

pomegranate juice and your blood pressure will go down. (Butters, Tr. 2933).

510. According to Dr. Butters, the headline "Decompress," juxtaposed to the "blood pressure cuff" dressed bottle image, and a sub-headline "the antioxidant power of pomegranate juice, would not likely communicate that drinking POM Juice lowers blood pressure, and it would be far-fetched to interpret this text and imagery as making a medical claim. (PX0350 (Butters, Dep. at 148-50)).

511. Regarding CX0348 andCX0350 ("24 Scientific Studies"), Dr. Butters testified that a viewer of the "24 Scientific Studies" advertisement would find it reasonable to believe that the headline is accurate and that there must be 24 scientific studies on POMx. (Butters, Tr. 2940).

ii. Complaint Counsel's rebuttal expert Dr. Stewart

512. Complaint Counsel offered Professor David Stewart as a rebuttal witness to Dr. Butters. Dr. Stewart's area of expertise is advertising, marketing, consumer behavior, and survey methodology. Dr. Stewart is not an expert in linguistics, the subject of Dr. Butters' testimony. (Stewart, Tr. 3168-69).

513. Dr. Stewart was not asked by Complaint Counsel to conduct a facial analysis of the Challenged Advertisements to opine on what the advertisements meant. Dr. Stewart was asked to read and critique Dr. Butters' report, and to reach a conclusion as to whether or not he agreed with Dr. Butters' conclusions, and why. (Stewart, Tr. 3169, 3226).

514. Dr. Stewart opined that "[I]t is not possible to determine that an advertisement does or does not communicate certain implied messages simply from linguistic analysis." (CX1295 (Stewart Expert Report at 0006)).

515. According to Dr. Stewart, linguistic analysis fails to take into account the individual characteristics of the viewer and how that consumer processes information; it looks only at the advertisement stimulus. (Stewart, Tr. 3171-73).

516. According to Dr. Stewart, Dr. Butters' analysis ignores research related to how consumers use information, process advertising messages, and make decisions in the market place. (CX1295 (Stewart Expert Report at 0006); Stewart, Tr. 3170-71).

517. According to Dr. Stewart, well-educated, affluent, health-conscious consumers are more likely to be more attentive to health claims and more likely to draw pragmatic inferences about the benefits of POM products. (CX1295 (Stewart Expert Report at 0012-13)). However, Dr. Stewart defined a "pragmatic" inference as a meaning that is neither express, nor implied by the advertisement, and may or may not even follow, logically. (Stewart, Tr. 3227-28).

518. Dr. Stewart disagreed with Dr. Butters that a typical consumer would necessarily

discern a difference between "can" and "will." According to Dr. Stewart, when viewing an advertisement the typical consumer is looking at the totality of the advertisement including: the illustration, the headline, the text, and carrying away a net impression based on all of that information. The potential meaning of "can" versus "will" is defined by its context, according to Dr. Stewart. (Stewart, Tr. 3190-91).

519. Dr. Stewart disagreed with Dr. Butters over the effect of such words as "initial" or "pilot." In Dr. Stewart's opinion, the typical consumer would likely have little understanding of what "initial" or "pilot" means, particularly in the context of being referred to as having been published in a major journal. In such circumstances, according to Dr. Stewart, juxtaposing terms such as "initial" or "pilot" with mentions of a well-respected medical school (UCLA), "leading universities," reference to professional journals in which support of the claims is found, reference to a Nobel laureate, and reference to the sum of money spent on research that is represented as supporting the advertising claims (*e.g.*, $25 million), have the effect of establishing the credibility of claims for the POM products. (CX1295 (Stewart Expert Report at 0016-17); Stewart, Tr. 3191).

520. Dr. Stewart opined that the Bovitz Study (*see* subsection c, *infra*), which studied headlines from billboard advertisements, contradicts the notion that humorous headlines, such as "Amaze your cardiologist" and "Floss your arteries," do not communicate any claims, as Dr. Butters concluded. (Stewart, Tr. 3202, 3204-06, 3230-31; *see* F. 497-489, 502-503).

b. Findings of fact regarding advertising interpretation, based upon testimony of Dr. Butters and Dr. Stewart

521. More educated, affluent people, who are concerned about their health, are likely to be more discerning and careful readers of an advertisement. (Butters, Tr. 2829-30).

522. Better educated people are more likely to better understand an advertisement. (Stewart, Tr. 3240).

523. According to the New Oxford Dictionary ("NOAD") the meaning of "defend" (*see* CX0274/1426 Ex. C), includes to "resist an attack made on (someone or something) and protect from harm or danger." (Butters, Tr. 2899-2901).

524. In linguistic terms, "I'm off to save prostates" would not imply that a product will protect or rescue from disease. (Butters, Tr. 2898; PX0350 (Butters, Dep. at 125)).

525. In linguistics terms, the word "may" is a shortened way of saying "may or may not." (Butters, Tr. 2822-23).

526. According to an ordinary desktop dictionary, "can" does not mean "will." (Butters, Tr. 2915).

527. Whether a consumer will discern a difference between "can" and "will" depends on the context and the totality of the advertisement. (Stewart, Tr. 3190-91).

528. Some academic literature indicates that the use of qualifiers, such as "can," "could," "might," or "up to" "encourage the audience of the advertisements to infer that a stronger claim is intended than the one that is actually entailed." Dr. Butters disagrees with this assertion. (Butters, Tr. 2916-19; *see also* CX1295 (Stewart Expert Report at 0016-17) (discussing study finding use of the word "may" rather than the stronger term "will" created greater credence for the claim)).

529. In linguistic terms, to "prevent" a disease means to keep the disease from happening. (Butters, Tr. 2818).

530. In linguistic terms, the word "treat" means medical treatment. (Butters, Tr. 2825).

531. In linguistic terms, the phrase, "backed by research" totaling a certain dollar amount, such as used in CX0475/1426 Ex. A, could be interpreted to mean there has been completed research with some results, or that there has been a certain dollar amount of research done so far and that research is ongoing. (Butters, Tr. 2876-78).

532. In the field of linguistics, hyperbole is a term used to refer to extreme exaggeration, and is not meant literally. (Butters, Tr. 2824).

533. Readers discount puffery and hyperbole because an advertisement using either, on its face, is an exaggeration; however, the fact that puffery and hyperbole are not to be taken literally does not mean that they cannot convey a claim that is serious. (Butters, Tr. 2824; Stewart, Tr. 3230).

534. Parody and humor have the effect of capturing the attention of the advertisement viewer, to help them connect with the message in the printed portion of the advertisement. (Butters, Tr. 2866).

535. Humor can induce further processing of an advertisement and a search for further information. (Stewart, Tr. 3229-30).

536. Contemporary speakers of American English would include "heart disease" within their understanding of the meaning of "heart trouble." (Butters, Tr. 2850-51).

537. Contemporary speakers of American English could interpret the phrase "erectile function" to relate to the ability of men to achieve and maintain erections. Erectile function and the absence of erectile dysfunction are closely related. (Butters, Tr. 2851 (discussing CX0351 and CX0355).

538. Contemporary speakers of American English could interpret the phrase "prostate health" to include the condition of not being diseased. (Butters, Tr. 2851).

539. Contemporary speakers of American English could interpret the phrase "heart health" to include the condition of not being diseased. (Butters, Tr. 2851).

540. In the proper context, a visual of an intravenous drip bottle could be a symbol for drugs and medicine. (Butters, Tr. 2947).

541. The caduceus symbol, showing snakes curling around a staff, is a symbol that people associate with medicine. (Butters, Tr. 2944).[3]

542. Academic marketing and psychology literature indicate that the meaning of a particular communication really resides in the recipient, not in the actual stimulus. Consumers are not simply passive recipients of messages but are active processors. (Stewart, Tr. 3170).

543. To determine what a consumer would take away from the POM advertising, it is very important to know the characteristics of the viewer of the advertisements, including prior beliefs and prior knowledge, and how the consumer would process the information, and generally what the consumer brings to the viewing situation – all of which are really important in understanding the totality of what people will take away from an advertising message. (Stewart, Tr. 3171-73).

c. Bovitz Billboard Survey

544. In March 2009, at the request of Ms. Resnick, POM engaged the Bovitz Research Group ("Bovitz") to design a consumer survey to evaluate the relative effectiveness of the then-running "Super Hero" advertising campaign compared to POM's earlier "Dressed Bottle" advertising campaign. (CX0286; CX1378 at 0049 (Kuyoomjian, Ocean Spray Dep. at 191-92)).

545. The target POM consumer for purposes of the survey was identified for Bovitz as "Higher HH income $75k+", 25 to 64, concerned about their health and willing to buy premium, health products." In recruiting participants, the survey eliminated individuals with incomes below $75,000. Individuals who did not score high on a scale measuring certain attitudes and lifestyle choices related to health and diet were also disqualified from participation. (CX0286 at 0002-03; CX0369 at 0003).

546. The Bovitz Survey used a forced exposure methodology (*i.e.*, showing the advertisement for which one wants to ascertain the consumer takeaway, to the survey respondents) which, although not the typical, natural way that consumers are exposed to advertising, is a valid method for a survey measuring advertising communication. (CX0369 at 0004-07; Mazis, Tr. 2693-95; Reibstein, Tr. 2509-10).

547. The Bovitz Survey exposed survey respondents only to POM's billboard advertising. (Reibstein, Tr. 2572-73, 2575; Stewart, Tr. 3207, 3209; PX0295a15 at 0005-06).

---

[3] The following is an image of a caduceus symbol: 

548. The Bovitz Survey compared consumers' perceptions of the following ten billboard advertisements from POM's Super Hero and Dressed Bottle advertising campaigns (hereinafter, "Bovitz Stimuli"), as follows:

> Super Hero campaign advertisements:
> Holy Health! $25 million in medical research.
> I'm off to save PROSTATES!
> 100% PURE pomegranate juice to the rescue!
> BACK OFF …impostor juices!
> Risk your health in this economy? NEVER!
>
> Dressed Bottle campaign advertisements:
> Cheat Death.
> The Antioxidant Superpower.
> Decompress.
> Heart therapy.
> Forever young.

(PX0295a15at0010-11).

549. The billboard advertisements from the Dressed Bottle campaign use humorous headlines and images. (Stewart, Tr. 3205).

550. Each of the Bovitz Stimuli also included a tagline related to antioxidants, such as "The Antioxidant Superpower" and the "The antioxidant power of pomegranate juice." The Bovitz Stimuli contained no additional text. (PX0225 at 0005-06).

551. In the Bovitz Survey, a total of 150 target consumers and 100 existing POM users were exposed to the billboard advertisements from each campaign, identified in F. 544. (PX0225 at 0003-04).

552. Four of the billboard advertisements described in F. 548 (*i.e.*, "Heart therapy," "Decompress," "Cheat death" and "I'm off to save prostates") share headlines and imagery that appear in certain of the Challenged Advertisements in this case. (*See* CX0109 at 0001 and CX0463 ("Heart therapy banner advertisement"), CX0103 at 0001 ("Decompress"), CX0036 at 0001 and CX0188 at 0001 ("Cheat death"), and CX0274 at 0001 and CX0466 ("I'm off to save PROSTATES!" banner advertisement)).

553. The headline of one test billboard included a reference to "$25 million in . . . medical research," (F. 548), which reference appears in some of the Challenged Advertisements. (*See, e.g.*, CX0274).

554. The participants were shown various advertisements, in a variety of configurations, and asked a series of questions, including: "Other than trying to get you to buy the product,

what do you think is the main idea" that the advertisement "is trying to get across to you?" (CX0369 at 0005-11).

555. Fourteen percent of the general target audience and seventeen percent of POM Juice users in the Bovitz Survey, when shown an advertisement picturing a POM Juice bottle inside a blood pressure cuff, with the headline "Decompress" and a sub-headline "POM Wonderful Pomegranate Juice. The Antioxidant Superpower," said the ad's main idea was "helps/lowers blood pressure." (PX0295a15 at 0011, 0018, 0046; Stewart, Tr. 3213-14).

556. Other "main ideas" identified in the Bovitz Survey by those shown the billboard advertisement picturing a POM Juice bottle inside a blood pressure cuff, with the headline "Decompress" and a sub-headline "POM Wonderful Pomegranate Juice. The Antioxidant Superpower," include: (1) 64% of the general population and 73% of the POM population stated that the "main idea" of the billboard was "healthy/health benefits/juice is good for you"; (2) 16% of the general population and 20% of the POM population responded "antioxidants"; and (3) 6% of the general population and 13% of the POM population said "calming/relieves stress/relaxing." (PX0295a15 at 0018, 0046).

557. Forty-three percent of the general target audience and forty-eight percent of POM Juice users in the Bovitz Survey, when shown an advertisement picturing a POM Juice bottle saying, "I'm off to save PROSTATES!" and a sub-headline "The Antioxidant Superpower," said the advertisement's main idea was "good for prostates." (PX0295a15 at 0010, 0017, 0045).

558. Other "main ideas" identified in the Bovitz Survey by those shown the billboard advertisement picturing a POM Juice bottle saying, "I'm off to save PROSTATES!" and a sub-headline "The Antioxidant Superpower," include: (1) 31% of the general population and 48% of the POM population said the "main idea" of the "I'm off to save PROSTATES!" billboard was "healthy/health benefits/juice is good for you" and (2) 12% of the general population and 28% of the POM population said "antioxidants." (PX0295a15 at 0017, 0045).

559. Twenty-two percent of the general target audience and thirty-one percent of POM Juice users in the Bovitz Survey, who were shown an advertisement picturing a POM Juice bottle saying, "HOLY HEALTH! $25 million in medical research" and a sub-headline "The Antioxidant Superpower," said the advertisement's main idea was "$25 million spent on research/research based." (PX0295a15 at 0010, 0017, 0045).

560. Other "main ideas" identified in the Bovitz Survey by those shown the "HOLY HEALTH!" billboard advertisements were: (1) 57% of the general population and 46% of the POM population said "healthy/health benefits/juice is good for you;" (2) 12% of the general population and 9% of the POM population responded "antioxidants." (PX0295a15 at 0017, 0045).

561. According to Dr. Stewart, a test of headlines and images in the context of a billboard advertisement provides some insight into understanding what messages were communicated by the image and the headline. Other text that is added to a lengthier print advertisement might modify the messages communicated by the image and headline. (Stewart, Tr. 3205-06).

562. Bovitz Survey respondents were also exposed to all five tested advertisements from the "Super Hero" campaign or all five tested advertisements from the "Dressed Bottle" campaign and asked: "Based on the ads you just saw, what are the specific benefits, if any, of drinking POM Wonderful?" (CX0369 at 0008-09; Stewart, Tr. 3214-16).

563. Professor Reibstein testified that the question posed in F. 562 was a leading, biased question because it directed the survey participants to select a "specific benefit" which pressures them to identify a "specific benefit" even if they had not perceived a particular benefit. (Reibstein, Tr. 2515-16). Dr. Stewart testified that this question was open-ended and not leading. (Stewart, Tr. 3216).

564. Of the survey respondents exposed to the five "Dressed Bottle" advertisements, which included the images and headlines of the "Decompress" print advertisement (CX0103) and the "Heart Therapy" print and banner advertisements (CX0109; CX0463), 38% of the general target audience said that a benefit of drinking POM Juice was "good for your heart" and 21% said a benefit was "helps/lowers blood pressure." (PX0225 at 0014; Stewart, Tr. 3216-17).

565. Bovitz Survey respondents who were exposed to the five "Super Hero" advertisements, which included an advertisement picturing a POM Juice bottle saying, "HOLY HEALTH! $25 million in medical research," were asked a close-ended question, "Based on the ads you just saw, which of the following do you think are true about POM Wonderful?" Survey respondents were provided a multiple-choice list and told to select as many or as few that applied. (CX0369 at 0010-11). Specifically, question 16 provided the following choices:

1. Backed by medical research
2. Is good for cardiovascular health
3. 100% pure pomegranate juice
4. Contains all natural ingredients
5. Is good for prostate health
6. Like "health in a bottle"
7. Contains naturally occurring antioxidants
8. Is the original pomegranate juice
9. Is good for you
10. Will help you stay healthy
11. Will help you live longer
12. Is better than other pomegranate juices
13. Has proven health benefits
14. Tastes good

566. In response to Question 16, 63% of the general population and 78% of POM Juice users included the choice, "has proven health benefits." (PX0295a15 at 0033, 0034).

567. Complaint Counsel's expert, Dr. Stewart, acknowledged that because Question 16 was a closed-ended question, there is the possibility of yea-saying, *i.e.*, the tendency to give a yes or more socially desirable response in an effort to be agreeable. (Stewart, Tr. 3218-19).

568. According to Dr. Reibstein, by providing respondents with a list of choices in response to Question 16 of the Bovitz Survey, survey respondents were cued to select from attributes that they may not otherwise have thought of, and do not have the option of attributes that do not appear on the list. This tends to inflate results. (Reibstein, Tr. 2518-19).

569. According to Dr. Reibstein, the Bovitz Survey is methodologically flawed and unreliable because it had no control and, thus survey respondents might have had preconceived perceptions about pomegranate juice before being exposed to POM's billboard advertisements. (Reibstein, Tr. at 2510-11).

570. Dr. Stewart testified he was "comfortable" with open-ended questions without a control, although he also testified that, without a control, you cannot draw a firm inference that an advertisement had a particular effect. (Stewart, Tr. 3241-42).

571. Dr. Reibstein opined that the Bovitz Survey is methodologically flawed and unreliable because the sample size of only 100 POM users and 150 target consumers exposed to each category of advertisements was too small to reach statistical significance at the 95% confidence level. (Reibstein, Tr. 2512-13).

572. None of the survey respondents in the Bovitz Survey answered that the main idea of the billboard advertisements was prevention, risk reduction, or treatment of any specific disease. The most common "main idea" communicated (at least 90%) was that POM Juice had general health benefits. (Reibstein, Tr. 2516-17; PX0225 at 0012-13).

573. Dr. Reibstein testified that the Bovitz Survey is methodologically flawed and unreliable because Question E (F. 574), which asked about health-related beliefs, resulted in accepting only recruits who were extremely health-focused, rather than merely health-oriented. According to Dr. Reibstein, such respondents would be more inclined to find health-oriented messages, particularly in light of the methodology of forced exposure and copy test questions cueing health. (Reibstein, Tr. 2511-12).

574. Question E of the Bovitz Survey stated as follows:

> Listed below are some statements that may or may not describe you. Using the scale provided, please indicate the extent to which each of the following statements describes you.

(RANDOMIZE ROWS)	Describes me perfectly	Describes me well	Describes me somewhat	Describes me a little	Does not describe me at all
I use my diet to manage my health	5	4	3	2	1
High fiber foods are a regular part of my diet	5	4	3	2	1
I regularly work out to stay fit	5	4	3	2	1
I try to include plenty of fruits and vegetables in my diet	5	4	3	2	1
I believe that what I eat can directly affect my health	5	4	3	2	1
I am the first of my friends to try new gadgets and technology	5	4	3	2	1
I prefer to watch movies at home instead of a theater	5	4	3	2	1
I am adjusting my lifestyle to be conscious of the environment	5	4	3	2	1
I enjoy cooking and trying new recipes that I find online	5	4	3	2	1
I like to stay up on current events	5	4	3	2	1

To qualify for participation in the survey, respondents had to respond with a "5" or a "4" on the rating scale with respect to at least three of the five health-related statements (*i.e.*, Questions 1 through 5). (CX0369 at 0002).

3. Television interviews

575. On November 20, 2008, Mrs. Resnick appeared on NBC's *The Martha Stewart Show*. Martha Stewart invited Mrs. Resnick to be interviewed on *The Martha Stewart Show*. (CX1426, Ex. E-6; L. Resnick, Tr. 137).

576. On February 19, 2009, Mrs. Resnick appeared on CBS' *The Early Show* in a segment on Cashing in on Ideas. (CX472 at 0003).

577. On March 20, 2009, *Newsweek* published on its website two pages of excerpts from an interview with Mrs. Resnick titled, "*Striking Out On Your Own. Is now a good time to start a company?*" (CX1426, Ex. F).

578. On June 17, 2008, Mr. Tupper provided a television interview on the Fox Network Business Channel. (CX1426, Ex. E-7; Tupper, Tr. 919).[4]

4. Summary of findings on advertising claims

579. In determining whether Respondents disseminated advertisements and promotional materials making the claims alleged in the Complaint, each of the Challenged Advertisements has been reviewed. Extrinsic evidence as to how the Challenged Advertisements would be interpreted by a reasonable consumer has also been considered.

580. Respondents disseminated advertisements and promotional materials that impliedly represented either that drinking eight ounces of POM Juice daily, taking one POMx Pill daily, and/or taking one teaspoon of POMx Liquid daily, is clinically proven to treat, prevent, or reduce the risk of heart disease, by reducing arterial plaque, lowering blood pressure, and/or improving blood flow to the heart, as alleged in paragraph 12 of the Complaint. The following advertisements and promotional materials contain one or more of the foregoing representations:

- CX0016 (print advertisement) (prevent/reduce the risk only) (F. 293);
- CX0029 (print advertisement) (F. 299);
- CX1426 (Compl. Ex. I) (package insert) (F. 338);
- CX1426 (Compl. Ex. M) (POMx Heart Newsletter)(F. 346);
- CX0473 (Pomwonderful.com website: April 2009 (Compl. Ex. E-2); October 2009, December 2009 and January 2010 (F. 368, 380); Pompills.com website: April 2009 (Compl. Ex. E-8), January 2010 (Compl. Ex. E-9) (F. 387); pomegranatetruth.com website (Compl. Ex. E-1)(F. 411));
- CX0013 (press release) (F. 417); and
- CX0044 (press release) (F. 422).

581. Respondents disseminated advertisements and promotional materials that impliedly represented either that drinking eight ounces of POM Juice daily, taking one POMx Pill daily, and/or taking one teaspoon of POMx Liquid daily, is clinically proven to treat,

[4] As explained in Section III.C, *infra*, the four television interviews that Complaint Counsel challenges as "advertisements" (*see* Complaint ¶ 9, I-J; CCB Appendix A) are not actionable as "advertisements" under the FTC Act. *See* Section III.C.1. Thus, the interviews are hereinafter not included in the term, "Challenged Advertisements," and this Initial Decision does not include any findings regarding any claims allegedly made in those interviews.

prevent or reduce the risk of prostate cancer by prolonging prostate-specific antigen ("PSA") doubling time, as alleged in paragraph 14 of the Complaint. The following advertisements and promotional materials contain one or more of the foregoing representations:

- CX0314 (magazine wrap) (F.310);
- CX0372 (magazine wrap) (F. 310);
- CX0379 (magazine wrap) (F. 310);
- CX0380 (magazine wrap) (F. 310);
- CX1426 (Compl. Ex. N) (POMx Prostate Newsletter) (F. 351);
- CX1426 (Compl. Ex. I) (package insert) (F. 331);
- CX0473 (Pomwonderful.com website: April 2009 (Compl. Ex. E-2); October 2009, December 2009, and January 2010 (F 368, 380); Pompills.com website: April 2009 (Compl. Ex. E-8), January 2010 (Compl. Ex. E-9) (F. 387)); and
- CX0065 (press release) (F. 429).

582. Respondents disseminated advertisements and promotional materials that impliedly represented either that drinking eight ounces of POM Juice daily, taking one POMx Pill daily, and/or taking one teaspoon of POMx Liquid daily, is clinically proven to treat, prevent or reduce the risk of erectile dysfunction, as alleged in paragraph 16 of the Complaint. The following advertisements and promotional materials contain one or more of the foregoing representations:

- CX0351 (print advertisement) (F. 325);
- CX0355 (print advertisement) (F. 325);
- CX0473 (Pomwonderful.com website: April 2009 (Compl. Ex. E-2); October 2009, December 2009, and January 2010 (F. 368, 380); Pompills.com website: April 2009 (Compl. Ex. E-8), January 2010 (Compl. Ex. E-9) (F. 387)); and
- CX0128 (press release) (treatment only) (F. 433).

583. Respondents disseminated advertisements and promotional materials that impliedly represented either that drinking eight ounces of POM Juice daily, taking one POMx Pill daily, and/or taking one teaspoon of POMx Liquid daily, treats, prevents or reduces the risk of heart disease, by reducing arterial plaque, lowering blood pressure, and/or improving blood flow to the heart, without also representing clinical proof of these effects, as alleged in paragraph 19 of the Complaint. The following advertisements contain one or more of the foregoing representations:

- CX0031 (print advertisement) (F. 443);
- CX0033 (print advertisement) (F. 455);
- CX0034 (print advertisement) (F. 463); and
- CX0036 (print advertisement) (F. 474).

584. The findings described in F. 580-583 are based upon the overall, common-sense, net impression of the advertisements themselves, and full consideration of any applicable extrinsic evidence. As to advertisements cited in F. 580-583, the weight of the applicable extrinsic evidence fails to sufficiently contradict the overall, common-sense, net impression gleaned from the advertisements themselves.

585. The following Challenged Advertisements were found to have made claims alleged in the Complaint, but the preponderance of the evidence fails to prove that these advertisements made all the claims asserted by Complaint Counsel. *See* Appendix A to Complaint Counsel's Post-hearing Brief. These advertisements and claims are: CX0031 ("clinically proven" claim not found); CX0034 ("clinically proven" claim not found); CX0065 (press release) (heart disease claim not found); CX0351 and CX0355 (prostate cancer and heart disease claims not found). It is not reasonably clear from the face of the advertisements alone that a significant minority of consumers, acting reasonably under the circumstances, would interpret these advertisements as making the identified claims. A review of each of these advertisements, considering the interplay of all the elements of each such advertisement, failed to allow a confident conclusion that a significant minority of reasonable consumers would interpret the advertisements as making the identified claims. Among other reasons, the foregoing advertisements: do not mention heart disease, prostate cancer, or erectile dysfunction; use vague, non-specific, substantially qualified, and/or otherwise non-definitive language; use language and/or images that, in the context of the advertisement, are inconsistent with the alleged claim; and/or do not draw a sufficiently clear connection for the reader, such as through associated explanatory text, between the health effects or study results referred to in the advertisements and the diseases alleged in the Complaint. Moreover, applicable extrinsic evidence fails to demonstrate that these advertisements make the identified claims.

586. Based on a thorough review of all the Challenged Advertisements, none expressly (*i.e.*, unequivocally and directly) states that "drinking eight ounces of POM Juice daily" or "taking one POMx Pill daily," or "taking one teaspoon of POMx Liquid daily"(1) "treats," "prevents," or "reduces the risk" of "heart disease," including by reducing arterial plaque, lowering blood pressure, and/or improving blood flow to the heart, or that these effects are "clinically proven"; (2) "treats," "prevents" or "reduces the risk" of "prostate cancer," including by prolonging prostate-specific antigen doubling time, or that these effects are "clinically proven"; or (3) "treats," "prevents," or "reduces the risk" of erectile dysfunction, or that these effects are "clinically proven."

587. As to the Challenged Advertisements not identified in F. 580-583 as making the representations alleged in the Complaint, after a thorough review it is not reasonably clear from the face of these advertisements that a significant minority of consumers, acting reasonably under the circumstances, would interpret these advertisements as making the claims alleged in the Complaint. A review of these advertisements, considering the interplay of all the elements of each such advertisement, failed to allow a confident conclusion that a significant minority of reasonable consumers would interpret these advertisements as making the claims alleged in the Complaint. These

advertisements, which are all print advertisements except where noted, are: CX0103; CX0109; CX0188, CX0192; CX0260; CX0274; CX0475; CX0120; CX0122; CX0169; CX0180; CX0279; CX0280; CX0328; CX0331; CX0337; CX0342; CX0348; CX0350; CX0353; CX0463 (banner advertisement) and CX0466 (banner advertisement).

588. Among other reasons, the advertisements identified in F. 587: use language that is vague, non-specific, substantially qualified, and/or otherwise non-definitive; use language and/or imagery that in the context of the advertisements is inconsistent with the alleged claims; fail to mention specific diseases; and/or fail to draw a sufficiently clear connection for the reader, such as through associated explanatory text, between health effects or study results referred to in the advertisements and the diseases alleged in the Complaint.

589. As to the advertisements identified in F. 587, the weight of the applicable extrinsic evidence (*see* Section II.E.2, *infra*) fails to demonstrate that these advertisements make the claims alleged in the Complaint.

590. Having fully considered each of the advertisements identified in F. 587, as well as any extrinsic evidence pertaining thereto (*see* Section II.E.2, *infra*), the preponderance of the evidence fails to demonstrate that a significant minority of reasonable consumers would interpret these advertisements as making the claims alleged in the Complaint.

591. The evidence fails to show that CX0473 (pomegranatetruth.com website) made the prostate cancer and erectile dysfunction claims alleged in the Complaint because the web capture of this website did not include content pertaining to such claims. (F. 415).

F. Level of Required Substantiation

1. Types of studies

592. There are four study types for examining the relation between a food or nutrient and a disease outcome: (a) *in vitro* studies; (b) animal studies; (c) human observational studies; and (d) human clinical studies. (CX1293 (Stampfer Expert Report at 0008)).

593. "Basic science" refers to test-tube, animal studies, and preclinical research. (Dreher, Tr. 528).

a. *In vitro* studies

594. *In vitro* studies are those where blood elements or cells are removed from the body and tested in a controlled laboratory environment, such as a test tube. They are used to identify potential biologic mechanisms and generate hypotheses for studies in humans. (CX1293 (Stampfer Expert Report at 0008); CX1291 (Sacks Expert Report at 0015-16); *see* Melman, Tr. 1112). Human metabolism and disease processes are very complicated and cannot be replicated in a petri dish, and therefore, many *in vitro* studies produce

results that cannot be replicated in humans. (CX1291 (Sacks Expert Report at 0015-16); Sacks, Tr. 1450; *see also* Stampfer, Tr. 725-26; deKernion, Tr. 3063-64).

b. Animal studies

595. Animal studies are tools for identifying potential treatments, mechanisms, and side effects. Animals are not the same as humans, either biologically or psychologically, and therefore, many findings of dietary or drug effects in animals are not confirmed in human testing. (CX1291 (Sacks Expert Report at 0016); Sacks, Tr. 1451; Melman, Tr. 1112-13; CX1289 (Melman Expert Report at 0011); *see* PX0355 (Ornish, Dep. at 66)).

596. Animal studies alone are not sufficient to show that a tested product will prevent or treat human disease. (Sacks, Tr. 1451-52; Melman, Tr. 1112-13; CX1289 (Melman Expert Report at 0011); Goldstein, Tr. 2644; PX0349 (Burnett, Dep. at 57, 112-13)).

597. Animal studies are very informative and provide for some clinical insights. (PX0349 (Burnett, Dep. at 111); PX0352 (Goldstein, Dep. at 122-24); Goldstein, Tr. 2644; Heber, Tr. 2086, 2149; CX1352 (Heber, Dep. at 243); Heber, Tr. 2086; 2149, 2182; PX0192 (Heber Expert Report at 0015, 0041-42, 0051-59). In an animal study, researchers can isolate mechanisms of action and accomplish toxicity or safety testing, as well as examine specific mechanisms by taking out their organs and cells, which cannot be done in humans. (PX0361 (Sacks, Dep. at 89-91). Results from such animal studies have potential for benefit of therapy at the human level. (PX0206 (Miller Expert Report at 10-11, 13); Miller Tr. 2194; PX0349 (Burnett, Dep. at 112); Burnett, Tr. 2262-63; Heber, Tr. 2086, 2149; CX1352 (Heber, Dep. at 243); Heber, Tr. 2086; 2149, 2182; PX0192 (Heber Expert Report at 0015, 0041-42, 0051-59).

598. Although there are limitations to extrapolating from animal studies to human studies, studies on animals have value in determining therapeutic efficacy. (PX0025 (Ornish Expert Report at 0007)).

599. Dr. Sacks, Complaint Counsel's cardiology expert, testified that he considers all levels of science in issuing national guidelines for the prevention or treatment of cardiovascular disease. (PX0361 (Sacks Dep. at 71)). Similarly, Complaint Counsel's erectile dysfunction expert, Dr. Melman, testified that based on the results of his gene therapy erectile dysfunction product in an animal model, he was "personally satisfied" that it would also work in humans. (PX0360 (Melman, Dep. at 56-57)).

c. Human observational studies

600. Human observational studies are large human studies that compare intake of various levels of nutrients (for example, low vitamin C versus high vitamin C) with various endpoints, such as disease outcomes, over time. (CX1293 (Stampfer Expert Report at 0008); Stampfer, Tr. 719; *see* Heber, Tr. 2168).

601. Human observational studies can support a conclusion that there is an association between a nutrient and a disease of interest, but generally do not prove causation, due to the potential, even in well-designed studies, for unidentified biases or inadequately controlled confounding factors. (CX1293 (Stampfer Expert Report at 0008-09); Stampfer, Tr. 720-21; *see* Sacks, Tr. 1418-19).

d. Human clinical studies

602. Human clinical studies are those in which investigators assign the exposure level to participant – meaning that the investigators tell the subjects how much of a particular nutrient to consume, in contrast to observational studies, where the investigators study existing exposure levels within a particular population. (CX1293 (Stampfer Expert Report at 0009)).

603. There is a typical progression in human clinical studies, from exploratory research to randomized clinical trials. (PX0025 (Ornish Expert Report at 0010, 0024) ("Science usually progresses when someone publishes a study of a series of patients with a nonrandomized control group that shows an unprecedented finding which is then replicated by one or more subsequent randomized controlled trials[;]" "[t]here is a logical progression in science which often begins with a pilot study that has no control group")).

604. Some researchers describe the progression of research in terms of "phases," where: a Phase I trial tests treatments in a small number of patients to find a safe dose; a Phase II trial tests the intervention in a larger number of people to identify specific effects; a Phase III trial tests the treatment in a larger number of people, to compare it to "standard treatment"; and a Phase IV trial tests a treatment in several hundred to thousands of people to assess long-term safety and effectiveness. (CX1287 (Eastham Expert Report at 0009); CX1341 (Pantuck, Dep. at 28-29); *see also* Burnett, Tr. 2262).

605. Typically, researchers conduct pilot or exploratory studies. A pilot study is designed to investigate whether there is any evidence of a treatment effect. Such research can reveal potential changes from an intervention, allows the researchers to see if people can tolerate the intervention or if it causes unexpected side effects, and paves the way for more definitive research. (CX1338 (Padma-Nathan, Dep. at 87-88, 155); CX1193 at 0001; Melman, Tr. 1116; Stampfer, Tr. 747-48; CX1342 (Hill, Dep. at 45-48)).

606. Pilot studies are generally considered by scientists and clinicians in the scientific community to be valid, accurate, and reliable studies. (CX1336 (Davidson, Dep. at 232-33); CX1342 (Hill, Dep. at 48-49, 53); CX1339 (Ornish, Dep. at 23); CX1358 (Aviram, Dep. at 17)).

607. A "pilot" study does not mean that it is not as scientifically valid as a larger study. (CX1339 (Ornish, Dep. at 23, 119-20)). A small number of participants do not weaken the importance of the results, especially if they are in agreement with *in vitro*, mechanistical studies and in animal models. (CX1358 (Aviram, Dep. at 18)).

608. A reason a researcher conducts a "pilot" study is because he or she is not certain how many subjects it will take to adequately power the study. If there is no effect shown, then this allows the investigators to address any concerns regarding the study. (CX1342 (Hill, Dep. at 46-48)).

2. Randomized clinical trials

609. Well-designed, well-conducted, randomized, double-blinded, placebo-controlled human clinical studies are referred to by experts in the field of clinical testing as "RCTs." (CX1291 (Sacks Expert Report at 10)).

610. It is standard practice, in human research, to begin with a *protocol*. (Stampfer, Tr. 760; Sacks, Tr. 1436-37; Heber, Tr. 2044-45). A protocol describes the key features of a study, such as objectives, methodology, statistical analysis plan, the definition of the *p* value (probability), and primary outcome variables (endpoints). (Sacks, Tr. 1436-37; Stampfer, Tr. 760; *see* Ornish, Tr. 2367). The purpose of identifying the primary outcomes in advance is to prevent a researcher from using positive results and ignoring negative ones, resulting in bias. (Sacks, Tr. 1475; CX1291 (Sacks Expert Report at 0021)).

611. A *controlled* study is one that includes a group of patients receiving the purported treatment ("treatment" or "active" group) and a control group ("placebo" or "control" group). (CX1291 (Sacks Expert Report at 0011)). A control group provides a standard by which results observed in the treatment group can be evaluated. (CX1287 (Eastham Expert Report at 0013)). A control group allows investigators to distinguish between real effects from the intervention, and other changes, including those due to the mere act of being treated ("placebo effect"), the passage of time, change in seasons, other environmental changes, and equipment changes (such as calibration changes). (CX1291 (Sacks Expert Report at 0011); Burnett, Tr. 2265; Eastham, Tr. 1268; *see* CX1293 (Stampfer Expert Report at 0009); Ornish, Tr. 2367). The control group should be approximately the same size and meet the same criteria as the treatment group. (Eastham, Tr. 1268-69; CX1287 (Eastham Expert Report at 0013); CX1291 (Sacks Expert Report at 0011); Melman, Tr. 1095; CX1289 (Melman Expert Report at 0009)). It also should receive the same measurements and attention from the researchers as the treatment group. (CX1291 (Sacks Expert Report at 0011)).

612. *Randomization* means assigning subjects to the active product group or the control group in a random fashion, whether using a computer program, random number table, or coin toss. It is another way to control for bias. (Burnett, Tr. 2264-65; CX1291 (Sacks Expert Report at 0011); CX1339 (Ornish, Dep. at 20); Eastham, Tr. 1266; Melman, Tr. 1096). It increases the likelihood that the treatment and control groups are similar in relevant characteristics, so that any difference in the outcome between the two groups can be attributed to the treatment. (CX1291 (Sacks Expert Report at 0011-12); CX1293 (Stampfer Expert Report at 0009); CX1287 (Eastham Expert Report at 0012-13); CX1339 (Ornish, Dep. at 20) ("[B]y randomizing people, if there were some

unknown factor that was biasing your outcomes, it would be likely to be distributed across both groups")). It also prevents the investigator from deciding who gets which treatment, which can introduce bias into the study. (CX1345 (deGroof, Dep. at 62); Melman, Tr. 1096).

613. A *placebo* is an inactive product or treatment given to the control group, in lieu of the intervention being tested. (Stampfer, Tr. 708; Eastham, Tr. 1267-68; Melman, Tr. 1094-95). For example, in a study of a pill, the placebo would be a pill that looks like the intervention, but does not contain the active ingredient. (Stampfer, Tr. 708). A placebo should be identical, in all ways possible, to the active treatment. (CX1291 (Sacks Expert Report at 0011); Melman, Tr. 1095). A double blind study, *see* F. 614, blinds participants and investigators as to whether study participants are in the active or placebo group. (CX1293 (Stampfer Expert Report at 0009); Melman, Tr. 1095-96).

614. *Blinding* refers to steps taken to ensure that neither the study participants nor the researchers conducting the outcome measurements are aware of whether a patient is in the active group or the control group. (CX1291 (Sacks Expert Report at 0012); Melman, Tr. 1097).

615. *Double-blinding*, that is, blinding of both the patients and investigators, is optimal to prevent bias arising from actions of the patients or investigators. (CX1293 (Stampfer Expert Report at 0009); Stampfer Tr. 708-09; Eastham, Tr. 1267; Melman, Tr. 1098; CX1287 (Eastham Expert Report at 0013); *see also* Heber, Tr. 2044). In some instances, the blinding of patients is not possible. A study that is unblinded can still have value. (Sacks, Tr. 1435-36; PX0361 (Sacks, Dep. at 104-05); Ornish, Tr. 2345; Eastham, Tr. 1327, 1339).

616. Once a randomized controlled trial is completed and all the data is collected, data for the control and active treatment groups is compared through use of appropriate *statistical analyses*. (Eastham, Tr. 1272; CX1287 (Eastham Expert Report at 0014); CX1291 (Sacks Expert Report at 0012-13)). If the results of the treatment group are *statistically significant* from those of the control group at the end of the trial, it can be concluded that the tested product is effective. This analysis is called a *between-group analysis*. (CX1291 (Sacks Expert Report at 0012-13); Burnett, Tr. 2269).

617. A *within-group* analysis, where a researcher compares the treatment group participants' "before" data to their "after" data, has much less scientific value, because it relies on the assumption that without the intervention there would have been no change in the study participants' condition. (Stampfer, Tr. 714).

618. Evaluating data from a clinical trial for *statistical significance* is the standard practice to demonstrate that a study's hypothesis has been proven. (Burnett, Tr. 2269; CX1287 (Eastham Expert Report at 0014)). *Statistical significance* is recognized as being attained if the statistical test for probability, referred to as the "*p*" value, is less than or equal to 0.05 ($p \leq 0.05$), which means that there is only a 5 percent or less chance that the difference between the treatment and placebo groups is due to chance. (CX1291

(Sacks Expert Report at 0012); Eastham, Tr. 1273; Ornish, Tr. 2368; Melman, Tr. 1102-03; CX1289 (Melman Expert Report at 0010)). It means that the results demonstrated would occur no more than one time out of 20, and therefore, other causes of the result, such as chance, are less likely as an explanation. (Stampfer, Tr. 710-11).

619. Statistical significance is an arbitrary convention in the context of studying a whole food. (Ornish, Tr. 2340, 2368; Goldstein, Tr. 2598-99 (choosing a significance level is technically an arbitrary task, and "in specific situations a different value could be utilized")).

620. Results that do not have a *p*-value of less than 0.05 can still evidence a clinically meaningful benefit that is scientifically supportable. (PX0352 (Goldstein, Dep. at 108-09); Goldstein, Tr. 2599; PX0189 (Goldstein Expert Report at 0013); PX0349 (Burnett, Dep. at 67, 138-39); Burnett, Tr. 2270-71; CX1350 (Liker, Dep. at 190-91); PX0361 (Sacks, Dep. at 109); Sacks, Tr. 1608-09).

621. *Validated* endpoints or surrogate markers are those outcomes that, while not direct endpoints, have been shown to be so closely linked to a direct endpoint that a change in the surrogate marker is confidently predictive of a change in the disease. (*See* CX1291 (Sacks Expert Report at 0013); *see* CX1287 (Eastham Expert Report at 0010) ("Changes in a surrogate are expected to reflect changes in a clinically meaningful endpoint")). *Validated* measures or assessment tools are those that have been established as reliable through rigorous assessments involving a large number of individuals. (Burnett Tr. 2266-67; Melman, Tr. 1100).

622. Certain validated measures, like the International Index of Erectile Function ("IIEF"), were originally intended for pharmaceutical products and "not necessarily designed for a nutraceutical [a food product that provides medical or health benefits]." (PX0352 (Goldstein, Dep. at 67-69); Goldstein, Tr. 2603-04, 2633).

623. Certain non-validated measures are very "informative and . . . valuable to use in clinical studies." (Burnett, Tr. 2294).

624. *Clinical significance* means that the treatment makes a real difference in a patient's life. (Melman, Tr. 1103; Eastham, Tr. 1274; PX0361 (Sacks, Dep. at 109)). A result may also be clinically significant even if it did not reach statistical significance. (PX0352 (Goldstein, Dep. 108-09); Goldstein, Tr. 2599; PX0189 (Goldstein Expert Report at 0013); PX0349 (Burnett, Dep. at 67, 138-39); Burnett, Tr. 2270-71; CX1350 (Liker, Dep. at 190-91). A result may be statistically significant, but not clinically significant. (Melman, Tr. 1104; Eastham, Tr. 1274).

625. *Replication* is intended to ensure that the results obtained in one study are not due to chance. Even with the safeguards contained in an RCT, the results contained in any one study may be due to chance or may not be generalizable due to uniqueness of the study sample. (Sacks, Tr. 1446; CX1291 (Sacks Expert Report at 0014-15)).

3. Testimony from Complaint Counsel's experts on whether RCTs are required

a. Dr. Meir Stampfer

626. Dr. Stampfer provided the following opinion regarding the appropriate level of evidence of substantiation: randomized, double blind, placebo-controlled trials are needed for nutrient supplements when they are used as medical interventions to prevent or treat diseases. (CX1293 (Stampfer Expert Report at 0029)).

627. Dr. Stampfer testified that if there is a claim that a cause and effect relationship (causal link) between a nutrient or food and a disease has been established, then one has to have evidence to back it up. (Stampfer, Tr. 830-31).

628. Dr. Stampfer testified that the level of scientific evidence required to support a claim depends on the claim being made. (Stampfer, Tr. 830-31).

629. Dr. Stampfer explained that it is an efficacy claim to say that a product reduces the risk of a disease, but it is not an efficacy claim to say that users of a product have a lower incidence of a particular disease. To state that users of a product have a lower incidence does not mean that use of the product caused them to have a lower incidence. (Stampfer, Tr. 798).

630. Dr. Stampfer further testified that a statement that studies indicate that a product lowers the risk of heart disease and diabetes does not imply that a causal link is established. (Stampfer, Tr. 817).

631. Dr. Stampfer testified that if the claim does not imply a causal link, for example, if the claim is that there is some evidence to suggest the possibility that nuts may reduce the risk of diabetes, then evidence short of RCTs can support that claim. (Stampfer, Tr. 830-31; CX1293 (Stampfer Expert Report at 0029-30) (it may be appropriate to use evidence short of randomized clinical trials for crafting public health recommendations regarding nutrient guidelines even when causality cannot be established, because everyone eats and the public should be given advice based on the best evidence available. This advice should distinguish between recommendations based on good evidence of a causal relation from those that are based on evidence that is suggestive but falls short of a firm casual conclusion.)).

632. Dr. Stampfer further testified that in a nutritional context, a hypothesis about disease causation can, rarely, if ever, be directly tested in humans using the RCT design. (Stampfer, Tr. 831-32; PX0362 (Stampfer, Dep. at 73, 99); CX1293 (Stampfer Expert Report at 0030) (long term trials of diet and disease outcomes are often unfeasible due to the financial and participant burden required to perform such studies, but it is indisputable the randomized clinical trial is the best study design that permits strong causal inference concerning the relationship between an administered agent (whether drug or nutrient) and any specific outcome)).

633. Dr. Stampfer also testified, that the failure to act, in the absence of conclusive RCT evidence, increases the risk of forgoing benefits to the public that might have been achieved with little risk and little cost and that one should "definitely" make that potential benefit available to the public rather than withhold it. (Stampfer, Tr. 837-38).

634. In a recently published article titled "*Evidence-based criteria in the nutritional context*," Dr. Stampfer opined that the general principles of evidence-based nutrition "can provide a sufficient foundation for establishing nutrient requirements and dietary guidelines in the absence of RCTs for every nutrient and food group." (Stampfer, Tr. 831; RX5007 at 483). Dr. Stampfer also opined that because RCT study designs may not be "available" (economically or scientifically) for nutrients, "nutrient related decisions could be made at a level of certainty somewhat below that required for drugs." (RX5007 at 481).

635. Dr. Stampfer also stated in the article "*Evidence-based criteria in the nutritional context*" that some of the intellectual fathers of evidence based medicine "stressed" that evidence based medicine was "not restricted to randomized trials and meta-analyses." (RX5007 at 483). Dr. Stampfer further stated that "certain features of [evidence-based medicine] seem ill-suited to the nutrition context." (RX5007 at 479). He also opined that "to fail to act in the absence of conclusive RCT evidence increases the risk of forgoing benefits that might have been achieved with little risk and at low cost." (RX5007 at 481).

636. In the article "*Evidence-based criteria in the nutritional context*," Dr. Stampfer noted that some of the differences between the evaluation of drugs and nutrients are: "(i) medical interventions are designed to cure a disease *not* produced by their absence, while nutrients prevent dysfunction that would result from their inadequate intake; (ii) it is usually not plausible to summon clinical equipoise for basic nutrient effects, thus creating ethical impediments to many trials; (iii) drug effects are generally intended to be large and with limited scope of action, while nutrient effects are typically polyvalent in scope and, in effect size, are typically within the "noise" range of biological variability; (iv) drug effects tend to be monotonic, with response varying in proportion to dose, while nutrient effects are often of a sigmoid character, with useful response occurring only across a portion of the intake range; (v) drug effects can be tested against a nonexposed (placebo) contrast group, whereas it is impossible and/or unethical to attempt a zero intake group for nutrients; and (vi) therapeutic drugs are intended to be efficacious within a relatively short term while the impact of nutrients on the reduction of risk of chronic disease may require decades to demonstrate – a difference with significant implications for the feasibility of conducting pertinent RCTs." (RX5007 at 479; PX0362 (Stampfer, Dep. at 78)).

637. Dr. Stampfer admitted that he has made public health recommendations about foods that were not supported by RCTs. (Stampfer, Tr. 810, 813-14; PX0362 (Stampfer, Dep. at 173)).

b. Dr. Frank Sacks

638. Dr. Sacks provided the following opinion regarding the appropriate level of evidence of substantiation: appropriately analyzed results of well-designed, well-conducted, randomized, double-blinded, controlled human clinical studies, demonstrating significant changes in valid surrogate markers of cardiovascular health would be necessary (a) to substantiate that a product, including a conventional food or dietary supplement, can treat, prevent or reduce the risk of heart disease and/or (b) to support a claim that clinical studies, research, or trials prove that a product treats, prevents or reduces the risk of heart disease. In addition, Dr. Sacks opined that at least two well-designed studies, conducted by different researchers, and each showing strong results, are needed to constitute reliable evidence. (CX1291 (Sacks Expert Report at 0010-11, 0014-15)).

639. Dr. Sacks testified that most scientists in the fields of nutrition, epidemiology and the prevention of disease believe that at least two well-designed RCTs, conducted by independent researchers, and each showing strong results, are needed to constitute reliable evidence that an intervention causes a result. (Sacks, Tr. 1446; CX1291 (Sacks Expert Report at 0014-15)).

640. Dr. Sacks testified that pomegranate juice has not been proven for safety and that double-blinded, placebo-controlled tests would be necessary to prove pomegranate juice to be safe. (Sack, Tr. 1534).

641. Dr. Sacks acknowledges that in some instances, such as studies on foods, the blinding of patients is not possible, and that if a study becomes unblinded or does not have a placebo, it can still have value. (Sacks, Tr. 1435; PX0361 (Sacks, Dep. at 104-105, 111, 137)).

642. In an article titled "*The Importance of Population-Wide Sodium Reduction as a Means to Prevent Cardiovascular Disease and Stroke: A Call to Action From the American Heart Association*" published in their journal (Circulation. 2011 Mar 15;123(10):1138-43), Dr. Sacks, as one of the authors, wrote: "Some scientists still question the evidence supporting population-wide sodium reduction. Common arguments include the absence of a major trial with hard clinical outcomes. It is well-known, however, that such trials are not feasible because of logistic, financial, and often ethical considerations." (Sacks, Tr. 1561; PX0361a03). In writing about "financial considerations" in this article, Dr. Sacks conceded that he meant the cost of conducting a major trial. (Sacks, Tr. 1561).

643. Dr. Sacks has never researched whether a single fruit, such as the pomegranate, has health benefits, but instead has only studied "fruits and vegetables as a category." (PX0361 (Sacks, Dep. at 54, 56)).

644. Dr. Sacks served as the Chairman of the Design and Analysis Committee for the DASH ("Dietary Approaches to Stop Hypertension") diet sponsored by the National Heart, Lung and Blood Institute, part of the National Institute of Health. The DASH study was

a multi-center study to look at the effect of fruits and vegetables in lowering blood pressure and the effect of a total dietary approach in lowering blood pressure, including the reduction of sodium intake. The DASH diet showed that diets high in fruits and vegetables, among other things, substantially lowered blood pressure in subjects compared to the control group. (PX0361a03 at 002; PX0361 (Sacks, Dep. at 48-49); Sacks, Tr. 1417-18).

645. Dr. Sacks testified that you do not need RCTs to test the benefit of food categories that are included in a diet already tested, like the DASH diet, which includes pomegranates. However, Dr. Sacks also opined that you do need two RCTs to test pomegranate juice. (Sacks, Tr. 1546-47).

646. Dr. Sacks also testified that *in vitro* studies can be competent and reliable evidence of an agent's effect on a particular mechanism. (Sacks, Tr. 1578; PX0361 (Sacks, Dep. at 123-24)).

647. Dr. Sacks further testified that there are common clinical recommendations today that have not been proven by RCTs and that major trials with hard clinical outcomes are often not feasible because of the costs of conducting them. (Sacks, Tr. 1559-61).

c. Dr. James Eastham

648. Dr. Eastham provided the following opinion regarding the appropriate level of evidence of substantiation: qualified experts in the field of urology, including the prevention and treatment of prostate cancer, and in the field of clinical testing relating to the prevention and treatment of prostate cancer, would require claims that the POM Products treat, prevent, or reduce the risk of prostate cancer, or are clinically proven to do so, to be supported by at least one well-conducted, randomized, double-blind, placebo-controlled clinical trial involving an appropriate sample population and with an appropriate endpoint. (CX1287 (Eastham Expert Report at 006, 012)).

649. Dr. Eastham testified that even if a product is safe and might create a benefit, like a fruit juice, he would still require an RCT to justify claims that Respondents are charged with making. (Eastham, Tr. 1325-31).

650. Dr. Eastham testified that studies of disease prevention should involve 10,000 to 30,000 men and that such studies are "incredibly expensive" and in the range of $600 million. (Eastham, Tr. 1328).

651. Dr. Eastham testified additionally that animal or *in vitro* studies alone do not provide sufficient scientific evidence to support a claim that a product prevents or treats prostate cancer, even where the agent being tested is nontoxic. (Eastham, Tr. 1284-85).

652. Dr. Eastham has performed over 200 radical prostatectomies per year for a number of years before there were any RCTs showing that they worked. (Eastham Tr. 1331-32; PX0358 (Eastham, Dep. at 154-55)). Dr. Eastham performed these radical operations

without RCTs despite the fact that the side-effects of this operation are significant and include impotence, incontinence, bleeding, embolisms, and infection, plus risks of general anesthetic. (Eastham, Tr. 1331-32).

653. Dr. Eastham testified that he has removed hundreds of prostates despite all the above stated risks and without RCT substantiation, yet he would not consider the use of pomegranate juice to treat, prevent or reduce the risk of prostate cancer unless supported by RCTs. (Eastham, Tr. 1332).

d. Dr. Arnold Melman

654. Dr. Melman provided the following opinion regarding the appropriate level of evidence of substantiation: to constitute competent and reliable scientific evidence demonstrating efficacy in preventing, reducing the risk of, or treating erectile dysfunction, experts in the field of erectile dysfunction would require at least one clinical trial, involving several investigatory sites, which is well-designed, randomized, placebo-controlled, and double-blinded. (CX1289 (Melman Expert Report at 0004-05)).

655. Dr. Melman testified that the only kind of science to support claims that a product helps with erectile dysfunction are two double-blind placebo based randomized trials, conducted in two separate institutions, with a group large enough to produce a statistically significant ($p < 0.05$) result. Dr. Melman testified that you cannot properly make public claims that a product helps with erectile dysfunction in absence of such trials. (Melman, Tr. 1135, 1138-39; CX1289 (Melman Expert Report at 0008-11)).

656. Dr. Melman also testified that the men's sexual partners must also confirm the result; that for a study to claim any improvement in participants, the men must have reached orgasm; and that the sexual partner must achieve sexual satisfaction. (Melman, Tr. 1139-43).

657. Dr. Melman testified that "pomegranate juice is a drug," and therefore the FDA standard for pharmaceutical drugs should apply. (PX0360 (Melman, Dep. at 17-19); Melman, Tr. 1141).

658. Dr. Melman conceded that he has never conducted any clinical work on a food product, including pomegranates. (Melman, Tr. 1164-65).

659. Dr. Melman is developing a gene-transfer therapy for erectile dysfunction called hMaxi-K which is injected into the penis. (Melman, Tr. 1148, 1192). Dr. Melman announced to the public, in an interview with the *New York Observer*, that his hMaxi-K produced spontaneous normal erections in men suffering from erectile dysfunction. (Melman, Tr. 1154). Dr. Melman acknowledged that people have died or gotten very sick from gene-transfer therapy. (Melman, Tr. 1158).

660. While Dr. Melman testified that Respondents must have at least one clinical trial, involving several investigatory sites, which is well-designed, randomized, placebo-

controlled, and double-blinded before they can publicize the positive effects of pomegranate juice on men with erectile dysfunction, Dr. Melman publicized preliminary results of studies on his gene-transfer therapy based only on the results of an animal study. (Melman, Tr. 1149-55).

4. Testimony from Respondents' experts on whether RCTs are required

a. Dr. Denis Miller

661. Dr. Miller provided the following opinion regarding the appropriate level of evidence of substantiation: because pomegranates are a food, an appropriate level of scientific substantiation regarding the health benefit claims of pomegranates should be flexible, and consider several factors (including the risk of harm) with the desirability of getting information to the public, the validity of the science, costs of the science, and the nature of the claim. (PX0206 (Miller Expert Report at 15)).

662. Dr. Miller opined that the standard for substantiating claims for pure foods which are clearly safe need not be as rigorous as that for a new drug or anticancer agent, but should be based on reliable and competent scientific data that confirm its safety, and support a relevant and beneficial effect; and that valid, scientifically conducted basic science could be enough to support a claim, depending on the claim, so long as the product is not claimed to be a substitute for conventional drug therapies or medical care. (PX0206 (Miller Expert Report at 15); Miller, Tr. 2194).

663. Dr. Miller opined that if the product is a whole food or a derivative of a whole food and it is obviously safe, there should be a cost benefit analysis to determine whether it makes sense to report possible, or probable benefits of consumption, and to err on the side of giving more information to the public and medical community, so long as the claim does not suggest (by use of absolutes or in other ways) that an individual forgo conventional medical care or treatment based on the consumption of the product and/or suggest that the underlying science is valid. (PX0206 (Miller Expert Report at 7-8)).

664. Dr. Miller opined that retrospective or prospective observational cohort or case-control studies are not feasible to study the benefits of a food and that a double-blind, placebo controlled trial evaluating POM Products as prostate cancer protective agents would take decades and thousands of patients and would have to control for other naturally occurring, dietary antioxidants, anti-inflammatory, and anticancer agents as well as life-style activities (*e.g.*, exercise, smoking, alcohol use), genetic predisposition, racial and ethnic factors, benign prostatic hypertrophy, and other factors that might have an effect on carcinogenesis of prostate cancer. (PX0206 (Miller Expert Report at 0014)).

665. Dr. Miller opined that the claim being made about a product is relevant to the level of substantiation required. (Miller, Tr. 2195, 2210).

666. Dr. Miller opined that even if a food were marketed for the treatment or prevention of a disease, the level needed to substantiate claims about a food is more relaxed or less rigorous than it would be for a drug because with a drug, one would have to consider the safety of the agent, the efficacy of the agent, and the risk-benefit ratio. (Miller, Tr. 2210-11).

667. Dr. Miller testified that if one were claiming a fruit juice prevents prostate cancer, and there was reliable scientific data to support that claim, one could make that claim without an RCT. (Miller, Tr. 2201).

668. Dr. Miller testified that you do not need to go through the process of clinical testing and randomized clinical trials to establish the safety and efficacy of a food when there is already reliable scientific evidence supporting that. (Miller, Tr. 2205-06).

669. Dr. Miller opined that if a dietary supplement is derived from a pure food it should require the same level of substantiation as a food. In the alternative, if a dietary supplement is "a mixture of fifty different minerals and elements and vitamins," then it is different than a food and would require a different level of substantiation. (Miller, Tr. 2213).

670. Dr. Miller testified that because a food is not patentable, it is not reasonable to require the maker of a potentially beneficial foodstuff to conduct a prohibitively expensive RCT to claim that it is beneficial to health. (PX0206 (Miller Expert Report at 16)).

b. Dr. David Heber

671. Dr. Heber provided the following opinions regarding the appropriate level of evidence of substantiation: (1) double-blind placebo-controlled trials have limited usefulness for nutritional research; (2) the nutritional complexity of pomegranate juice and extract makes controlled studies less suitable for researching the health benefits of pomegranate juice and extract; (3) prospective randomized controlled trials demand that a nutrient act like a drug and that is an unreasonable requirement for nutritional studies because nutrients occur in a food matrix; and (4) the prospective randomized trial cannot practically be imposed as a requirement for nutritional science. (PX0192 (Heber Expert Report at 0013-16)).

672. Dr. Heber testified that most experts in the field of nutrition consider competent and reliable science to support health claims for pomegranate juice based upon the totality of evidence, which does not necessarily include RCTs. (Heber, Tr. 2166, 2182).

673. Dr. Heber testified that in dealing with nutrients, RCTs are often infeasible and too expensive; that the drug standard should not be applied to nutrients; and that most experts in the field of nutrition believe that RCTs have some significant drawbacks when it comes to the study of nutrient substances like pomegranates. (Heber, Tr. 1948-50).

c. Dr. Dean Ornish

674. Dr. Ornish provided the following opinion regarding the appropriate level of evidence of substantiation: it is important to carefully examine the totality of scientific evidence in determining whether or not pomegranate juice in its various forms is beneficial and that in a nutritional context, *in vitro* and animal studies may be more effective in testing the efficacy of a nutrient. (PX0025 (Ornish Expert Report at 0005); Ornish, Tr. 2327-31).

675. Dr. Ornish testified that new drugs, which always have toxicities and side effects, need to be held to a higher standard than a juice that is derived from a fruit that has been around for thousands of years. (Ornish, Tr. 2324-25, 2340, 2381).

676. Dr. Ornish testified that if a fruit or beverage is held to the standard required of drugs, no one would be able to meet that standard. No manufacturer would spend billions of dollars to test a fruit unless it is a drug like Lipitor, where one could make billions of dollars a year and it would be worthwhile to make such an investment. (Ornish, Tr. 2324-25).

677. Dr. Ornish opined that there is a world of difference between offering juice as a healthy lifestyle choice or as an *adjunct* to conventional treatments versus offering it as a replacement for conventional medical care. (PX0025 (Ornish Expert Report at 0008)).

678. Dr. Ornish also opined that "it is an extreme position to state that the therapeutic efficacy of a fruit juice or extract of pomegranate juice should be held to the same standard of evidence as a new drug." Dr. Ornish further opined that the study of pomegranates or pomegranate juice is different than studying a new drug, in which harmful side-effects, both short-term and long-term, are the rule rather than the exception. (PX0025 (Ornish Expert Report at 0008)).

679. Dr. Ornish opined that RCTs, even when conducted perfectly, do not control for all sources of bias and may inject new ones unique to RCTs. For example, in studying a fruit or food, it is hard to do double-blind, randomized, placebo-controlled trials. Once a participant is assigned to the control group, and they know what the intervention is, they can consume the food or juice anyway, whereas one would not be able to do so with an experimental drug. (PX0025 (Ornish Expert Report at 0008); Ornish, Tr. 2328-29, 2356).

680. Dr. Ornish also testified that RCTs have shown that angioplasties and stents do not prevent heart attacks or prolong life, yet the number of these procedures performed is greater than ever. (PX0025 (Ornish Expert Report at 0007); Ornish, Tr. 2380-81).

681. Dr. Ornish opined that while there are limitations to extrapolating from *in vitro* and animal studies to human studies, it is false to say this research has no value in determining therapeutic efficacy. (PX0025 (Ornish Expert Report at 0007)).

d. Dr. Jean deKernion

682. Dr. deKernion provided the following opinion regarding the appropriate level of evidence of substantiation: if you have a drug with toxicities, it is extremely important to have a test with a placebo group, because it gives one a valid measure of the toxicity of the drug. But in the case of something like fruit juice, that has low or no toxicity at all, is it not necessary to use an RCT or placebo-controlled kind of test. (deKernion, Tr. 3060).

e. Dr. Arthur Burnett

683. Dr. Burnett provided the following opinion regarding the appropriate level of evidence of substantiation: (1) because pomegranate juice is a harmless fruit product that creates no material risk of harm and assuming that drinking pomegranate juice is not advocated as an alternative to following medical advice, information of pomegranate juice's likely benefit may be communicated to consumers; and (2) studies such as double blinded, placebo-based tests are not required before permitting this information to be given to the public. (Burnett, Tr. 2272-74; PX0149 (Burnett Expert Report at 0006-07)).

684. Dr. Burnett testified that the standard of substantiation is different for a product that is directly associated as a treatment for erectile dysfunction and for a product that claims to have helpful benefits for or improves one's erectile function. (Burnett, Tr. 2260-62, 2303).

f. Dr. Irwin Goldstein

685. Dr. Goldstein provided the following opinion regarding the appropriate level of evidence of substantiation: health care practitioners who treat patients concerned with erectile health would not hold pomegranate juice to the standards of safety and efficacy traditionally required by the FDA for approval of a pharmaceutical (including performance of large, double-blind, placebo-controlled pivotal clinical trials) before recommending pomegranate juice to their patients. (PX0189 (Goldstein Expert Report at 0003, 0014)).

686. Dr. Goldstein testified that when studying pomegranate juice and its effect on erectile function, RCT studies are not necessary because the safety of natural fruit juice is not questionable. Furthermore, Dr. Goldstein questioned whether one could make a placebo pomegranate juice. By contrast, Dr. Goldstein testified that RCTs are needed for pharmaceutical drugs, which are unnatural and developed in laboratories, to assess safety and efficacy. (Goldstein, Tr. 2599-01, 2619).

687. Dr. Goldstein testified that an article he co-authored stated that RCTs are considered the criterion standard for determining causality, but that that article was written in the context of the pharmaceutical industry and pharmaceutical drugs like Viagra, Levitra and Cialis that have been studied with randomized clinical trials for determination of their safety and efficacy. Dr. Goldstein further testified that it would be ideal if there

could be randomized clinical control data for nutraceuticals, but that in reality, that is not going to happen or it is not possible. (Goldstein, Tr. 2613-14).

5. Determinations on the required level of substantiation

a. Type of claims

688. The level of scientific evidence required to support a claim depends on the claim being made. (Stampfer, Tr. 830-31; Miller, Tr. 2195, 2210).

689. Claims of efficacy can be made only when a causal relation with human disease is established. (CX1293 (Stampfer Expert Report at 0030)).

690. A claim that users of a product have a lower incidence of disease is not the same thing as a claim that use of the product caused them to have a lower incidence of disease. (Stampfer, Tr. 798).

691. A claim that studies indicate that a product lowers the risk of heart disease and diabetes does not imply that a causal link is established, *i.e.*, that the product caused users to have lower risk of heart disease and diabetes. (Stampfer, Tr. 817).

692. If the claim does not imply a causal link, for example, if the claim is that there is some evidence to suggest the possibility that nuts may reduce the risk of diabetes, then evidence short of RCTs can support that claim. (Stampfer, Tr. 830-31; CX1293 (Stampfer Expert Report at 0029-30)).

693. If the claim does not suggest (by use of absolutes or in other ways) that an individual should forgo conventional medical care or treatment based on the consumption of a safe product, one can relax the requirement for an RCT. (Miller, Tr. 2201-02; PX0206 (Miller Expert Report 7-8)).

b. Type of product

694. The level of scientific evidence required to support a claim depends on the product being promoted. (Miller, Tr. 2196, 2198; PX0206 (Miller Expert Report at 8)).

695. The potential risk of the product must be weighed against the potential benefit and harm of keeping information from the public. (Sacks, Tr. 1559; PX0361 (Sacks, Dep. at 137)). In recommending a food or drug, you have to take into account the risk of harm from the product. (Stampfer, Tr. 829).

696. RCTs are needed for pharmaceutical drugs to assess safety and efficacy because pharmaceutical drugs are unnatural, developed in laboratories, and have toxicities. (Goldstein, Tr. 2600-01, 2620; deKernion, Tr. 3060).

697. Pharmaceutical drugs, which are not known to be safe and always have toxicities and side effects, are held to a higher standard than a juice that is derived from a fruit that has been around for thousands of years. (Ornish, Tr. 2324-25, 2340, 2381; PX0025 (Ornish Expert Report at 0008); Goldstein, Tr. 2600-01, 2620; deKernion, Tr. 3060).

698. The standard applied to new drugs should not be applied to nutrients as long as the product is not claimed to be a substitute for conventional drug therapies or medical care. (PX0206 (Miller Expert Report at 15); Miller, Tr. 2194; Heber, Tr. 1948-50; PX0025 (Ornish Expert Report at 0008)).

699. Pomegranate juice is a natural fruit product with health promoting characteristics. The safety of pomegranate juice is not in doubt. (Miller, Tr. 2194, 2201; PX0206 (Miller Expert Report at 10); Heber, Tr. 1948-50; PX0025 (Ornish Expert Report at 0007)).

c. Feasibility of RCTs

700. RCTs can be beneficial, but they are not perfect and, when dealing with nutrition, they have their own set of limitations as well. (Ornish, Tr. 2329).

701. In a nutritional context, a hypothesis about disease causation can rarely, if ever, be directly tested in humans using the RCT design. (Stampfer, Tr. 832-33; PX0362 (Stampfer, Dep. at 73, 98); CX1293 (Stampfer Expert Report at 0029-30); PX0361 (Sacks, Dep. at 111, 137); PX0192 (Heber Expert Report at 0009-12)).

702. In studying a drug, RCTs are possible because placebos can be used and subjects, therefore, do not know if they are getting a drug or not. (Ornish, Tr. 2328).

703. In studying a fruit or food, it is difficult to do double-blind, randomized, placebo-controlled trials because the subjects know what they are consuming. Once a participant is assigned to the control group, and they know what the intervention is, the participant can consume the food or juice anyway, whereas one would not be able to do so with an experimental drug. (PX0025 (Ornish Expert Report at 0008); Ornish, Tr. 2328-29, 2356; Goldstein, Tr. 2600-01, 2620).

704. In a nutritional context, RCTs are extremely expensive and often not feasible because of the costs of conducting them. (Sacks, Tr. 1559-61; Stampfer, Tr. 810, 813-14; Heber, Tr. 1948-50; PX0192 (Heber Expert Report at 0013-16); Goldstein, Tr. 2613-14; (Eastham, Tr. 1328) (the standard studies for chemoprevention should involve 10,000 to 30,000 and are "incredibly expensive," costing in the range of $600 million)).

705. Because a food, unlike a pharmaceutical drug, is not patentable, it is not reasonable to require the maker of a potentially beneficial foodstuff to conduct an RCT to claim that it is beneficial to health. (PX0206 (Miller Expert Report at 16)). No manufacturer would spend billions of dollars to test a fruit unless it is a drug where one could make billions of dollars a year and was worthwhile to make such an investment. (Ornish, Tr. 2324-25).

d. Conditions where RCTs are necessary

706. RCTs are needed for a nutrient supplement if one makes a claim that the product causes the effect of treating, preventing, or reducing the risk of a disease and offers the nutrient supplement as a replacement to medical care to prevent, treat or reduce the risk of disease. (PX0206 (Miller Expert Report at 15); Miller, Tr. 2194; PX0025 (Ornish Expert Report at 0008); *see also* CX1293 (Stampfer Expert Report at 0029); Stampfer, Tr. 830-31).

707. RCTs are not required to convey information about a food or nutrient supplement where: the safety of the product is known; the product creates no material risk of harm; and the product is not being advocated as an alternative to following medical advice. (PX0149 (Burnett Expert Report at 0006-07); deKernion, Tr. 3060; Goldstein, Tr. 2600-01, 2620; PX0025 (Ornish Expert Report at 0008)).

e. Necessary substantiation

708. If a dietary supplement is derived from a pure food, it should require the same level of substantiation as a food. By contrast, if a dietary supplement is "a mixture of fifty different minerals and elements and vitamins," then it is different than a food and requires a different level of substantiation. (Miller, Tr. 2213).

709. Because pomegranate juice is a food, the appropriate level of scientific substantiation regarding health benefit claims of pomegranate juice in its various forms should be flexible, and consider several factors, including the risk of harm, the validity of the science, costs of the science, and the nature of the claim, including whether it is offered as a substitute or replacement for a conventional therapy. (Miller, Tr. at 2201; PX0206 (Miller Expert Report at 11, 15). *See also* PX0025 (Ornish Expert Report at 0005); Ornish, Tr. 2329-31).

G. Substantiation for Respondents' Heart Disease Claims

1. Substantiation standard for heart disease claims

710. Experts in the field of cardiovascular health would not require RCTs to substantiate health benefit claims for harmless pure fruit products like pomegranate juice. (Ornish, Tr. 2327-30; *see also* Miller, Tr. 2194, 2201; *but see* Sacks, Tr. 1545-48) (testifying that RCT trials are not necessary to test the benefit of food categories that are included in a diet that has already been tested, like the DASH diet; that pomegranates are in the fruit category and, thus, do not need to be tested with RCTs; but that pomegranate juice is different from pomegranates and thus held to a higher standard).

711. Experts in the field of cardiovascular health would require that a product be scientifically evaluated through rigorous scientific and clinical studies, which does not necessarily include RCTs, to make claims that the product can treat, prevent or reduce

the risk of heart disease. (Heber, Tr. 1948-49, 2058, 2085, 2166, 2182 (food products must be evaluated on the totality of the scientific evidence that is competently performed, which includes *in vitro* animal studies and human studies, along with basic science about nutritional uptake on metabolism). *But see* Sacks CX1291 (Sacks Expert Report at 0010) (requiring "well-designed, well-conducted, randomized, double-blinded, controlled human clinical studies" with strong "*p*" values)).

712. To substantiate a claim that a food or a diet supplement can treat heart disease, one needs appropriately analyzed data showing significant changes in valid surrogate markers of cardiovascular health and the study subjects must have established cardiovascular disease ("CVD") or coronary heart disease ("CHD"). To substantiate a claim that a food or a diet supplement can prevent or reduce the risk of heart disease, the study subjects may be persons with *or* without CVD or CHD. (*See* CX1291 (Sacks Expert Report at 0010-11 (also stating requirement of RCTs)).

713. The same level of evidence stated in F. 711-712 is needed to show that clinical studies, research, or trials prove that a product treats heart disease. (*See* CX1291 (Sacks Expert Report at 0011).

714. There must be a sufficient number and diversity of subjects tested in a study to conclude that the measured effect of a product on heart disease can be generalized to a larger population. The study also must be of sufficient duration to show that the effect will last. (CX1291 (Sacks Expert Report at 0014)).

2. Overview of cardiovascular disease

715. A heart attack occurs when there is a sudden rupture of inflamed plaque which covers about 50 percent of the inner surface (lumen) of a coronary vessel. (Heber, Tr. 1959).

716. Plaque is the end result of decades of damage to the blood vessel, which begins with oxidation. The process of plaque formation begins when a protein called low-density lipoprotein ("LDL") or so-called "bad cholesterol," which circulates through the blood, becomes oxidized. (Heber, Tr. 1959).

717. When the LDL cholesterol gets oxidized, the chemical nature of the protein changes, causing the protein to reside and deposit in the wall of the blood vessel, where it accumulates. (Heber, Tr. 1959; CX1358 (Aviram, Dep. at 5)).

718. Regular cholesterol passes in and out of the arteries, but the oxidized cholesterol remains there. (Heber, Tr. 1959-60).

719. Macrophages (white blood cells that respond to inflammation by digesting cellular debris) come in and they eat up this oxidized cholesterol. (Heber, Tr. 1960).

720. Macrophages have ravenous appetites which do not stop, and they continue to accumulate until they become what are called foam cells, which are full of cholesterol

and actually burst into the area, bringing in more cells and more inflammation. (Heber, Tr. 1960).

721. Oxidation is followed by inflammation, which is followed by damage to the interior of the blood vessel. This damage is detected as yellow streaks in the coronary arteries. As this process progresses, plaque forms and begins to fill those lumen. (Heber, Tr. 1960).

722. Plaque can have different characteristics; it can be stable or unstable. Unstable plaque is full of oxidized cholesterol and macrophages, reft with inflammation. (Heber, Tr. 1960).

723. By blocking inflammation and oxidation, it is possible to stabilize plaque. (Heber, Tr. 1960; PX0192 (Heber Expert Report at 0033)).

724. Inhibitors of the oxidation process are called antioxidants. (CX1358 (Aviram, Dep. at 5)). Punicalagin, an ellagitannin, is the most abundant polyphenol that accounts for more than 50% of the antioxidant activity. (PX0025 (Ornish Expert Report at 0008)).

725. Several studies have indicated that pomegranate juice has antioxidant and anti-atherosclerotic properties due to the presence of multiple polyphenols such as tannins, flavonols, anthocyanins and ellagic acid. (PX0025 (Ornish Expert Report at 0008)).

726. Antioxidants are well known to enhance the biological actions of nitric oxide ("NO") by virtue of their capacity to improve endothelial NO synthase ("eNOS"). (PX0055 at 0002; PX0056).

727. Antioxidants are well known to increase and prolong cellular concentrations of NO by protecting it from oxidation. Antioxidants accomplish this task by neutralizing free radicals. (PX0055 at 0002; PX0056 at 0002; PX0057; PX0059 at 0001, 0004; PX0190 at 0006).

728. The negative effects on NO caused by shear stress (the force of friction caused by perturbed blood flow around atherosclerosis) and on the expression of oxidation-sensitive genes can be mitigated by antioxidants. (PX0055 at 0002; PX0056).

729. Dr. Louis Ignarro demonstrated that POM Juice and POMx were able to attenuate the effects of perturbed shear stress and atherogenisis. However, POMx was significantly more effective at enhancing the expression of endothelial nitric oxide synthase (eNOS – an enzyme necessary for cellular NO production), decreasing oxygen-sensitive gene expression, and reducing lesion size. (PX0056).

730. Antioxidants enhance the bioavailability of NO. (Heber, Tr. 1816; CX0908 at 0001, 0002; PX0058).

731. NO helps maintain healthy blood vessels, which improves blood flow to almost every organ in the body, including the heart. (Heber, Tr. 1816, 1969).

3. Respondents' basic science studies

732. Respondents have sponsored many published studies in cellular and animal models evaluating the effects of pomegranate juice and/or its extracts on cardiovascular function. (PX0007; PX0008; PX0010; PX0015; CX0543; PX0017; PX0022; PX0055; PX0056, PX0057; PX0058; PX0059; CX0053).

a. Dr. Aviram's *in vitro* and *in vivo* studies

733. The earliest heart studies on pomegranate juice were carried out by Dr. Aviram at the Technion Institute in Israel. (Heber, Tr. 1957).

734. Dr. Aviram is a professor and head of the Lipid Research Laboratory at the Technion Faculty of Medicine, Rappaport Institute for Research in the Medical Sciences and Rambam Medical Center, in Haifa, Israel. (CX1116 at 0001).

735. Dr. Aviram is considered an internationally renowned researcher, pioneer, and one the leading experts in the world on cholesterol, lipid oxidation and the protective role of dietary antioxidants related to cardiovascular disease. (Heber, Tr. 1957-58).

736. Dr. Frank Sacks, Complaint Counsel's expert on cardiovascular health, acknowledges that Dr. Aviram's basic science is good and that Technion is a good research institution. (Sacks, Tr. 1571).

737. For the last 30 years, Dr. Aviram's major research focus has been on dietary antioxidants and antioxidants in general, especially their role in cardiovascular disease. (CX1358 (Aviram, Dep. at 5)).

738. Before studying pomegranates, Dr. Aviram examined a number of antioxidants from plants, including lycopene from tomatoes, green tea, citrus fruits, and red wine. (Heber, Tr. 1958).

739. Dr. Aviram published a red-wine study, which explained partially the "French paradox," that people in France, even though they eat fatty foods like people in Finland, they do not get heart attacks in France compared to Finland. It was shown epidemiologically that it has to do with drinking red wine, because red wine contains antioxidants from the skin of the grape. (CX1358 (Aviram, Dep. at 5)).

740. Dr. Aviram was approached by POM and asked to do the same type of study that he did for red wine, and other fruits and vegetables, but now for pomegranates. (CX1358 (Aviram, Dep. at 6)).

741. After a year of studying in 1998 or 1999, Dr. Aviram concluded that pomegranate juice had greater antioxidant potencies than red wine. (CX1358 (Aviram, Dep. at 6)).

742. High-density lipoprotein cholesterol ("HDL" or so-called "good cholesterol") contains an antioxidant enzyme, called "paraoxonase" or "PON1" which acts to protect the body against oxygen radicals. (Heber, Tr. 1961).

743. Dr. Aviram found that pomegranate juice benefits the activity of paraoxonase or PON1 by increasing its binding to HDL cholesterol. (Heber, Tr. 1961).

744. Beginning in 2000 and continuing until as recently as 2010, Dr. Aviram's *in vitro* and *in vivo* research on pomegranate juice and/or POMx pills showed reduction in oxidation of LDL cholesterol; lessening the uptake of oxidized and native LDL cholesterol by macrophage foam cells; diminishing the size of atherosclerotic lesions and foam cells; inhibition of macrophage cholesterol biosynthesis; decrease in macrophage oxidative stress; protection against cellular lipid peroxidation; reduction of serum lipids and glucose levels; improvement of PON1; and lessening of platelet aggregation. (PX0007; PX0008; PX0010; PX0015; CX0543; PX0017; PX0022; CX0053).

745. Dr. Sacks acknowledges that some of Respondents' *in vitro* studies have shown pomegranate juice's favorable effects on the mechanisms involved in cardiovascular disease and that *in vitro* studies, like Dr. Aviram's, can be competent and reliable evidence of an agent's effect on a particular mechanism. (Sacks, Tr. 1578).

746. Dr. Sacks agrees that Dr. Aviram's *in vitro* studies showed that pomegranate juice inhibits macrophage uptake of oxidized LDL, which is one component of atherosclerosis, and a significant reduction in atherosclerotic vessels, but that changes in macrophage levels are not a reliable surrogate marker of heart health. (Sacks, Tr. 1572, 1579, 1622).

b. *In vitro* and *in vivo* studies on nitric oxide

747. Respondents have also sponsored research in the area of nitric oxide and understanding its role in cardiovascular health. (PX0055; PX0056; PX0057; PX0058; PX0059).

748. Respondents have sponsored *in vitro* and *in vivo* research by Dr. deNigris, Dr. Napoli, and, Dr. Ignarro to conduct basic research on the effects of pomegranate juice on nitric oxide in the human body. (PX0055; PX0056; PX0057; PX0058; PX0059).

749. Nitric oxide is produced by the cells lining the heart blood vessels and by the cells lining the blood vessels of many organs around the body. Nitric oxide opens up tiny blood vessels and helps, among other things, preserve blood flow to the heart. (Heber, Tr. 1966-68).

750. Nitric oxide is beneficial in that it improves blood flow to almost every organ in the body that is dependent upon blood flow. (Heber, Tr. 1969-70).

751. In their *in vitro* and *in vivo* studies, Dr. deNigris, Dr. Napoli, Dr. Ignarro, and others found that pomegranate juice and/or POMx pills demonstrated: increasing and preserving levels of nitric oxide and decreasing expression of genes associated with stress and progression of atherosclerosis; reducing LDL oxidation, size of atherosclerotic plaques, and formation of foam cells; reversing effects of shear stress, which can damage the endothelial cells or thin layer of cells that line the interior of blood vessels; decreasing cellular production and release of oxygen radicals in the vascular wall; inhibiting activation of oxidation-sensitive genes; and improving biological activity of nitric oxide. (PX0055; PX0056; PX0057; PX0058; PX0059).

c. Experts' analysis on Respondents' basic research

752. Complaint Counsel's expert witness, Dr. Sacks, opined the following regarding Respondents' basic research:

- *in vitro* studies do not provide reliable scientific evidence of what effects a treatment will have inside the human body;
- animal studies cannot be generalized to describe what effects a treatment has on human subjects and, thus, do not provide reliable scientific evidence on whether an agent can treat, prevent or reduce the risk of cardiovascular disease in humans;
- *in vitro* and animal studies need to be replicated in humans to show an effect on preventing or treating a disease; and
- there is value in conducting *in vitro* and animal studies because it is possible to isolate mechanisms of action and accomplish toxicity or safety testing.

(CX1291 (Sacks Expert Report at 0015-16); PX0361 (Sacks, Dep. at 91)).

753. Respondents' expert witness, Dr. Ornish, opined the following regarding Respondents' basic research:

- *in vitro* and animal studies are important in considering the totality of evidence in determining whether or not pomegranate juice in its various forms is beneficial; and
- *in vitro* and animal studies have value in determining therapeutic value, but there are limitations to extrapolating from *in vitro* and animal studies to humans.

(PX0025 (Ornish Expert Report at 005, 007)).

d. Determinations on Respondents' basic research

754. Respondents' basic and animal science shows that pomegranate juice and/or its extract may be beneficial toward cardiovascular health by, among other things, reducing the oxidation of LDL cholesterol and its uptake, diminishing the size and scope of atherosclerotic legions, macrophages, and foam cells, lessening platelet aggregation, and enhancing the presence of nitric oxide. (PX0007, PX0008, PX0010, PX0015, CX0543, PX0017, PX0022, CX0053, PX0055, PX0056, PX0057, PX0058, PX0059).

755. The basic research relied upon by Respondents is part of the totality of evidence that must be examined in evaluating the effects of the POM Products, but *in vitro* and animal studies need to be replicated in humans to show an effect on preventing or treating a disease. F. 752-753.

4. Overview of Respondents' clinical trials and surrogate markers in clinical studies on heart disease

756. Respondents have sponsored approximately ten published studies on humans evaluating the effect of pomegranate juice and/or its extracts on cardiovascular health. (PX0004; PX0005; CX0611; PX0014; PX0020; PX0021; PX0023; PX0038; PX0127; PX0139). Two of these published human studies, the Davidson CIMT Study and the Ornish MP Study (discussed below), were designed as RCTs. In addition, Respondents conducted several unpublished human studies on POM Juice and POMx Pills related to cardiovascular health, also discussed below.

757. Respondents worked with Dr. Aviram and two other pre-eminent research scientists in the field of cardiovascular health to evaluate the potential benefits of pomegranate juice and/or its derivatives in humans: Dr. Dean Ornish and Dr. Michael Davidson. (PX0014; PX0023).

758. The qualifications of Dr. Ornish, who also testified as an expert for Respondents, are set forth in F. 227-230.

759. Dr. Davidson is the Clinical Professor of Medicine and Director of Preventive Cardiology at the University of Chicago Medical Center, Medical Director of Radiant Research, Chicago, and a practicing physician who typically treats patients with cholesterol abnormalities, coronary artery disease, or clinical atherosclerosis. Dr. Davidson has been involved, in some manner, in over 700 clinical studies over the past 25 years. (JX0003 at 0004; CX1134 at 0001; CX1336 (Davidson, Dep. at 218-21)).

760. Dr. Sacks regards Dr. Davidson as one of the foremost clinical researchers in the cardiovascular field with a superb reputation for top-quality clinical trial research in cardiovascular disease. (Sacks, Tr. 1490).

761. In considering whether a study shows a benefit to cardiovascular disease, it is important to look at what endpoints have been measured. There are two kinds of endpoints: direct endpoints and surrogate markers. (CX1291 (Sacks Expert Report at 0013)).

762. In the case of heart disease, direct endpoints are heart attack, unstable angina, or the need for coronary artery bypass or angioplasty. Surrogate markers are measurements that are closely linked to the disease process such that a change in a surrogate marker can confidently be predictive of a change in the disease. (CX1291 (Sacks Expert Report at 0013)).

763. Blood pressure and LDL cholesterol are recognized as valid surrogate markers of cardiovascular health in clinical guidelines and by the FDA. (Ornish, Tr. 2334; Sacks, Tr. 1441; CX1291 (Sacks Expert Report at 0013)).

764. LDL cholesterol is a risk factor for heart disease, but is not actually heart disease. For that reason, Dr. Ornish testified, LDL cholesterol cannot be a valid surrogate. (Ornish, Tr. 2334). Dr. Heber further explained, when a person has a biomarker such as high LDL cholesterol which increases his or her risk, it is very distal or far away from the actual event of a heart attack which may be affected by many other factors, such as inflammation and oxidation. (Heber, Tr. 1974). There are a number of people who have low cholesterol levels, but get heart disease. (Ornish, Tr. 2334-35). About 50 percent of the people who die from a heart attack actually have cholesterol in the normal range. (Heber, Tr. 1974). There are people who have high cholesterol levels who do not have heart disease, and the same is true with high blood pressure. (Ornish, Tr. 2334-35).

765. While the FDA, for the purposes of drug registration and testing, only accepts a limited number of surrogate markers, the number of indicators that physicians and scientists use is much greater and indicators can be at many points along the pathway of heart disease. (Heber, Tr. 1973).

766. Most experts (but not all) also recognize C-reactive protein, HDL cholesterol, and triglycerides as valid surrogate markers. (Sacks, Tr. 1441; CX1291 (Sacks Expert Report at 0013)).

767. Carotid intima media thickness, or "CIMT," testing measures the combination of the vessel muscle and atherosclerosis (arterial plaque). There is a moderate connection between a reduction in the intima-media thickness and a reduction in atherosclerosis. (CX1291 (Sacks Expert Report at 0013); Sacks, Tr. 1442-43)).

768. Dr. Sacks acknowledged that the CIMT test is "a worthy test" and is relevant to cardiovascular health, but noted there is disagreement among experts on the prognostic value of CIMT. (Sacks, Tr. 1589-90; CX1291 (Sacks Expert Report at 0013)).

769. Dr. Sacks opined that if CIMT measures show consistent improvement, this would be an indicator that a treatment may be beneficial, but that he would be reluctant to rely on

CIMT improvements alone, if these were the only evidence that an intervention treated heart disease. Dr. Sacks referenced a recent article in a leading cardiology journal that analyzed CIMT in relation to cardiovascular events and found that among a meta-analysis of 41 randomized trials, "there was no significant relationship between IMT regression and CHD [coronary heart disease] . . . events . . . CBV [cerebrovascular] events. . . and for all-cause death." From this, Dr. Sacks opined, there is broad consensus that at least two types of imaging studies must be obtained to make inferences on benefit to cardiovascular disease. (CX1291 (Sacks Expert Report at 0014)).

770. Myocardial perfusion (MP) is a measure of blood flow to the heart. Dr. Sacks opined that change in MP is not recognized as a surrogate marker of therapeutic effects on CHD. Even where blood flow is shown to be improved, it will not necessarily result in improved cardiovascular health, such as reductions in heart attack and stroke. (CX1291 (Sacks Expert Report at 0020-21)).

771. Dr. Ornish opined that when researchers measure myocardial perfusion, researchers are actually measuring what matters most. How much blood flow the heart receives is really the "bottom line" in coronary heart disease. (PX0025 (Ornish Expert Report at 0012); Ornish, Tr. 2334-35).

5. Cardiovascular studies sponsored by Respondents

a. Aviram 2000 Study

772. In 2000, in a study titled, "*Pomegranate juice consumption reduces oxidative stress, atherogenic modifications to LDL, and platelet aggregation: studies in humans and in atherosclerotic apolipoprotein E-deficient mice*" by Aviram M, Dornfeld L, Rosenblat M, Volkova N, Kaplan M, Coleman R, Hayek T, Presser D, and Fuhrman B (Am. J. Clin. Nutr. 2000: 71;1062-76), ("Aviram 2000 Study "), Dr. Aviram and his colleagues examined the effect of pomegranate juice consumption on the atherogensis process (the development of fatty plaques in the walls of arteries) in humans, animal models, and cells.

773. The Aviram 2000 Study consisted of two human studies: one involving 13 subjects who consumed pomegranate juice daily for two weeks; and one involving 3 subjects who consumed increasing doses for 10 weeks. The authors concluded that the study "showed the antiatherogenic capabilities of PJ [pomegranate juice] in 3 related components of atherosclerosis, plasma lipoproteins, arterial macrophages, and blood platelets. The potent antioxidative capacity of PJ against lipid peroxidation may be the central link for the antiatherogenic effects of PJ on lipoproteins, macrophages, and platelets." (PX0004 at 0001-02, 0004-05, 0014).

b. Aviram ACE/BP Study

i. About the Aviram ACE/BP Study

774. In 2001, in a study titled, "*Pomegranate juice consumption inhibits serum angiotensin converting enzyme activity and reduces systolic blood pressure*" by Aviram M and Dornfeld L, (Atherosclerosis 158 (2001) 195-198) ("Aviram ACE/BP Study"), Dr. Aviram and his co-workers conducted a study with ten elderly, hypertensive patients who drank 50 ml. of pomegranate concentrate daily, for two weeks. (CX0542 at 0002; CX1358 (Aviram, Dep. at 21)).

775. The Aviram ACE/BP Study measured angiotensin converting enzyme ("ACE") activity and blood pressure. (CX0542 at 0001). ACE is an enzyme that alters the function of angiotensin, which relates to blood pressure for each patient. (Stampfer, Tr. 742).

776. The Aviram ACE/BP Study was unblinded and had no control group; instead, each patient's "before" measures were compared to his or her "after" measures. (CX1358 (Aviram, Dep. at 22-24); CX0025 at 0012).

777. According to the Aviram ACE/BP Study, seven of the ten patients experienced a statistically significant 36% reduction in serum ACE activity from their baseline measure. (CX0542 at 0001). The article does not reveal what happened to the ACE levels of the other three patients or analyze the overall results in all ten patients. (CX1291 (Sacks Expert Report at 0016-17); CX0542 at 0002-03; *see also* Stampfer, Tr. 741-42; CX1293 (Stampfer Expert Report at 0017-18)). Dr. Aviram testified that there was "no effect" from pomegranate juice on the other three patients' ACE levels. (CX1358 (Aviram, Dep. at 23)).

778. The Aviram ACE/BP Study reports that all ten patients experienced a statistically significant 5% reduction in systolic blood pressure from their baseline blood pressure measure. (CX0542 at 0002-03; CX1291 (Sacks Expert Report at 0016-17)).

779. The Aviram ACE/BP Study concludes that, "pomegranate juice consumption can offer a wide protection against cardiovascular disease." (CX0542 at 0003).

ii. Experts' analysis on the Aviram ACE/BP Study

780. Complaint Counsel's experts criticized the Aviram ACE/BP Study on the following grounds:

- the sample size of ten patients is too small to provide reliable evidence that the observed effects would be generally applicable to a larger population

- the two-week period of the study was too short to provide reliable

evidence that the reported improvement in ACE activity and blood pressure would be enduring; and

- ACE (one of the study endpoints) is not a recognized surrogate marker of cardiovascular disease.

(CX1291 (Sacks Expert Report at 0017); *see also* Stampfer, Tr. 748).

781. Complaint Counsel's experts also testified that although blood pressure reduction is a validated surrogate for heart disease, the Aviram ACE/BP Study does not provide competent and reliable evidence to support a claim of effectiveness for heart disease because it was not a blinded, placebo-controlled study. According to these experts, given the lack of a control group, it is not possible to conclude what caused the reported improvements in the subjects' blood pressure levels; and without a control group, this study was simply an observational study on patients given pomegranate juice concentrate. (CX1291 (Sacks Expert Report at 0017); Sacks, Tr. at 1452-54; *see also* Stampfer, Tr. 748, 771; CX1293 (Stampfer Expert Report at 0019)).

782. Dr. Ornish's response to Complaint Counsels' experts' criticism (F. 780-781) is that the Aviram ACE/BP Study should be viewed in the larger context of other studies in this area, as its findings are congruent with, and supportive of, other research. (PX0025 (Ornish Expert Report at 0009)).

783. Dr. Ornish testified that there is a common misconception that a larger study is a better study, but the opposite can be argued. When a study has a smaller number of patients, the treatment has to be that much more powerful and that much more consistent for it to be statistically significant. (Ornish, Tr. 2362-63; CX1339 (Ornish, Dep. at 22-23)).

784. Dr. Aviram explains that comparing the statistics from each patient after treatment to his or her own statistics before treatment is a valid method to conduct a study. (CX1348 (Aviram, Dep. at 12-13)).

785. A study with a small number of subjects or conducted without a placebo does not weaken the importance of the result, especially if the results are in agreement with previously published findings conducted through *in vitro*, mechanistic, and animal models. (CX1348 (Aviram, Dep. at 18)).

iii. Determination on the Aviram ACE/BP Study

786. The Aviram ACE/BP Study does not provide competent and reliable scientific evidence to support claims that the POM Products treat, prevent or reduce the risk of heart disease. (*See* F. 774-785).

c. Aviram CIMT/BP Study

i. About the Aviram CIMT/BP Study

787. The carotid arteries are located on each side of the neck and provide the main blood supply to the brain. Carotid artery stenosis ("CAS") is a narrowing or constriction of the inner surface (lumen) of the carotid artery, usually caused by atherosclerosis. (JX0003 at 0001).

788. Stenosis occurs when a person has more than a 50 percent blockage in one of the carotid arteries. To remove a blockage in the carotid artery, a person undergoes an operation called an endarterectomy, where the buildup is removed and a graft is placed in the artery. CAS is a risk factor for heart disease. (Heber, Tr. 1963).

789. In 2004, Dr. Aviram and his co-workers investigated, among other things, the effects of pomegranate juice consumption by patients with CAS in a study titled, "*Pomegranate juice consumption for 3 years by patients with carotid artery stenosis reduces common carotid intima-media thickness, blood pressure and LDL oxidation*" by Aviram M, Rosenblat M, Gaitini D, Nitecki S, Hoffman A, Dornfeld L, Volkova N, Presser D, Attias J, Liker H, and Hayek T, (Clin Nutr. 2004; 23:423-33), ("Aviram CIMT/BP Study"). (CX0611).

790. In the Aviram CIMT/BP Study, a group of ten patients with severe CAS consumed 50 ml. of concentrated pomegranate juice daily for one year and five of them continued for up to three years. A second group of nine patients who did not consume pomegranate juice acted as a control. (CX0611 at 0001-02).

791. In the Aviram CIMT/BP Study, in the control group that did not consume pomegranate juice, the patients' carotid intima-media thickness increased by 9% during one year, whereas, pomegranate juice consumption resulted in a significant CIMT reduction, by up to 30%, after one year. (CX0611).

792. In the Aviram CIMT/BP Study, in two out of the ten patients on pomegranate juice (after 3 and 12 months) due to clinical deterioration, carotid endartherectomy surgery was performed. Their carotid lesions were analyzed and compared to lesions obtained from seven patients that did not consume pomegranate juice (not the patients of the placebo group). The cholesterol content in carotid lesions from the two patients that consumed pomegranate juice was lower by 58% and 20%, respectively, in comparison to lesions obtained from CAS patients that did not consume pomegranate juice. The lipid peroxides content in lesions obtained from the patients after pomegranate juice consumption for 3 or 12 months was significantly reduced by 61% or 44%, respectively, as compared to lesions from patients that did not consume pomegranate juice. (PX0025 (Ornish Expert Report at 0011)).

793. Dr. Ornish testified that the findings in the Aviram CIMT/BP Study suggest that oxidative stress, including oxidation of LDL to a form that makes it more likely to cause arterial blockages and cause foam cell production in macrophages (macrophage-derived foam cells play integral roles in all stages of atherosclerosis) may have been reduced by pomegranate juice consumption in these patients. (PX0025 (Ornish Expert Report at 0011)).

794. The Aviram CIMT/BP Study reports that the pomegranate juice group members' systolic blood pressure was significantly ($p < 0.05$) reduced by 12% after one year of pomegranate juice consumption compared to their baseline values. In the group that did not consume pomegranate juice, blood pressure was unchanged. (CX0611 at 0005).

795. The CIMT and blood pressure changes described in the Aviram CIMT/BP Study are *within-group* analyses. The Study did not provide any *between-group* statistical analysis, that is, analysis of changes in CIMT and blood pressure between the active and control groups at the end of the study. (Sacks, Tr. 1456-57; CX0163 at 0017 (stating that between group analysis was not performed for any of the outcomes)). Dr. Aviram explained that each subject in the study served as his or her own control. (CX1358 (Aviram, Dep. at 27-28, 32)).

796. The Aviram CIMT/BP Study concluded: "pomegranate juice consumption (by patients with carotid artery stenosis) possess anti-atherosclerotic properties, as it substantially decreased serum oxidative stress and, in parallel, reduced common carotid intima-media thickness." (CX0611 at 0009).

797. The Aviram CIMT/BP Study also concluded that the "results of the present study thus suggest that PJ [pomegranate juice] consumption by patients with CAS decreases carotid IMT and systolic blood pressure and these effects could be related to the potent antioxidant characteristics of PJ polyphenols." (CX0611 at 0002).

ii. Experts' analysis on the Aviram CIMT/BP Study

798. Dr. Sacks testified that a qualified scientist would not be able to conclude with any credibility that the Aviram CIMT/BP Study's reported improvements in the treatment group were caused by their consumption of pomegranate juice and not some other factor because of: the lack of a randomized, placebo-controlled group; the fact that the patients in the active and control groups received different treatment; the small sample size, and the lack of any between-group statistical analysis. (Sacks, Tr. at 1459, 1585; CX1291 (Sacks Expert Report at 0019)).

799. Dr. Sacks concedes that he has no basis to disagree with Dr. Aviram's numbers. (Sacks, Tr. 1589-90).

800. Dr. Stampfer concluded the Aviram CIMT/BP Study does not support Respondents' heart disease prevention and treatment claims or their lower blood pressure claims. (CX1293 (Stampfer Expert Report at 0018)).

801. Dr. Ornish responds to Complaint Counsels' experts' criticism (F. 798-800) that the Aviram CIMT/BP Study should be viewed in the larger context of other studies in this area, as its findings are congruent with and supportive of other research. (PX0025 (Ornish Expert Report at 0010-11)).

802. Dr. Ornish agreed that the Aviram CIMT/BP Study was limited in scope and opined: "Thus, while not at all conclusive, the study suggests a benefit." He further testified that the Aviram CIMT/BP Study (2004) was "very provocative and interesting and laid the groundwork for even more conclusive studies." (PX0025 (Ornish Expert Report at 0010-11); PX0355 (Ornish, Dep. at 107)).

803. Dr. Heber also testified that small studies can be more informative than large studies. (Heber, Tr. 1963).

iii. Determination on the Aviram CIMT/BP Study

804. The Aviram CIMT/BP Study does not provide competent and reliable scientific evidence to support claims that the POM Products treat, prevent or reduce the risk of heart disease. (*See* F. 789-803).

d. Ornish MP Study

805. Dr. Dean Ornish and the Preventative Medicine Research Institute ("PMRI") conducted two studies for Respondents: (1) Sumner M, et al., *Effects of Pomegranate Juice Consumption on Myocardial Perfusion in Patients with Coronary Heart Disease*, 96 Am. J. Cardiology 810 (2005) ("Ornish MP Study") (CX1198; *see* JX0003 ¶ B.16); and (2) the Ornish CIMT Study (unpublished, 2005). (CX0754; *see* JX0003 ¶ B.16).

806. These studies (F. 805) were the only studies ever conducted by Dr. Ornish to consider whether a single food product has health benefits. (Ornish, Tr. 2464).

807. The contract setting forth the terms of the two studies conducted by Dr. Ornish (F. 805) was a September 19, 2003, letter agreement between the Resnicks, as Trustees of the Stewart and Linda Resnick Revocable Trust, and Dr. Ornish's organization, PMRI. (CX0613 at 0001). Attached to the letter agreement were protocols for the two studies. Although the Ornish MP Study budget was $708,436, and the CIMT Study budget was $496,390, the funding of these studies was cut short. (Ornish, Tr. 2431-35, 2436, 2441, 2454).

i. About the Ornish MP Study

808. In the Ornish MP Study, Dr. Ornish and his colleagues investigated whether the daily consumption of pomegranate juice for three months would affect myocardial perfusion (or blood flow) in 45 patients who had coronary heart disease and myocardial ischemia

(narrowing of the arteries) in a randomized, placebo-controlled, double-blind study. (PX0023 at 0001; Ornish, Tr. 2336).

809. In the Ornish MP Study, patients were randomly assigned into one or two groups: a pomegranate juice group (240 ml./day, approximately 8 ounces) or a placebo group that drank a beverage of similar caloric content, amount, flavor, and color. (PX0023 at 0001-02).

810. The Ornish MP Study provides data on three imaging measures at baseline and three months for myocardial perfusion: the summed rest score, or "SRS" (imaging results before the pharmacologic or exercise challenge), the summed stress score, or "SSS" (imaging results after the pharmacologic or exercise challenge) and the summed difference score, "SDS" (calculated by subtracting the SRS from the SSS). (CX1198 at 0003 (Table 2); CX1291 (Sacks Expert Report at 0020)).

811. The Ornish MP Study indicated that after three months there was a significant (p = 0.05) improvement of 17% in the SDS score in the POM Juice group, as compared to an average worsening of 18% in the control group. The comparative benefit of the pomegranate juice group to the placebo group in the Ornish MP Study was about 35 percent. (PX0023 at 0001; Ornish, Tr. 2337-38; Heber, Tr. 1972).

812. Those differences (F. 811) were statistically significant and the results were published in the *American Journal of Cardiology*. (PX0023; Ornish, Tr. 2337-39; Heber, Tr. 1971-72).

813. The Ornish MP Study also indicated that there were no statistically significant differences between the two groups in SSS and SRS, and no significant changes in blood pressure, cholesterol, LDL, HDL, or triglycerides. (CX1198 at 0003-04, Table 3 (notation below table); CX1291 (Sacks Expert Report at 0024)).

814. A conclusion of the Ornish MP Study was that "[t]he results of this study demonstrate, for the first time, that daily consumption of pomegranate juice for 3 months may decrease myocardial ischemia and improve myocardial perfusion in patients who have ischemic CHD [coronary heart disease] as measured by the SOS." (PX0023 at 0004).

815. Another conclusion of the Ornish MP Study was that "[a]lthough the sample in this study was relatively small, the strength of the design and the clinically significant and statistically significant improvements in myocardial perfusion observed in the experimental group over a rather short period suggest that daily consumption of pomegranate juice may have important clinical benefits in this population. (PX0023 at 0004).

816. The American Heart Association ("AHA") rejected the Ornish MP Study abstract in August 2004. Dr. Ornish asked the AHA's chairman of scientific sessions to reconsider, but the chairman responded that "[m]ultiple qualified, blinded graders scored this abstract below acceptable range." (CX0672, CX0680).

817. In November 2004, the *Journal of the American Medical Association* ("JAMA") rejected the Ornish MP Study manuscript. In response to Dr. Ornish's request for feedback, the Deputy Editor of JAMA responded that "the study appears very preliminary, with small sample size, apparent baseline imbalances between groups, use of an intermediate endpoint as main outcome measure, and modest differences with large variability." (CX0699 at 0001-02).

818. Dr. Ornish then submitted the Ornish MP Study manuscript to the *American Journal of Cardiology*. The editor accepted it without external peer-reviews. (CX1339 (Ornish, Dep. at 200); CX0715).

ii. Experts' analysis on the Ornish MP Study

819. In trial testimony and in his expert report, Dr. Ornish acknowledged that "some problems" occurred during the Ornish MP Study that were not "optimal." (Ornish, Tr. 2394; PX0025 (Ornish Expert Report at 0016)).

820. In the Ornish MP Study, although 41 patients completed the study, the published report provided data on only 39 patients. Complaint Counsel's experts opined that alterations in the original sample size may be critical when there is a borderline "*p*" value. (CX1291 (Sacks Expert Report at 0022); Sacks Tr. 1478-79; Ornish, Tr. 2394; *see* CX1198 at 0003 (Table 2); CX0664 at 0001).

821. Dr. Ornish agrees that a mistake was made in the Ornish MP Study in not reporting data on 41 patients, but opined that when data on all 41 patients was analyzed, the difference in SDS remained statistically significant and, therefore, the conclusions of the study remain valid. If anything, according to Dr. Ornish, the results were more statistically significant and even stronger because the sample size was slightly larger. (PX0025 (Ornish Expert Report at 0015); Ornish, Tr. 2347-48; 2394).

822. Dr. Sacks criticized the Ornish MP Study because two subjects in the placebo group did not receive a placebo treatment. They were tested at baseline and three months, with no intervention, and their data was included in the final study results. (Sacks, Tr. 1475-77; CX1339 (Ornish, Dep. at 168-70); CX0580 (patients' names *in camera*)).

823. Dr. Ornish explained that, initially, the two patients had been randomized to the control group in the Ornish MP Study and their measurements taken at baseline. As a result of funding issues, however, the study was put on hold. Three months later, the myocardial perfusion study resumed. Because these patients were already in the control group and their measurements taken at baseline, the decision was made to include them in the control group. Dr. Ornish explained his rationale for doing so as follows: "effectively, having nothing is the same as having a placebo beverage. I think it is probably worth putting in context that in any study there are things that are not optimal because you are dealing with human beings and all the vagaries of that and particularly in a study where the funding was changed midstream . . . . But the question is whether those things are

considered likely to have impacted the validity of the study, including in this case the answer is no." (CX1339 (Ornish, Dep. at 169-71); PX0025 (Ornish Expert Report at 0016)).

824. Complaint Counsel's experts criticize the Ornish MP Study on the additional ground that that six patients were unblinded before their three-month test dates – meaning the study patients discovered which beverage they were consuming. Dr. Ornish testified that the unblinding of the patients did not undermine the validity of the study or its conclusions. Dr. Ornish further testified that the expectation that an intervention is beneficial has the potential for confounding the outcome of a study, but such an outcome was unlikely to have occurred in this study because at the time that the study was conducted, there was not an awareness in the general population that pomegranate juice was beneficial or even that the subjects were drinking pomegranate juice (the study was titled a "beverage study"). (Ornish, Tr. 2345-46, 2403-09; (CX1339 (Ornish, Dep. at 146-49); PX0025 (Ornish Expert Report at 0016)).

825. Drs. Sacks and Stampfer testified that the Ornish MP Study did not use a recognized surrogate marker of heart disease. (CX1291 (Sacks Expert Report at 0020-21); Sacks, Tr. 1464 (myocardial perfusion, a measure of blood flow, is not used as the primary outcome in studies of treatment efficacy for coronary heart disease); Stampfer, Tr. 771-72 (blood flow is a research tool but not a recognized surrogate marker)). Even where blood flow is shown to have been improved, it will not necessarily result in improved cardiovascular health, such as reductions in heart attack and stroke. (CX1291 (Sacks Expert Report at 0020-21)).

826. Dr. Sacks also testified that proper blood flow from the coronary artery and to the heart is fundamental to lowering the risk of cardiovascular disease. (Sacks, Tr. 1593).

827. Dr. Ornish opined that blood flow is essential to life, an important measure of heart disease, and the "bottom line" in coronary heart disease (along with how well the heart is pumping blood) and, thus, when researchers measure myocardial perfusion, researchers are actually measuring what matters most. (PX0025 (Ornish Expert Report at 0012); Ornish, Tr. 2331-35).

828. Dr. Ornish further explained: Blood carries oxygen and nutrients that feed the heart. If the blood flow the heart (perfusion) is reduced, then the heart is no longer receiving enough blood flow to maintain itself. Coronary heart disease, which is the most common form of heart disease, occurs when the heart does not get enough blood to fuel itself and blood carries oxygen, which is the fuel for the heart. If the reduction in blood flow is temporary, then the person often experiences angina, or chest pain. If this reduction in blood to the heart lasts more than a few hours, then that portion of the heart that is underperfused may die and turn in to scar tissue – this is commonly referred to as a "heart attack." (PX0025-0012; Ornish, Tr. 2331-35).

829. Respondents' experts testified that in comparing myocardial perfusion and LDL cholesterol, myocardial perfusion is more closely connected as a surrogate marker for

cardiovascular disease. When a person has a biomarker like high LDL cholesterol which increases his or her risk, that is far away from the actual event of a heart attack, which may be affected by many other factors, such as inflammation and oxidation. There are a number of people who have low cholesterol levels, but get heart disease. About 50 percent of the people who die from a heart attack actually have cholesterol in the normal range. There are people who have high cholesterol levels who do not have heart disease, and the same is true for blood pressure. When measuring myocardial perfusion, researchers are actually measuring what matters most, which is how much blood flow the heart is receiving. (Ornish, Tr. 2334-35; Heber, Tr. 1974).

830. Dr. Ornish also opined that the degree of blockage is only one of several mechanisms that affect perfusion, or blood flow to the heart. Other mechanisms include changes in vasomotor tone (how dilated or constricted the coronary arteries are), platelet aggregation (how sticky the platelets are that can form blood clots that may partially or completely occlude the flow of blood to the heart), and collateral blood flow (the heart can grow new blood vessels that provide additional blood flow around partial or even completely blocked arteries if the blockage occurs slowly overtime). (PX0025 (Ornish Expert Report at 0012)).

831. Dr. Sacks testified that another problem with the Ornish MP Study was that the primary endpoint measurement indicated in the published study as the main proof of benefit (SDS) was not identified as the primary endpoint in the protocol. The protocol for the Ornish MP Study provided for measurement of perfusion, but did not identify whether the primary endpoint would be SSS, SRS, SDS or some other imaging measurement. (CX1291 (Sacks Expert Report at 0021); *see also* CX0613 at 0009-10). Dr. Ornish conceded that he did not specify that changes in SDS would be the primary endpoint measure. (PX0025 (Ornish Expert Report at 0014); *see also* Sacks, Tr. 1475).

832. Dr. Ornish explained in response to Dr. Sacks' criticism (F. 831) that although the Ornish MP Study did not specify that changes in SDS would be the primary endpoint measure, it was not necessary to do so since SDS is a measure of how much of the heart was not receiving enough blood flow. Because SDS is derived by subtracting SRS from SSS, it is a way of factoring out the amount of infarcted or hibernating myocardium, so Dr. Ornish could focus on what he was most interested in: SDS. PX0025 (Ornish Expert Report at 0014)).

833. The 35 percent improvement in myocardial perfusion indicated in the Ornish MP Study pertained only to the SDS scores, and not to the SRS and SSS data. (Sacks, Tr. 1622-24). Dr. Sacks and Dr. Stampfer both stated that the .05 "*p*" value of the reported SDS improvement is not very persuasive where, as here, there were three possible outcome measures (SSS, SRS, and SDS) and only one just met significance. (CX1198 at 0003; Sacks, Tr. 1467 ("when there are . . . multiple outcomes . . . then a *p*-value of .05 . . . doesn't convey the same level of confidence than in a situation where there is one primary outcome"); CX1291 (Sacks Expert Report at 0021-22); Stampfer, Tr. 751 ("[T]he second reason I don't put a lot of weight on this is that the results were only

slightly significant just for one of the three endpoints that was not specified as the primary outcome in advance.")).

834. Dr. Ornish testified that while the Ornish MP Study did indicate a statistically significant change in the SDS, Dr. Ornish did not ignore the SSS and SRS measures that were shown in Table 2 of the study. The Ornish MP Study examined all three measurements in an effort to divine the SDS, as the primary hypothesis was that pomegranate juice would result in an improvement in SDS, a measure of the heart not receiving enough blood. (PX0023 at 0003; PX0025 (Ornish Expert Report at 0001); PX0355 (Ornish, Dep. at 128-29; 139)).

835. Complaint Counsel's experts also criticized the Ornish MP Study based on the large discrepancy in the blood flow values between the placebo and active groups at baseline. The baseline SSS for the placebo group was 9.6 ± 6.5, and the baseline SSS of the juice group was 6.4 ± 3.5, meaning that the placebo group was sicker than the juice group when the study started. (CX1198 at 0003 (Table 2); CX1291 (Sacks Expert Report at 0022-23); Sacks, Tr. 1469-72, 77; Stampfer, Tr. 750-52). Study documents from Dr. Ornish's clinic files show that the difference between the baseline SSS values of the placebo and juice groups was so large as to be statistically significant. (CX0701 at 0001 (email from M. Sumner to M. Eller, forwarded to D. Ornish, stating, "[t]here was a baseline difference in SSS between the experimental and the control groups (p <. 04). We don't have to mention this, but we should keep this in mind.")).

836. Complaint Counsel's experts further opined that the imbalance in baseline values in the Ornish MP Study shows that randomization did not produce an active group and a placebo group that were similar on relevant characteristics. (Stampfer, Tr. 751-52; CX1293 (Stampfer Expert Report at 0019); CX1291 (Sacks Expert Report at 0023)). It could be predicted that the control group, having worse coronary perfusion than the POM Juice group at baseline, would have a more accelerated form of the disease and show worsening on follow-up. (CX1291 (Sacks Expert Report at 0022-23); Sacks, Tr.1469-72, 77; *see also* Stampfer, Tr. 751 ("[H]ere, the placebo group was worse off at the start, and it's easy to imagine that if you're worse off at the start, you are going to get worse faster over time. So, the evidence isn't persuasive.")). Dr. Sacks stated that the baseline difference should have been reported in the publication. (Sacks, Tr. 1477; CX1291 (Sacks Expert Report at 0023)).

837. Dr. Ornish testified that although there was a difference in SSS at baseline, the Ornish MP Study employed an "analysis of variance," which took into account any baseline differences. The Ornish MP Study stated: "To test for the effects of experimental condition and time (and their interaction) on medical characteristics, 2 (experimental vs. placebo) X 2 (baseline vs. 3 months) analyses of variance for repeated measurements were run," which built into the analysis controlling for baseline differences. Further, when researchers recruit randomly and look at a number of different measures, it is not uncommon that one difference may be statistically significant in the group. Even if there had been a difference in SSS at baseline, this would not have undermined the

validity of the study, particularly since it was not Dr. Ornish's primary endpoint measure. (Ornish, Tr. 2343-44, 2394; PX0025 (Ornish Expert Report at 0015)).

838. Dr. Sacks criticized the Ornish MP Study on the additional basis that blood pressure, cholesterol, inflammatory biomarkers, and oxidative stress were not improved. (CX1291 (Sacks Expert Report at 0024)).

839. Dr. Ornish himself concluded that "blood pressure . . . did not improve" in the Ornish MP Study. (PX0025 (Ornish Expert Report at 17)).

840. Dr. Ornish also explained, the fact that other factors such as blood pressure and cholesterol did not improve in the Ornish MP Study does not in any way provide evidence that pomegranate juice was not beneficial, as its effects may have been mediated via other pathways. (PX0025 (Ornish Expert Report at 0017-18)).

841. Dr. Heber testified that in the Ornish MP Study, even though there was no change in blood pressure, one could not conclude that there was no effect of pomegranate juice on blood pressure, because the primary endpoint was blood flow, not blood pressure. (Heber, Tr. 2101-02).

842. In any clinical study, it is routine to take a blood pressure, pulse, body temperature, among others, to make sure patients are healthy. Although blood pressure is measured in many studies, a specific claim on blood pressure requires a very specific study involving special equipment and personnel. (Heber, Tr. 2101, 2040).

843. Dr. Sacks notes that Dr. Ornish's study originally was designed to last for 12 months, with measurements at baseline, three months, and 12 months, but was halted after three months. Dr. Sacks opined that the study was terminated under unusual circumstances because, according to correspondence, at the time, the *p*-value was considered significant rather than at the time the trial was originally set to end. Dr. Sacks further opined that the shortened study period and failure to report the planned duration is inconsistent with widely-accepted standards for conduct of clinical trials and undermines any confidence in the findings. (CX1291 (Sacks Expert Report at 0023-24); Sacks, Tr. 1474-75).

844. Dr. Ornish testified that the Ornish MP Study was terminated after three months only because the Resnicks did not provide the funding that they had previously committed to this study, not because the *p*-value was statistically significant at three months. Dr. Ornish further opined that while he did not have 12 months of follow-up data, this does not undermine the confidence in the three-month findings of the Ornish MP Study. (PX0025 (Ornish Expert Report at 0017)).

845. Complaint Counsel's experts concluded: The interpretation of the Ornish MP Study that is most consistent with principles of clinical study design and conduct is that the pomegranate juice treatment had no effect on any measure of cardiac health. (CX1291 (Sacks Expert Report at 0024)). Experts in the field of cardiovascular disease would

not consider the Ornish MP Study to support the proposition that pomegranate juice provides a heart disease benefit, either in terms of prevention or treatment. (Sacks, Tr. 1472, 1526-28). In light of the problems in the design and conduct of the study, and the discrepant results of the SSS, SDS, and SRS measures, the study does not even support the conclusion that pomegranate juice had a favorable effect on coronary perfusion (blood flow to the heart). CX1291 (Sacks Expert Report at 0024); CX1293 (Stampfer Expert Report at 0018-19)).

846. Respondents' experts concluded the following about the Ornish MP Study:

- Myocardial perfusion (or blood flow to the heart) is a good predictor or surrogate for cardiac events and a better scientific test than coronary angiography. (PX0025 (Ornish Expert Report at 0012); Ornish, Tr. 2331-34; Heber, Tr. 1973-74).

- SDS is considered a valid surrogate for coronary heart disease and the Ornish MP Study showed SDS, but not SRS or SSS, because SDS measures the primary endpoint, how much blood flow the heart is getting when compared to rest and stress. (Ornish, Tr. 2341-42).

- Differences at baseline for SRS and SSS did not affect the outcome of the Ornish MP Study. (Ornish, Tr. 2343-44, 2394; PX0025 (Ornish Expert Report at 0015).

- Omissions of patient data did not alter the results of the Ornish MP Study. (PX0025 (Ornish Expert Report at 0015); Ornish, Tr. 2347-48; 2394).

- The unblinding of patients or lack of a placebo does not diminish the validity of the Ornish MP Study. (Ornish, Tr. 2345-46; PX0025 (Ornish Expert Report at 0016); CX1339 (Ornish, Dep. at 148-49)).

- The results of the Ornish MP Study are valid even though they were tested over only a three-month period. (PX0025 (Ornish Expert Report at 0017).

847. Dr. Ornish concluded that the Ornish MP Study constitutes credible and reliable science showing that pomegranate juice lessens the risk of cardiovascular problems, that in people who have already had heart disease, it improves the blood flow and reverses the progression of heart disease; and if you can begin to reverse a disease, it would only make sense that pomegranate juice would work even better to help prevent heart disease in the first place. (Ornish, Tr. 2354-55).

iii. Determination on the Ornish MP Study

848. The Ornish MP Study does not provide competent and reliable scientific evidence to support claims that the POM Products treat, prevent or reduce the risk of heart disease. (*See* F. 808-846).

e. Ornish CIMT Study

i. About the Ornish CIMT Study

849. The second study Dr. Ornish conducted for Respondents, the Ornish CIMT Study, was completed in 2005 and is unpublished. (JX0003 ¶ B.16).

850. The Ornish CIMT Study was a randomized, double-blind, placebo-controlled 73-person study that measured CIMT, blood pressure, and other related mechanisms for 12 months. The primary endpoint of the Ornish CIMT Study was to investigate the effects of pomegranate juice on CIMT and indices of arterial stiffness for the common carotid arteries (CCA) in patients with at least one cardiovascular risk factor. The treatment group drank one cup (eight ounces) of pomegranate juice concentrate daily, and the control group drank one cup of placebo beverage, daily, for one year. (CX0754 at 0002; CX0613 at 0020).

851. The Ornish CIMT Study was designed to include 200 patients, not 73 patients. Dr. Ornish estimated that he would need at least 200 patients to show a statistically significant difference in CIMT however, because recruitment took longer than anticipated (since most patients with heart disease ended up having angioplasty, stents, and/or bypass surgery at a much higher rate than anticipated), the funding was cut, so Dr. Ornish was only able to recruit 73 patients, from which 56 patients' pre and post data was collected. (Ornish, Tr. 2352; PX0355a007 at 0002).

852. The primary purpose of the Ornish CIMT Study was to determine if pomegranate juice will affect the progression of early/subclinical carotid atherosclerosis. (PX355a0006 at 0004; PX0355a007 at 0010).

853. On or about October 21, 2004, PMRI finished its data collection. (CX0697). Commenting on the study data, Dr. Sumner of PMRI stated, "very few significant interactions . . . a mixed, but relatively disappointing bag so far." (CX0717 at 0001; CX1344 (Sumner, Dep. at 151-52)).

854. On March 24, 2005, Dr. Sumner stated, "I am looking into additional ways to analyze the data" and suggested sending "the IMT results to [another researcher] to check before [sending] them to Harley [Liker]/the Resnicks." (CX0717 at 0001; *see also* CX0718 at 0001). The next day, another PMRI employee suggested having a biostatistician analyze the data "before concluding the juice had a null effect." (CX0719 at 0001).

855. Dr. Ornish testified that it would be wrong to classify the Ornish CIMT Study as a "null" study. Instead, Dr. Ornish explained that the study was underpowered because PMRI knew from the beginning that they needed 200 patients. Thus, the study ended with an indeterminate finding, not a clearly nonsignificant finding. (Ornish, Tr. 2456-61).

856. The final analysis for the Ornish CIMT Study results was conducted in approximately June 2005 and the results of the study were provided to Dr. Ornish. (CX1344 (Sumner, Dep. at 168-69); CX0752).

857. In the Ornish CIMT Study, Dr. Ornish observed an improvement in the carotid artery significant to the 0.13 level as opposed to the 0.15 level. Dr. Ornish testified that if that degree of change had occurred in the larger number of patients he had projected (*i.e.*, 200 instead of 73), it would have been at the 0.05 level or less and, thus, would have reached statistical significance. (Ornish, Tr. 2352-54).

858. According to the Ornish CIMT Study unpublished final report, there were no significant changes in the treatment group relative to the placebo for CIMT thickness or elastic properties. (CX0754 (transmitting "Bev 2 Summary 6-16-05.doc")).

859. In the Ornish CIMT Study unpublished final report, there also were no significant differences in the treatment group relative to the placebo group over time for any of the other heart-related measurements, including systolic and diastolic blood pressure, cholesterol, LDL, HDL, or triglycerides. (CX0754 at 0003, 0005; CX1291 (Sacks Expert Report at 0024-25); Stampfer, Tr. 754-55; CX1293 (Stampfer Expert Report at 0019-20)).

ii. Experts' analysis of the Ornish CIMT Study

860. Complaint Counsel's expert opined that the Ornish CIMT Study appears to have been well-designed and well-conducted. (Sacks, Tr. 1485-88, 1603; CX1291 (Sacks Expert Report at 0026)).

861. Dr. Sacks described the results of this study as "convincingly null, showing that pomegranate juice treatment did not improve CIMT or the other tested parameters" including elasticity of the arteries, blood pressure, or cholesterol. (Sacks, Tr. 1484-86; CX1291 (Sacks Expert Report at 0026); *see also* CX1293 (Stampfer Expert Report at 0019-20); Stampfer, Tr. 755).

862. Dr. Sacks opined that the null results of the Ornish CIMT Study confirm that the purportedly positive results of Dr. Aviram's unrandomized, uncontrolled 19-patient CIMT/BP Study lack credibility. (Sacks, Tr. 1486-88; CX1291 (Sacks Expert Report at 0026)).

863. Dr. Ornish opined that it would be more accurate to see the Ornish CIMT Study as a validation of the studies by Dr. Aviram and Dr. Davidson, since the differences in

CIMT would have been statistically significant if the findings measured in 73 patients were found in the 200 patients that Dr. Ornish originally planned to enroll. (PX0025 (Ornish Expert Report at 0019)).

864. Dr. Ornish testified that the Ornish CIMT Study was an indeterminate study that cannot be relied upon: "It neither proves or disproves. It would be, again, as wrong to say that it proves as it would be for Dr. Sacks to assert that it disproves it." (PX0355 (Ornish, Dep. at 192-93)).

865. Dr. Heber did not consider the results of the Ornish CIMT Study in reaching his conclusions on the adequacy of Respondents' substantiation, because it was "incomplete." Dr. Heber observed that the Ornish CIMT Study "had inadequate power at that number of subjects," so no conclusions could be drawn from the study. (PX353 (Heber, Dep. at 180-81); Heber, Tr. 2133-34).

866. Dr. Heber opined: "The failure of any clinical trial to show a difference cannot be interpreted as a negative finding, however. Only a probability that any difference has been excluded can be calculated, using the so-called beta type II error calculation, which was not done by Dr. Stampfer." (PX0192 (Heber Expert Report at 0053)).

867. Dr. Sacks admits that the lack of statistical significance for a positive result in the Ornish CIMT Study is not proof of a negative and does not mean pomegranate juice is not beneficial. (Sacks, Tr. 1608-09).

iii. Determination on the Ornish CIMT Study

868. The Ornish CIMT Study does not provide competent and reliable scientific evidence to support claims that the POM Products treat, prevent or reduce the risk of heart disease. (*See* F. 849-867).

f. Davidson CIMT Study

869. In 2003, Dr. Liker approached Dr. Davidson about conducting a CIMT study and a brachial artery reactivity testing study for Respondents. From the beginning, Dr. Liker indicated that the he wanted the study to be randomized, double-blind, and placebo-controlled. (CX1336 (Davidson, Dep. at 92-93); CX0586).

870. In a summary of cardiovascular studies sent to a scientific consultant for POM, Dr. Liker described the Aviram ACE/BP Study, the Aviram CIMT/BP Study, the Ornish MP Study (2005), and the unpublished Ornish CIMT Study, and stated that POM was still exploring its research options "in its efforts to understand whether or not the consumption of pomegranate juice offers cardiovascular benefits." (CX0579 at 0003-04).

871. Dr. Davidson conducted two studies for Respondents: (1) Davidson MH., et al., *Effects of Consumption of Pomegranate Juice on Carotid Intima-Media Thickness in Men and*

Women at Moderate Risk for Coronary Heart Disease, 104 Am. J. Cardiology 936 (2009) ("Davidson CIMT Study") (CX1065; *see* JX0003 ¶ B.17); and (2) Davidson MH, *The Effects of Pomegranate Juice on Flow-Mediated Vasodilation* (unpublished, 2004) ("Davidson BART/FMD Study") (CX0684; *see* JX0003 ¶ B.17). The cost for the two studies, sponsored by the Stewart and Lynda Resnick Revocable Trust, was $2,940,494. (CX1134 at 0001).

i. About the Davidson CIMT Study

872. The Davidson CIMT Study was an 18-month, 289-person randomized, double-blinded, placebo-controlled clinical trial conducted at two clinical research sites in accordance with good clinical practice guidelines and under a protocol approved by an institutional review board. (PX0014 at 0001-02).

873. The Davidson CIMT Study was designed to test the effect of pomegranate juice on CIMT progression rates in subjects at moderate coronary heart disease risk. (PX0014 at 0001-02).

874. The Davidson CIMT Study analyzed the results of 289 persons, but actually screened and enrolled 876 and 383 subjects, respectively. (PX0014 at 0002; CX1065 at 0001; CX1291 (Sacks Expert Report at 0027)).

875. Participants in the Davidson CIMT Study were middle-aged men and women with one or more coronary heart disease risk factors (high LDL, low HDL, hypertension or use of hypertension medication, or cigarette smoking) and were required to have a baseline posterior wall common CIMT measurement of > 0.7 and < 2.0 mm on ≥ 1 side (right or left). The study excluded persons with actual coronary heart disease or diabetes. (PX0014 at 0002; CX1065 at 0001-02; CX1291 (Sacks Expert Report at 0027)).

876. Participants in the Davidson CIMT Study drank eight ounces of pomegranate juice or placebo juice daily. Adherence to study product consumption was assessed at each visit by reviewing daily consumption diaries maintained by the subjects. (CX1065 at 0002).

877. The protocol for the Davidson CIMT Study called for ultrasound testing of the carotid artery at baseline, at 12 months, and at 18 months. (CX0716 at 0018-19). The primary outcome variable identified in the protocol was the difference between placebo and pomegranate juice in posterior wall common CIMT progression rate in mm/year, using non-contrast images, and a secondary outcome measurement was the difference between placebo and pomegranate juice in the anterior wall common CIMT progression rate in mm/year, using contrast images. (CX0716 at 0028). Exploratory endpoints included changes in blood pressure, lipids, and various measures of inflammation and oxidative stress. (CX0716 at 0011; CX1291 (Sacks Expert Report at 0027)).

878. The Davidson CIMT Study indicated the following:

- With the exception of apolipoprotein-B100, which decreased more with pomegranate juice than with control . . . , there were no differences between treatment groups for changes from baseline in traditional cardiovascular risk markers, including fasting lipoprotein lipids, blood pressures, or smoking status (data not shown).

- Of the 152 subjects (52%) agreeing to the optional administration of intravenous contrast agent for anterior wall imaging, as expected, baseline values for the anterior wall of the common carotid artery were larger than for the posterior wall.

- Anterior and posterior wall CIMT values and progression rates did not differ significantly between treatment groups at any time point.

- The composite measurement of CIMT showed a significantly smaller value at 12 months in the pomegranate juice group compared to the control group . . . However, this difference was no longer significant at the end of the treatment period.

- Exploratory analyses of several subgroups indicated significantly lower values for pomegranate juice versus control after treatment for anterior wall and/or composite CIMT values: subjects in the top tertiles for baseline triglycerides (TG), . . . total cholesterol/HDL cholesterol ratio .; composite. . . , TG/HDL cholesterol ratio . . . and apolipoprotein-B100 and the lowest tertile for HDL cholesterol. There were no significant differences between treatments in any of these subgroups at baseline for any CIMT measurements or after treatment in posterior wall CIMT values.

- Results of the present study showed no significant influence of 18 months of pomegranate juice consumption on CIMT progression in the overall study sample. However, results from *post hoc* exploratory analyses, which should be interpreted with caution, suggest that the rate of CIMT progression may have been slowed in subgroups characterized by more rapid CIMT progression, including those with increased levels of TG-rich lipoproteins, low levels of HDL cholesterol, and greater oxidative stress.

- Whether possible benefits of pomegranate juice consumption on CIMT progression in some subgroups relate to antioxidant activity is uncertain. A lack of significant improvements in most markers of oxidative stress argues against an important role for antioxidant activity. However, specific reactive oxygen/nitrogen species may be scavenged by pomegranate unique polyphenolic hydrolysable tannins. Indeed, a subgroup for whom there was an apparent benefit was the top tertile for baseline PD – AAPH, suggesting that antioxidant effects may have

played a role in the protection against CIMT progression by pomegranate juice consumption.

- Pomegranate juice and/or polyphenol consumption might favorably influence CIMT progression through effects on platelet activity, endothelial function, or shifts in the production of prostacyclin production. However, because none of these variables were measured in the present trial, their potential roles here are unknown.

(PX0014 at 0005-06).

879. The Davidson CIMT Study included a *post hoc* analysis of changes in the CIMT measurements for some of the study subpopulations and stated that there were significantly lower anterior and/or composite CIMT progression rates with higher CVD risk factors. (CX1065 at 0001, 0006; CX1336 (Davidson, Dep. at 57-69)).

880. Dr. Davidson initially submitted a manuscript of the study to the journal, *Arteriosclerosis, Thrombosis, and Vascular Biology*, in late 2008. That journal rejected the manuscript, concluding that it was a negative study. (CX1336 (Davidson, Dep. at 202-03) (discussing CX1016)).

881. In May 2009, Dr. Davidson submitted the manuscript (F. 880) to the *American Journal of Cardiology*. Two expert reviewers provided recommendations and comments. (CX1336 (Davidson, Dep. at 77-78); *see* CX1057 at 0024-27).

882. One reviewer of the manuscript (F. 880) stated that, given the large number of *post hoc* analyses performed, it would be appropriate to conduct a statistical correction for multiple comparisons. (CX1057 at 0025; CX1336 (Davidson, Dep. at 80-81)). Dr. Davidson did not do the statistical correction, but committed to revise the discussion section to emphasize "[t]he possibility of type I errors, the exploratory nature of these findings, and caution regarding interpretation of post-hoc subgroup analyses." (CX1336 (Davidson, Dep. at 73); CX1057 at 0025).

883. Another reviewer of the manuscript (F. 880) advised that "The study needs to be reported as a negative study as it is." (CX1057 at 0027). In response, Dr. Davidson "affirm[ed] that it was a negative study," and committed to revise the manuscript to emphasize that "caution is warranted" with regard to the subgroup findings, and that those findings "should be considered hypotheses that will need to be replicated in future trials designed to assess the efficacy of pomegranate juice consumption" in those subgroups. (CX1336 (Davidson, Dep. at 78-85); CX1057 at 0027).

ii. Experts' analysis of the Davidson CIMT Study

884. Dr. Sacks testified that the Davidson CIMT Study is the largest of the heart studies conducted on pomegranate juice; was carefully designed, in that the protocol identified the endpoints to be measured, the procedures to be followed, inclusion and exclusion

criteria, and the statistical analysis to be conducted; and that there was no evidence of critical problems in the conduct or analysis of the study (except its over-emphasis on the subgroup results). Dr. Sacks concluded that the Davidson CIMT Study is "competent and reliable evidence that consumption of pomegranate juice did not improve CIMT in subjects with one or more cardiovascular risk factors." (CX1291 (Sacks Expert Report at 0029)).

885. Dr. Ornish and Dr. Heber testified that the Davidson CIMT Study constitutes competent and reliable evidence that the consumption of POM Juice is beneficial to cardiovascular health by, among other things, reducing arterial plaque. (PX0025 (Ornish Expert Report at 0019-22); PX0192 (Heber Expert Report at 0039, 0053); Heber Tr. 1979-86; PX0014).

886. In his expert report, Dr. Sacks expressly stated the following regarding the Davidson CIMT Study:

- According to the Davidson [C]IMT report, at the end of the study, there were no significant differences in CIMT progression rates between the subjects in the pomegranate juice and control groups.

- The "composite rate" for all measured carotid artery walls had shown a significantly smaller value at 12 months in the pomegranate juice group, but this difference was no longer significant at the end of the study.

- Further, the anterior wall values and rates, and the posterior wall values and progression rates did not differ significantly at any point in the trial.

- There were also no statistically significant changes in the measured indicators of inflammation and oxidative stress, or in fasting lipoprotein lipids or blood pressure.

(CX1291 (Sacks Expert Report at 0028)).

887. Dr. Ornish agreed with Dr. Sacks' conclusion that the Davidson CIMT Study showed no significant differences in the overall CIMT progression rates between the active and placebo groups at 18 months. (PX0025 (Ornish Expert Report at 0019-20)).

888. In his expert report, Dr. Ornish expressly stated the following regarding the Davidson CIMT Study:

- the fact that these differences in CIMT measurements were not statistically significant at 18 months does not change the fact that these differences were statistically significant after 12 months;

- the bottom line is that pomegranate juice *did* show a statistically significant improvement in CIMT after 12 months in the measure that was most clinically relevant; and

- the Davidson CIMT Study does provide supporting evidence that there was statistically significant lower CIMT progression rates for pomegranate versus control subjects in those with higher cardiovascular disease risk factors.

(PX0025 (Ornish Expert Report at 0020-22)).

889. Dr. Heber acknowledged that the results at 18 months suggest that in subjects at risk with moderate coronary heart disease, pomegranate juice consumption had no significant effect on overall CIMT progression rate, opining as follows:

- No significant difference in overall CIMT progression rate was observed between pomegranate juice and control treatments.

- In exploratory analyses, in subjects in the most adverse tertiles for baseline serum lipid peroxides, triglycerides (TGs), high-density lipoprotein (HDL) cholesterol, TGs/HDL cholesterol, total cholesterol/HDL cholesterol, and apolipoprotein-B100, those in the pomegranate juice group had significantly less anterior wall and/or composite CIMT progression versus control subjects.

- In conclusion, these results suggest that in subjects at moderate coronary heart disease risk, pomegranate juice consumption had no significant effect on overall CIMT progression rate, but may have slowed CIMT progression in subjects with increased oxidative stress and disturbances in the TG-rich lipoprotein/HDL axis.

(PX0192 (Heber Expert Report at 0039)).

890. Dr. Ornish opined that a potential reason for lack of a change in the CIMT progression rate at 18 months was that participants in the Davidson CIMT Study may have stopped drinking the juice after 12 months. In his 34 years of directing RCTs, Dr. Ornish notes that it is very challenging to motivate patients to continue following any intervention for more than one year. Dr. Ornish further observes that it is not unusual for patients to be less than honest in describing their compliance as patients often describe that it is embarrassing and even humiliating to report that they have not done what they were supposed to do. (PX0025 (Ornish Expert Report at 0020-21); PX0355 (Ornish, Dep. at 202-03)).

891. Dr. Davidson evaluated the compliance with product consumption guidelines during the Davidson CIMT Study. He testified that his review of compliance diaries showed high

levels of compliance with product consumption. (CX1336 (Davidson, Dep. at 151-52); CX0788).

892. Dr. Stampfer provided the opinion that that the main result from the Davidson CIMT Study (2009) provides substantial evidence *against* the hypothesis that pomegranate juice can reduce the progression of CIMT. (CX1293 (Stampfer Expert Report at 0020-21); Stampfer, Tr. 758-59 ("So it seems clear that this is a null study, and that's what the authors concluded")).

893. Dr. Heber expressly disagrees with Dr. Stampfer's conclusion in (F.892) above: Dr. Stampfer contends that the CIMT benefit demonstrated in the subgroup of individuals at increased oxidant stress with increased triglycerides and low HDL does not override his conclusion that "the main result from this large trial provides substantial evidence against the hypothesis that pomegranate juice can reduce progression of CIMT." I disagree. The subgroup data is particularly important because the CIMT benefit was associated with the specific subgroup that had increased risk factors. (PX0192 (Heber Expert Report at 0053)).

894. The Davidson CIMT Study included a *post hoc* analysis of changes in the CIMT measurements for some of the study subpopulations. The Davidson CIMT Study described the subgroup analyses as "post hoc exploratory analyses, which should be interpreted with caution[.]" It stated that, "[b]ecause the decrease in CIMT progression in these subgroups was based on analyses that were not preplanned and had no correction for multiple comparisons . . . , these findings will need to be confirmed in future investigations." (CX1065 at 0001, 0006; CX1336 (Davidson, Dep. at 57-69)).

895. A *post hoc* analysis is one that is conceived after the researchers have seen the data and, thus, is generally a less valid approach than one planned for in the protocol, because it is more subject to bias. (Sacks, Tr. 1500-01).

896. Respondents' experts opined that in scientific research, *post hoc* analysis is routine. (Heber, Tr. 1984). Although the exploratory analysis was not called for by the protocol, such analyses, including those on subgroups, are commonly done. (CX1336 (Davidson, Dep. at 57, 221)).

897. With respect to the Davidson CIMT Study, Dr. Ornish opined: "While this is post hoc analysis, and thus not as rigorous as one stated a priori, it does provide supporting evidence that there was statistically significant lower CIMT progression rates for pomegranate versus control subjects in those with higher cardiovascular disease risk factors." (PX0025 (Ornish Expert Report at 0021)).

898. Dr. Sacks also noted that the subgroup analysis had not been corrected for multiple comparisons, as stated in the Davidson CIMT Study. (CX1291 (Sacks Expert Report at 0030)). When multiple endpoints are being measured, the *p*-value needs to be adjusted downward to correct for multiple comparisons. Without the correction, with each additional subgroup analyzed, the chances increase that one or more will turn out to

have a *p*-value of less than .05, by chance alone. (Sacks, Tr. 1505-06; Stampfer, Tr. 760-61). Dr. Davidson never did a correction for multiple comparisons on the subgroup analysis. (CX1336 (Davidson, Dep. at 73)).

899. Dr. Sacks further opined: because the subgroup data is hypothesis generating only, and has not been corrected for multiple comparisons, a qualified scientist could not rely on the *post hoc* analysis of the subgroup populations as reliable scientific evidence to support claims that POM Juice or POMx prevent, reduce the risk of, or treat heart disease in the subpopulations identified in Figure 3 of the Davis CIMT Study. (CX1291 (Sacks Expert Report at 0029-30)).

iii. Determination on the Davidson CIMT Study

900. The Davidson CIMT Study does not provide competent and reliable scientific evidence to support claims that the POM Products treat, prevent or reduce the risk of heart disease. (*See* F. 872-899).

g. Davidson BART/FMD Study

i. About the Davidson BART/FMD Study

901. The brachial artery is a major blood vessel of the arm. Brachial artery reactivity testing ("BART") is a measurement of how much the brachial artery dilates (enlarges) after a blood pressure cuff is inflated, and then released. This is also called flow mediated dilation ("FMD") testing. (JX0003 ¶ A.1-2; CX1336 (Davidson, Dep. at 34-35)).

902. Flow mediated dilation is the amount by which the brachial artery dilates (gets larger) after the blood pressure cuff is deflated. (JX0003 ¶ A.8).

903. Dr. Davidson conducted the Davidson BART/FMD Study on a subset of 45 Davidson CIMT Study participants. It was a 13-week, randomized, double-blind, placebo-controlled trial to evaluate the effect of consuming POM Juice or placebo on BART, also referred to as FMD testing. (JX0003 ¶ A.1; CX0684; CX0716 at 0010-11, 0074-81; CX1336 (Davidson, Dep. at 37, 102-03); Sacks, Tr. 1508-10; Stampfer, Tr. 764-66).

904. At the conclusion of the Davidson BART/FMD Study, there were no significantant differences between the treatment and placebo groups and no written report was prepared. (PX0019; CX0684 at 0001; CX1336 (Davidson, Dep. at 87-89); Sacks, Tr. 1510-13; CX1291 (Sacks Expert Report at 0030-31); CX1293 (Stampfer Expert Report at 0021); CX0695 at 0001; CX1336 (Davidson, Dep. at 125)).

905. The Davidson BART/FMD Study also took measurements of blood pressure and other vital signs. However, blood pressure, cholesterol, HDL cholesterol, non-HDL cholesterol, triglycerides, ACE, paraoxonase (PON), and thiobarbituric acid reactive substances (TBARS) were not primary or secondary endpoints of the Davidson

BART/FMD Study. (CX0684; CX0716 at 0010-11, 0074-81; Sacks, Tr. 1508-10; Stampfer, Tr. 764-66).

906. At the end of the Davidson BART/FMD Study, there were no significant differences between treatment and placebo groups in blood pressure, cholesterol, HDL cholesterol, non-HDL cholesterol, triglycerides, ACE, PON, and two TBARS measurements. (CX1336 (Davidson, Dep. at 86-88; CX0684 at 0005-13, 0019; CX1291 (Sacks Expert Report at 0031)).

ii. Experts' analysis of the Davidson BART/FMD Study

907. Complaint Counsel's expert, Dr. Sacks, opined that the Davidson BART/FMD Study appears to have been properly designed and conducted. The protocol identifies the endpoints to be measured, the procedures to be followed, inclusion and exclusion criteria, and the statistical analysis to be conducted. There is no indication of critical problems in the conduct of the study. (CX1291 (Sacks Expert Report at 0032)).

908. Dr. Sacks opined that although BART/FMD is not a valid or generally recognized surrogate marker of coronary heart disease, it does provide relevant information because FMD is a measure of nitric oxide. Dr. Sacks further opined that if pomegranate juice meaningfully affected nitric oxide metabolism, one would have expected to see a positive result in the FMD testing. (CX1291 (Sacks Expert Report at 0032); Sacks, Tr. 1510-12).

909. Dr. Sacks further opined that the Davidson BART/FMD Study finding of no statistically significant difference in blood pressure or ACE due to POM Juice consumption is inconsistent with Dr. Aviram's ACE/BP Study findings. (F. 774-779; Sacks, Tr. 1512-13; CX1291 (Sacks Expert Report at 0032)).

910. Dr. Heber testified that in the Davidson BART/FMD Study, the primary endpoint was flow-mediated dilation, not blood pressure, and, therefore, any results for blood pressure cannot be relied upon as negative evidence. (Heber, Tr. 2106-07).

911. Dr. Sacks concedes that just because the Davidson BART/FMD Study does not show statistically significant changes with respect to blood pressure and ACE, among other measurements, the absence of such evidence is not proof there is no effect. (PX0361 (Sacks, Dep. at 230)).

912. Respondents' experts explain that the absence of evidence is not evidence of absence, so the fact that a statistically significant change in ACE or blood pressure was not found does not mean that the result does not exist. (Heber, Tr. 1981; *see also* Sacks, Tr. 1608).

913. Respondents' experts opined that no conclusion can be drawn from the absence of statistically significant changes in the Davidson BART/FMD Study. (Heber, Tr. 1981; Sacks, Tr. 1608-09).

iii. Determination on the Davidson BART/FMD Study

914. The Davidson BART/FMD Study does not constitute competent and reliable scientific evidence supporting a claim that the POM Products treat, prevent or reduce the risk of heart disease. (*See* F. 903-913)

6. Additional biomarker studies sponsored by Respondents

a. The Overweight Studies

915. In 2006, POM sponsored Dr. James Hill, University of Colorado, Denver, to examine the safety and antioxidant activity of POMx on overweight individuals with increased waist size ("Denver Study"). Also in 2006, POM sponsored Dr.Heber and Accelovance to study the safety of POMx and the effect of POMx on biomarkers and inflammation in overweight people ("San Diego Study") (collectively, the "Overweight Studies") (CX0934; CX0819 at 0021-22; CX0859 at 0001).

i. About the Denver Study

916. In 2006, Dr. Hill and his colleagues conducted an unblinded, uncontrolled study of POMx capsules in Denver, Colorado, known as the Denver Study. (CX1291 (Sacks Expert Report at 0032-35); *see* Sacks, Tr. 1513-14).

917. The Denver Study enrolled 24 adults (19 females, 5 males) ages 40 to 70 with abdominal adiposity. Subjects received two POMx capsules per day for 28 days. (CX0877 at 0002-10; CX0934 at 0003-04).

918. The Denver Study measured a "wide range of biomarkers for oxidative stress and inflammation" at baseline and at four weeks, including TBARS (thiobarbituric acid reactive substances) and PON1 activity. TBARS is an important biomarker of oxidative stress in humans and strongly predictive of cardiovascular events in people with stable coronary artery disease, independent of traditional risk factors and inflammatory markers. High-density lipoprotein cholesterol ("HDL" or so called "good cholesterol") contains an antioxidant enzyme, called "paraoxonase" or "PON1" which acts to protect the body against oxygen radicals. Additional measurements included blood pressure, triglycerides, cholesterol, and C-reactive protein. Although the subjects' triglycerides, cholesterol, and C-reactive protein were measured, the study was not designed to assess those factors. (CX0877 at 0002-10; CX1342 (Hill, Dep. at 42-44); Heber, Tr. 1961; CX0934 at 0003-04).

919. Twenty-two subjects completed the Denver Study. According to the Preliminary Data Analysis, dated February 15, 2007, the participants gained an average of 1.3 pounds during the study, which Dr. Hill attributed to its being conducted during the holiday season. (CX0877 at 0002-03; CX1291 (Sacks Expert Report at 0032-33); CX1342 (Hill, Dep. at 99-103)).

920. TBARS was the primary endpoint chosen to assess the antioxidant activity of the POMx capsules in the Denver Study. (CX1342 (Hill, Dep. at 41-42)). The authors of the study concluded that POMx is safe and that there was evidence of antioxidant activity through a significant reduction in TBARS linked with cardiovascular disease risks. (CX0934 at 0004).

921. After adjusting the statistical analysis for the weight change, during the Denver Study TBARS decreased and free fatty acids increased. The study statistician stated that the change in TBARS was "of borderline significance [and had] not been adjusted for the number of comparisons made." (CX0877 at 0002-03, 0008 (TBARS); CX1291 (Sacks Expert Report at 0032-33)).

922. In the Denver Study, there was no change in PON1 and there were no statistically significant changes in blood pressure. The subjects' blood pressure was taken as a safety measure to protect the subjects, as the study was not designed to assess whether or not POMx capsules had an effect on blood pressure. (CX0877 at 0002-03, 0008, 0010; CX1291 (Sacks Expert Report at 0032-33); CX1342 (Hill, Dep. at 71-72, 97-103, 111-13, 118-19).

923. Although inflammation was not explored as the primary endpoint, the Denver Study concluded, "[w]e did not detect any effect of POMx on inflammation but identification of better biomarker assays for inflammation is needed . . . . [T]his pilot project suggests that a larger trial is warranted in abdominally obese subjects who may be at risk for development of metabolic diseases." (CX0877 at 0002-03; CX1291 (Sacks Expert Report at 0032-33); CX1342 (Hill, Dep. at 41-42); CX0934 at 0001).

ii. About the San Diego Study

924. The protocol for the San Diego Study was titled, *A Placebo-Controlled, Randomized, Double-Blind Study to Compare Antioxidant Levels in Normal Subjects with Elevated Waist Circumference When Administered 1 or 2 Pomegranate Dietary Supplement Capsules for 4 Weeks*. (CX0819 at 0014 (Protocol, July 14, 2006); CX1291 (Sacks Expert Report 0033-34)).

925. The San Diego Study was designed as a safety assessment. (CX0934 at 0001).

926. The San Diego Study recruited 64 generally healthy male and female subjects who took either two POMx capsules, two placebo capsules, or one placebo and one POMx capsule, per day, for four weeks. (CX0859 at 0010 (Clinical Study Report); CX1291 (Sacks Expert Report at 0033-34)).

927. Measurements in the San Diego Study included blood pressure, oxidized phospholipids, oxidized LDL/HDL, serum nitric oxide, and PON, but these were not primary endpoints. (CX0934 at 0001; CX0859 at 0003; CX1291 (Sacks Expert Report at 0033-34)).

928. A portion of the San Diego Study data was presented in a January 11, 2007 Clinical Study Report. (*See* CX0859). This document described the conduct of the study, adverse events, vital signs, and blood pressure data. It stated that "[t]here were no apparent treatment related changes in weight, systolic blood pressure, diastolic blood pressure, pulse rate, respirations, or temperature." The San Diego Study report also stated that the efficacy results of antioxidant and anti-inflammatory levels were shown separately. (CX0859 at 0018, 0020).

929. Dr. Heber prepared a slide presentation about the results of the San Diego Study in which he stated: "there were no changes in . . . markers of oxidative stress or inflammation that were studied," including in C-reactive protein, oxidized phospholipids, lipoprotein (a), and nitric oxide and that "[t]he variation among subjects suggests that a more focused study would be more likely to demonstrate significant changes." (CX1254 at 0026; CX1254 at 0001, 0006-26; Heber, Tr. 2119-21).

930. Dr. Heber sent this presentation (F. 929) to POM employees on January 9, 2007 with an accompanying email stating, "we have not proved or disproved efficacy at this point." By efficacy, Dr. Heber meant changes in biomarkers of oxidant stress or inflammation. (CX0858 at 0001). (CX1352 (Heber, Dep. at 107-11) (discussing CX1254)).

931. Dr. Heber's article on the San Diego Study results was published in late 2007 as Heber D. et al., *Safety and Antioxidant Activity of a Pomegranate Ellagitannin-Enriched Polyphenol Dietary Supplement in Overweight Individuals with Increased Waist Size*, J. Agric Food Chem., Vol. 55, No. 24 (2007). (*See* CX0934).

932. Dr. Hebers's article (F. 931) on the Overweight Studies stated that "[p]reliminary evidence of a reduction in TBARS was seen in the subjects who were studied at the Denver site . . . . TBARS are an important biomarker of oxidative stress. . . . [T]hese pilot studies demonstrate both the safety and efficacy of POMx . . . in humans. However, further studies need to be done to confirm the antioxidant properties of pomegranate ellagitannins administered as a dietary supplement." (CX0934 at 0003-04).

933. Dr. Heber acknowledged that the published article (F. 931) did not provide all of the results of the San Diego Study, including those concerning antioxidant stress or inflammation. Dr. Heber explained that the San Diego Study was primarily studying safety, "with the idea that we would explore the idea of whether any inflammatory markers or oxidant stress markers were elevated in those subjects." Dr. Heber further stated that they found that the studied population had a "great deal of variability" at baseline and four-week measurements. Dr. Heber further explained that there was no interest in publishing the results because the findings concerning anti-inflammatory effects were "indeterminate results, not negative results." (Heber, Tr. 2116-17).

iii. Experts' analysis of the Overweight Studies

934. Drs. Sacks and Stampfer concluded that the methodological shortfalls in the Denver Study – especially the lack of a control group – render its findings unreliable. (CX1291 (Sacks Expert Report at 0035); *see also* Sacks, Tr. 1519-21; Stampfer, Tr. 768-72).

935. Dr. Ornish agreed that there are limitations to the Denver Study and that it was a pilot study, which only provides preliminary findings to justify doing a larger study. Dr. Ornish further opined that the San Diego Study did not demonstrate efficacy since there were no significant changes in biomarkers. (PX0025 (Ornish Expert Report at 0024-25)).

936. Dr. Heber stated in his expert report that the Denver Study demonstrated the efficacy of POMx as an antioxidant. (CX0934 at 0004). At trial, however, he described the Denver Study as a "pilot study . . . not a conclusive demonstration." (Heber, Tr. 2116). Dr. Heber explained, anti-inflammatory effects "were indeterminate results, not negative results." (Heber, Tr. 2117).

937. With respect to the lack of statistically significant changes to blood pressure and other biomarkers, such as triglycerides, HDL, LDL, C-reactive protein, and PON, Dr. Sacks acknowledges that the absence of information does not prove the negative. (PX0361 (Sacks, Dep. at 223-24, 238, 243)).

iv. Determination on the Overweight Studies

938. The Overweight Studies do not constitute competent and reliable scientific evidence to support claims that the POM Products treat, prevent or reduce the risk of heart disease. (*See* F. 915-937).

b. The Diabetes Studies

i. About the Diabetes Studies

939. Respondents have also sponsored studies evaluating the effect of pomegranate juice and/or its derivatives on persons with diabetes, discussed below, (collectively, "the Diabetes Studies"). (PX0038; PX0127; CX0765).

940. The first of the Diabetes Studies, conducted by Dr. Rock, a member of Dr. Aviram's team, published as Rock, W, et al., *Consumption of Wonderful Variety Pomegranate Juice and Extract by Diabetic Patients Increases Paraoxonase I Association with High-Density Lipoprotein and Stimulates Its Catalytic Activities*, 56 J. Agric. Food Chem. (2008), looked at the relationship of PON1 and HDL cholesterol activity in 30 diabetic patients who used pomegranate juice or POMx Liquid for four to six weeks. It indicated a reduction in oxidative stress as measured by TBARS and improved PON. All measurements were comparisons to baseline. (PX0127; CX1291 (Sacks Expert Report at 0036-37); PX0192 (Heber Expert Report at 0038-39)).

941. The other two Diabetes Studies were conducted by Dr. Heber and Dr. Hill and were randomized, double-blind, placebo-controlled studies to evaluate the antioxidant effect of pomegranate extract capsule and pomegranate juice, respectively, in diabetic patients. (Heber, Tr. 2048-49, 2054; CX1352 (Heber, Dep. at 124-25); CX0949 at 0007-26 (protocol for diabetes extract study); CX1082 at 0007-21 (protocol for diabetes juice study); CX1284).

942. The POMx protocol called for enrolling 30 diabetics for 12 weeks. (CX949 at 0013). The POM Juice study protocol called for an enrollment of 40 diabetics for 12 weeks. (CX1082 at 0012).

943. The two Diabetes Studies conducted by Dr. Heber and Hill were completed, but the results were not published. (CX1352 (Heber, Dep. at 132-33); CX1342 (Hill, Dep. at 157)).

ii. Experts' analysis of the Diabetes Studies

944. Dr. Sacks testified that the Diabetes Studies do not constitute competent and reliable scientific evidence to support claims that POM Juice or POMx treat, prevent, or reduce the risk of heart disease because they are not RCTs, the study size is too small, and the duration is too limited in scope. (CX1291 (Sacks Expert Report at 0035-37); Sacks, Tr. 1521-24).

945. According to Dr. Heber, the two diabetes studies he conducted did not show a significant change in malondialdehyde, which is a TBARS measure, or in PON, both of which are heart-related biomarkers. (Heber, Tr. 2124 (malondialdehyde), 2137-38 (PON); CX1352 (Heber, Dep. at 161-70)).

946. Dr. Heber did not include the results of his two diabetes studies in his analysis of available human clinical evidence to substantiate heart benefits of POM Products. (PX0192 (Heber Expert Report at 0052-54)).

iii. Determination on the Diabetes Studies

947. The Diabetes Studies do not constitute competent and reliable scientific evidence to support claims that the POM Products treat, prevent or reduce the risk of heart disease. (*See* F. 939-946).

7. Experts' opinions based on the totality of the evidence

a. Summary of Complaint Counsel's experts' opinions

948. Dr. Sacks and Dr. Stampfer both opined that Respondents' research on pomegranate juice provides no evidence that POMx Pills or POMx Liquid will treat, prevent, or

reduce the risk of heart disease or that they are clinically proven to do so. (CX1291 (Sacks Expert Report at 0010, 0038); CX1293 (Stampfer Expert Report at 0017)).

949. Dr. Stampfer opined: Respondents' human clinical studies, including a large randomized clinical trial, failed to confirm the results of the animal and *in vitro* studies. Although some promising results appear in several of the smaller studies with important design limitations, the weight of the evidence strongly favors the null hypothesis of no effect. . . . The current data does not support the claims for heart disease prevention or treatment. (CX1293 (Stampfer Expert Report at 0022)).

950. Dr. Sacks opined: the evidence is not sufficient to support the conclusion that consumption of POM Juice, POMx Pills, or POMx Liquid treat, prevent, or reduce the risk of heart disease. (CX1291 (Sacks Expert Report at 0038-39)).

951. Dr. Sacks further opined: there is no reliable evidence that POM Juice, POMx Pills, or POMx Liquid reduce or delay the development of arterial plaque; improve blood flow to the heart (or other blood vessels); or reduce blood pressure. (CX1291 (Sacks Expert Report at 0038-39)).

952. Dr. Sacks opined, in addition, that clinical studies, research and/or trials do not prove that drinking POM Juice or taking one POMx Pill or one teaspoon of POMx Liquid, daily, prevents or reduces the risk of or treats heart disease, including by decreasing arterial plaque, lowering blood pressure, and/or improving blood flow to the heart. (CX1291 (Sacks Expert Report at 0010)).

b. Summary of Respondents' experts' opinions

953. Dr. Heber opined that based on basic scientific studies focusing on the hydrolysable tannins family, especially punicalagins and ellagitannins, POMx Pills and POMx Liquid are equivalent to POM Juice in providing health benefits to humans. (Heber, Tr. 2002-03; *see also* Heber, Tr. 2186-87 (studies show there is no difference between the antioxidant effect in pomegranate juice and that in POMx and that pomegranate juice and POMx have the same impact on oxidative stress)).

954. Dr. Heber also opined: the body of research on pomegranate juice and extract provides support for potential heart benefits for heart disease. (PX0192 (Heber Expert Report at 0015)).

955. Dr. Heber, in addition, opined that competent and reliable evidence shows that POM and POMx are likely to reduce the risk of cardiovascular disease. (Heber, Tr. 2012, 2087).

956. Dr. Heber further opined: there is credible scientific evidence that pomegranate juice and pomegranate extracts have significant health benefits for human cardiovascular systems, including: (1) decreases in arterial plaque; (2) lowering of blood pressure; and (3) improvement of cardiac blood flow, based on the biological mechanism of

prolonging the half-life of nitric oxide in the vasculature. (PX0192 (Heber Expert Report at 0044-45)).

957. Dr. Heber also stated in his expert report that he agreed with Dr. Stampfer that "claims that pomegranate juice and extract have not been proven absolutely effective to treat, prevent, or reduce the risk of heart disease . . . based solely on evidence from large double-blind placebo-controlled trials. . . But the entire body of scientific evidence should be considered when evaluating nutritional science." (PX0192 (Heber Expert Report at 0044)).

958. Dr. Ornish opined that in evaluating scientific research related to a whole food, as opposed to a drug, it is not necessary to reach statistical significance to convey information about the product; the convention of a finding that there be a five percent or less likely due to chance finding is an arbitrary convention; and that when you have a *p*-value of 0.05, there is a 95 percent probability of validity as opposed to chance and when you have a *p*-value of 0.058, there is a 94 percent validity as opposed to chance. (Ornish, Tr. 2340).

959. Dr. Ornish opined: taken as a whole, the preponderance of the scientific evidence from basic scientific studies, animal research, and clinical trials in humans reveals that the pomegranate in its various forms (including POM Wonderful 100% Pomegranate Juice, POMx Pills, or POMx Liquid) is likely to be beneficial in maintaining cardiovascular health and is likely to help reduce the risk of cardiovascular disease. (PX0025 (Ornish Expert Report at 0005)).

960. Dr. Ornish also opined: the universe of existing science provides significant evidence that pomegranate juice is likely to (1) reduce arterial plaque, (2) improve blood flow, and (3) reduce blood pressure. (PX0025 (Ornish Expert Report at 0005); PX0355 (Ornish, Dep. at 42); Ornish, Tr. 2374-75).

8. Conclusions

961. In considering whether a conventional food or dietary supplement is likely to have an effect on the risk or treatment of a disease, it is important to first look at the individual items of evidence, to determine whether they are reliable and probative. Then, it is important to look at the evidence as a whole. (CX1291 (Sacks Expert Report at 0038)).

962. There is insufficient competent and reliable scientific evidence to support the conclusion that the POM Products treat, prevent, or reduce the risk of heart disease, including by decreasing arterial plaque, lowering blood pressure, and/or improving blood flow to the heart; no clinical studies, research and/or trials prove these effects. (CX1291 (Sacks Expert Report at 0010, 0038-39); CX1293 (Stampfer Expert Report at 0022)).

H. Substantiation for Respondents' Prostate Cancer Claims

1. Substantiation standard for prostate claims

963. Because pomegranate juice is derived from a fruit, is known to be safe, and is not a pharmaceutical drug, physicians who treat patients concerned with prostate health would not hold pomegranate juice to the standards of safety and efficacy traditionally required by the FDA for approval of a pharmaceutical (performance of a large, randomized, double-blind, placebo controlled clinical trial) before recommending pomegranate juice to their patients. (PX0206 (Miller Expert Report)).

964. A claim that a fruit juice that is known to be safe, treats or prevents prostate cancer, if not offered as a substitute or a replacement for a conventional therapy, can be supported if there is reliable and competent scientific data that support the claimed beneficial effect. (PX0206 (Miller Expert Report at 11); Miller, Tr. at 2201).

965. Experts in the field of prostate health would not require RCTs to substantiate health benefit claims for harmless pure fruit products like pomegranate juice. (deKernion, Tr. 3060; *see also* Miller, Tr. 2201).

966. Experts in the field of prostate health would require that a product be scientifically evaluated through rigorous scientific and clinical studies, and believe that animal and *in vitro* studies alone are not sufficient to conclude that the POM Products treats, prevents, or reduces the risk of prostate cancer or that they have been clinically proven to do so. (CX1287 (Eastham Expert Report at 0006, 0012-15); CX1293 (Stampfer Expert Report at 0009-10)).

2. Background facts on prostates and the effects of pomegranates on prostates

a. Prostate function and prostate cancer

967. The prostate is a gland located in the male pelvis that is an organ of sexual function and fertility. (Eastham, Tr. 1236).

968. Prostate cancer occurs when cells of the prostate, typically the glandular cells, become cancerous, which means they have uncontrolled cell growth. (Eastham, Tr. 1236).

969. Last year about 220,000 men were diagnosed with prostate cancer in the United States. Approximately one in six men over the age of 60 will be diagnosed with prostate cancer each year. The average age of prostate cancer diagnosis is in the sixties. About 30,000 men die from prostate cancer each year. (Eastham, Tr. 1237-39).

970. Prostate cancer does not have a typical course. There are many prostate cancers that, while they are seen under the microscope, they do not represent a threat to the life expectancy or the quality of life of the patient. (Eastham, Tr. 1236).

971. Blood levels of prostate specific antigen (PSA) are measured in healthy men to assess their risk of prostate cancer. (Stampfer, Tr. 774).

972. PSA is a protein that is derived almost exclusively from the prostate and is widely used for screening for the risk of prostate cancer. (Stampfer, Tr. 774).

973. PSA is also used after diagnosis of prostate cancer to monitor the progression of disease. (Stampfer, Tr. 774).

974. The two mainstays of cure for prostate cancer are either radical prostatectomy (surgical removal of the prostate) or radiation therapy to the prostate. (Eastham, Tr. 1237; PX0060 at 0001).

975. Although the mainstays described in F. 974 are adequate for permanent disease control in many patients, a significant number of patients relapse and ultimately develop metastatic disease. (PX0060 at 0001).

976. Approximately one third of prostate cancer patients with clinically confined cancer that are treated with radical prostatectomy will develop a biochemical recurrence. (PX0060 at 0001).

977. There are limited treatment options for patients who have undergone primary therapy with curative intent and who have progressive elevation of their PSA without documented evidence of metastatic disease. (PX0060 at 0002).

978. Androgens are male steroid hormones that regulate prostate cancer cell growth. Hormone-type products increase testosterone levels and, basically, stop the conversion of testosterone to a more potent hormone, androgen. Compounds that contain hormone-type products can impact the PSA if they are used in large quantities. (Stampfer Tr. 773; Eastham Tr. 1242-44).

979. Early initiation of hormonal ablation is associated with significant morbidity and effect on quality of life, including fatigue, hot flashes, loss of libido, decreased muscle mass, and osteoporosis with long-term use. (PX0060 at 0002).

980. Strategies to delay clinical prostate cancer progression and prolong the interval from treatment failure to hormonal ablation would be of paramount importance. (PX0060 at 0002).

981. A combination of epidemiologic and basic science evidence strongly suggests that diet and plant-derived phytochemicals may play an important role in prostate cancer prevention or treatment. (PX0060 at 0002).

982. Epidemiologic studies suggest that a reduced risk of cancer is associated with the consumption of a phytochemical-rich diet that includes fruits and vegetables. (PX0060 at 0002).

983. Fresh and processed fruits and food products contain high levels of a diverse range of phytochemicals of which polyphenols, including hydrolyzable tannins (ellagitannins and gallotannins) and condensed tannins (proanthocyanidins), and anthocyanins and other flavonoids make up a large proportion. (PX0060 at 0002).

984. Several phytochemicals have been proposed as potential chemoprevention agents based on animal and laboratory evidence of antitumor effects. (PX0060 at 0002).

985. Suggested mechanisms of anticancer effects of polyphenols include the inhibition of cancer cell growth by interfering with growth factor receptor signaling and cell cycle progression, promotion of cellular differentiation, modulation of phosphodiesterase/ cyclooxygenase pathways, inhibition of kinases involved in cell signaling, and inhibition of inflammation. (PX0060 at 0002).

b. Mechanism of action of pomegranates in the prostate

986. The pomegranate (*punica granatum* L.) fruit has been used for centuries in ancient cultures for its medicinal purposes. (PX0060 at 0002).

987. Pomegranate fruits are widely consumed fresh and in beverage forms as juice and wines. Commercial pomegranate juice shows potent antioxidant and antiatherosclerotic properties attributed to its high content of polyphenols, including ellagic acid in its free and bound forms (as ellagitannins and ellagic acid glycosides), gallotannins, and anthocyanins (cyanidin, delphinidin, and pelargonidin glycosides) and other flavonoids (quercetin, kaempferol, and luteolin glycoside). (PX0060 at 0002).

988. Atherosclerosis means a build-up of plaque in arteries. (Stampfer, Tr. 700).

989. The most abundant of the polyphenols in pomegranates is punicalagin, an ellagitannin implicated as the bioactive constituent responsible for > 50% of the potent antioxidant activity of the juice. Punicalagin is abundant in the fruit husk and, during processing, is extracted into pomegranate juice in significant quantities reaching levels of > 2g/L juice. (PX0060 at 0002).

990. Ellagic acid and tannins have been shown previously to exhibit *in vitro* and *in vivo* anticarcinogenic properties, such as induction of cell cycle arrest and apoptosis, as well as the inhibition of tumor formation and growth in animals. (PX0060 at 0002).

i. *In vivo* research reporting reduced inflammation in prostate tumors

991. A large body of literature has linked inflammation to prostate carcinogenesis at all stages of the development of prostate cancer from normal tissue to advanced cancer. (PX0192 (Heber Expert Report at 0029); PX0070 at 0001).

992. Inflammation in the human is a key step in prostate cancer progression. (CX1352 (Heber, Dep. at 257-58); PX0070 at 0001).

993. Areas of chronic inflammation are almost universally present in pathologic specimens of the prostate, including biopsy cores in men prior to the diagnosis of prostate cancer, transurethral resection chips, and total prostatectomy specimens. (PX0192 (Heber Expert Report at 0029)).

994. Ninety-eight percent of prostate tumors removed at surgery for cancer have evidence of inflammation. (CX1352 (Heber, Dep. at 257-58); PX0192 (Heber Expert Report at 0029-30)).

995. *In vivo* research has demonstrated that pomegranate polyphenols reduce inflammation in prostate tumors. (CX1352 (Heber, Dep. at 257-58); Heber, Tr. 1992).

ii. *In vivo* research reporting nuclear factor κB decreased

996. One well-established signaling pathway mediating inflammatory responses relevant to cancer is the nuclear factor-*kappa*B (NF-κB) pathway. (PX0192 (Heber Expert Report at 0030); deKernion, Tr. 3046-47; Heber, Tr. 1992; PX0070 at 0001).

997. The unique protein NF-κB was the subject of Nobel Prize-winning research by Dr. David Baltimore who identified the protein's unique ability to both receive a signal from the outside of a cell and translate that signal into genetic programming of inflammatory proteins that are secreted by cells ("Dr. Baltimore's study"). (PX0192 (Heber Expert Report at 0030); Heber, Tr. 1992).

998. Dr. Baltimore's study involved *in vitro* and animal research. (PX0192 (Heber Expert Report at 0030)).

999. Dr. Baltimore's study showed that the activity of NF-κB is regulated by another protein inhibitor called IκB, which binds to and sequesters NF-κB family members in the fluid part of the cell away from DNA, called the cytoplasm. (PX0192 (Heber Expert Report at 0030); PX0070 at 0001).

1000. Dr. Baltimore's study showed that when the NF-κB pathway is activated, IκB is chemically modified by an enzyme called IκB kinase, which adds a phosphorus atom at

specific amino acids on the IkB protein (serine residues 32 and 36). (PX0192 (Heber Expert Report at 0030); PX0070 at 0001).

1001. Dr. Baltimore's study showed that once altered, the inhibitory protein IκB is degraded and NF-κB is free to move to the nucleus, where it functions to activate genetic mechanisms after binding to DNA, resulting in the secretion of proinflammatory signaling proteins. (PX0192 (Heber Expert Report at 0030); PX0070 at 0001).

1002. Dr. Baltimore's study showed that while normal activation of NF-κB is temporary in response to a stimulus meant to activate immune function, constant or constitutive activation has been observed in breast cancer, liver cancer, melanoma, Hodgkin's disease, and cervical cancer. (PX0192 (Heber Expert Report at 0030); PX0070 at 0001).

1003. Dr. Baltimore's study stated that direct genetic evidence in mouse models of colon and liver cancer have established that NF-κB activation within tumor cells or infiltrating inflammatory cells is required for tumor initiation or promotion. (PX0192 (Heber Expert Report at 0030); PX0070 at 0001).

1004. Dr. Baltimore's study reported that activation of NF-κB is observed in primary prostate cancer specimens as evidenced by its presence in the nucleus of cells where the genes reside and represents an independent risk factor for recurrence of prostate cancer after radical prostatectomy. (PX0192 (Heber Expert Report at 0030); PX0070 at 0001).

1005. Dr. Baltimore's study reported that pomegranate extract has been shown to inhibit NF-κB in normal human cells, including chondrocytes, epidermal keratinocytes, and vascular endothelial cells. (PX0192 (Heber Expert Report at 0031); PX0070 at 0002).

1006. Dr. Baltimore's study concluded that pomegranate extract inhibits both continuous (constitutive) and stimulated (cytokineinduced) NF-κB activity in prostate cancer cells *in vitro* and that the NF-κB inhibitory effect of pomegranate extract was necessary for the maximal cell killing effects of pomegranate extract. (PX0192 (Heber Expert Report at 0031); Heber, Tr. 1993; PX0070 at 0002).

1007. Respondents' experts testified that in tumors treated with pomegranate extract, the NF-κB decreased, therefore causing decrease of tumor growth. (deKernion, Tr. 3046-47; Heber, Tr. 1993).

1008. Respondents' experts testified that there is an absolute linear connection between the polyphenol mechanisms in pomegranate extract and the decrease in tumor growth. (deKernion, Tr. 3046-47; Heber, Tr. 1993).

1009. The mechanisms of action of the POM Products on inflammation and NF-κB contributes to the total body of research relied upon by Respondents. (PX0161 (deKernion Expert Report at 0011-12); PX0192 (Heber Expert Report at 0031); PX0206 (Miller Expert Report at 12); PX0070).

3. Basic science studies

a. Summary of the studies

1010. Respondents have conducted four *in vitro* studies and four animal studies relating to prostate cancer, according to their January 13, 2009 summary of their prostate cancer research to date. (CX1029 at 0004).

1011. POM's initial studies involved *in vitro* growing of human tumor cells in petri dishes in laboratories, adding POM and POM products and evaluating the effect on the human tumor cells. These initial studies showed a significant decrease in growth, increase in apoptosis, (programmed tumor death), and decrease in inflammation, factors which are all related to cancer. (deKernion, Tr. 3044).

1012. Subsequent research involved *in vivo* study wherein a human tumor was grown in immune deficient mice, an environment, which behaves as though it were in a human. In these studies which used LAPC4, a particular prostate tumor line, researchers demonstrated that when a prostate tumor is grown in mice and pomegranate extract and pomegranate products are added, the tumors markedly decreased. (deKernion, Tr. 3045). These studies were not of animal glands, but were studies of human prostate tissue put in animals. All of these studies indicated that POM had an antitumor effect on human tumors. (deKernion, Tr. 3049).

1013. In 2001, Agensys, a biotech company, performed early preclinical research for POM investigating the effect of pomegranate juice and prostate cancer. Agensys' unpublished research found that *in vitro* pomegranate juice consumption "substantially inhibits the proliferation of prostate cancer cells" and that pomegranate juice consumption "retards the growth of subcutaneous and orthotopic prostate tumors in mice." (deKernion, Tr. 3115; Tupper Tr. 1034; PX0065 at 0036-37).

1014. In a study titled, "*Pomegranate Ellagitannin-Derived Metabolites Inhibit Prostate Cancer Growth and Localize to the Mouse Prostate Gland*," Doctors Navindra Seeram, Arie Belledegrum, David Heber, and colleagues evaluated the effects of pomegranate extract on prostate cancer growth in severe combined immunodeficient mice injected with human prostate cancer cells. The study showed that pomegranate extract significantly inhibited prostate cancer in the mice as compared to the control. Researchers also found that ellagic acid and synthesized urolithins from the pomegranate extract were shown to inhibit the growth of human prostate cancer cells *in vitro*. The researchers concluded that the chemopreventive potential of pomegranate ellagitannins and localization of their bioactive metabolites in mouse prostate tissue suggest that the pomegranate may play a role in prostate cancer treatment and chemoprevention. The researchers also stated "[t]his warrants future human tissue bioavailability studies and further clinical studies in men with CaP [prostate cancer]." (PX0069).

1015. In a study titled, "*Pomegranate polyphenols down-regulate expression of androgen-synthesizing genes in human prostate cancer cells overexpressing the androgen receptor*," Doctors Hong, Seeram, and Heber examined the effects of pomegranate polyphenols from POMx Pills and POM Wonderful 100% pomegranate juice on the expression of androgen enzymes and androgen receptors. The study stated: recurrent prostate tumors advance to an androgen-independent state where they progress in the absence of circulating testosterone, leading to advanced cancer. The study also stated: during the development of the androgen-independent state, prostate cells are known to increase intracellular testosterone synthesis, which maintains cancer cell growth in the absence of significant amounts of circulating testosterone and that over-expression of androgen receptor to produce testosterone occurs in androgen-independent prostate cancer. The study found that POM polyphenols from either POMx Pills or POM Wonderful 100% pomegranate juice significantly inhibited gene expression and androgen receptors as a potential mechanism for maintaining healthy prostate cells. The researchers concluded that, "these results suggest that pomegranate polyphenols may be particularly helpful in the subgroup of patients with androgen-independent prostate cancer." (PX0068).

1016. A study by Doctors Rettig, Heber, et al., titled, "*Pomegranate extract inhibits androgen-independent prostate cancer growth through a nuclear factor-kappaB-dependent mechanism*," evaluated POMx Pills and POM Wonderful 100% pomegranate juice and found that their consumption was linked to reduction in cancer growth and decreased plasma PSA levels. The study found that one of the most well-established signaling pathways mediating inflammatory responses relevant to cancer is the NF-kB pathway, which serves as a predictor for recurrence of prostate cancer after radical prostatectomy, and that POMx inhibited NF-kB and cancer cell viability in a dose response fashion *in vitro* and Human LAPC4 prostate cancer xenograft mouse model. Based on the results reported, the researchers concluded "that pomegranate juice could have potential as a dietary agent to prevent the emergence of androgen-independence," thus potentially prolonging life expectancy of prostate cancer patients, and suggested "that this may be a high priority area for future clinical investigation." (PX0070).

1017. In a study by Dr. Sartippour, et al., titled, "*Ellagitannin-Rich Pomegranate Extract Inhibits Angiogenesis In Prostate Cancer In Vitro And In Vivo*," the *in vivo* results showed that POMx Pills inhibit prostate tumor growth compared to control in immunodeficient mice injected with human prostate cancer cells. The mice were given a dose comparable, using caloric demand scaling, to that found in POMx and taken by humans. The study reported that POMx was shown to significantly decrease the overall blood vessel density in mouse tumors. The study also stated that *in vitro* results showed that POMx Pills significantly inhibited proliferation of human prostate cancer cells at low ug/ml. concentrations. The researchers concluded, "these findings strongly suggest the potential of pomegranate ellagitannins for prevention of the multi-focal development of prostate cancer as well as to prolong survival in the growing population of prostate cancer survivors of primary therapy." (PX0071).

b. Complaint Counsel's experts' opinions of basic research on prostate cancer

1018. Complaint Counsel's experts testified that to substantiate a claim that a food or dietary supplement is an effective treatment for prostate cancer, experts in the field would require an RCT trial with an appropriate sample population of patients with the stage of the disease targeted by the study, and measuring a proper endpoint. (CX1287 (Eastham Expert Report at 0015)).

1019. Complaint Counsel's experts reviewed the available *in vitro* and animal research and concluded that RCTs with proper endpoints are needed to confirm the potential antioxidant effect on prostate cancer observed in a test tube or laboratory setting. (CX1293 (Stampfer Expert Report at 0022); CX1287 (Eastham Expert Report at 0021)).

c. Respondents' experts' opinions of basic research on prostate cancer

1020. Dr. deKernion explained that Respondents' animal studies were on human prostate tissue inserted in the animals and were not merely a study of animal glands. (deKernion, Tr. 3049).

1021. Dr. DeKernion testified that Respondents' *in vitro* and animal studies showed that pomegranate juice inhibited the growth of prostate cancer cells and actually killed cancer cells from humans that had been inserted into mice. (deKernion, Tr. 3044-47, 3120; PX0351 (deKernion, Dep. at 110).

1022. Dr. deKernion testified that while one cannot always extrapolate from *in vitro* and animal results to what the results would be in humans, the pre-clinical studies he reviewed indicated a strong likelihood that, in humans, pomegranate juice would at least inhibit the growth of prostate cancer cells. (deKernion, Tr. 3063-64; PX0161 (deKernion Expert Report at 0011-12)).

1023. Dr. deKernion also testified that that even where the animal and *in vitro* evidence is strong and shows that an agent's mechanism of action works, this evidence does not prove that an agent works in humans. (deKernion, Tr. 3063-64).

d. Determination on Respondents' basic research

1024. Experts in the field agree that even where the animal and *in vitro* evidence is strong and shows that an agent's mechanism of action works, this evidence alone does not prove that an agent works in humans. (deKernion, Tr. 3063-64; Stampfer, Tr. 722-25 (animal studies do not always correspond with what will occur in humans; one cannot assume that if an *in vitro* assay shows a certain result, the same result will occur in the human body)).

4. Human clinical studies

1025. Respondents have one human clinical study completed and published, the Pantuck Phase II Cancer Study (2006), and one ongoing human clinical study, the Carducci Dose Study, according to their January 13, 2009 summary of their prostate cancer research as of that date. (CX1029 at 0004).

a. Pantuck Phase II Prostate Cancer Study

i. Background to the Pantuck Study

1026. Dr. Allan J. Pantuck is an associate professor of Urology at UCLA Medical School and maintains a clinical practice at UCLA. He attended college at Columbia University, medical school at Robert Woods Johnson Medical School, and has a Masters Degree in Clinical Research from UCLA Medical School. (CX1090 at 0001; CX1341 (Pantuck Dep. at 20-21)).

1027. Dr. Pantuck's clinical appointments include: Attending Urologist at Harbor-UCLA Medical Center, Attending Urologist Wadsworth Veterans Affairs Medical Center, and Attending Urologist, UCLA Medical Center. (CX1090 at 0004).

1028. Dr. Pantuck's professional societies and memberships include the American Society of Clinical Oncology, American Urological Association, Jonsson Comprehensive Cancer Center, and the Society of Urologic Oncology. (CX1090 at 0002).

1029. Dr. Pantuck served as editor of Advances in the Management of Renal Cell Carcinoma and Proceedings of the Irish Society of Surgical Oncology (2003). Dr. Pantuck has been a reviewer for medical journals such as the British Journal of Urology International, The Journal of Urology, Clinical Cancer Research, and Urologic Oncology. (CX1090 at 0003).

1030. In 2001, Dr. Pantuck wrote a letter to Dr. Dornfeld and Dr. Harley Liker (Respondents' scientific advisors) setting forth his protocol concepts for two clinical studies studying the benefits of pomegranate juice in populations of men with prostate cancer. (CX0544 at 0001). According to the letter, "these pilot studies are designed to provide preliminary data to justify further development of pomegranate juice as a chemopreventative agent for prostate cancer." (CX0544 at 0001). One of the two proposed protocol concepts became the *Phase II Study of Pomegranate Juice for Men with Rising Prostate-Specific Antigen following Surgery or Radiation for Prostate Cancer* ("Pantuck Study"). (CX1341 (Pantuck, Dep. at 57)).

1031. The Pantuck Study began in 2003. (CX1128 at 0001). According to the protocol, the study was a single-center, three-year study in which approximately 40 patients with prostate cancer treated by radical prostatectomy or radiotherapy with a rising PSA would receive eight ounces of pomegranate juice daily. (CX0666 at 0004-05).

1032. By 2006, the Pantuck Study was complete and ready for publication. Dr. Pantuck first submitted the manuscript for the study to the *Journal of Clinical Oncology*. (CX1341 (Pantuck, Dep. at 107)). It was initially rejected. (CX1341 (Pantuck, Dep. at 107)). He subsequently submitted it to *Clinical Cancer Research*. (CX1341 (Pantuck, Dep. at 107)). One peer reviewer called the manuscript "excessively advocatory of pomegranate juice as a treatment for prostate cancer." (CX0790 at 0001). Dr. Pantuck addressed this concern and other comments by making various changes to the manuscript. (CX0790; CX0786).

1033. The Pantuck Study, titled, "*Phase II Study of Pomegranate Juice for Men with Rising Prostate-Specific Antigen Following Surgery or Radiation for Prostate Cancer*," Pantuck, et al., was published in the journal Clinical Cancer Research in July 2006. (CX0815).

1034. *Clinical Cancer Research* is an extremely well regarded peer-reviewed journal. The process and rigor for being published in *Clinical Cancer Research* is very high. It is considered one of, if not the, finest clinical cancer journals. (CX1352 (Heber Dep. at 268-69).

1035. Dr. Heber testified that the Pantuck Study is considered, "a very highly esteemed paper." (CX1352 (Heber, Dep. at 268)).

1036. The Pantuck Study was the first clinical trial of pomegranate juice in patients with prostate cancer. (CX0815 at 0001).

1037. According to the published study report, the Pantuck Study was "an open-label, single-arm clinical trial," meaning it was not an RCT and did not have a placebo group. (CX0815 at 0002).

1038. The Pantuck Study cost $479,236.50. (CX1128 at 0001).

ii. About the Pantuck Study

1039. The Pantuck Study included 46 patients who had been diagnosed with prostate cancer. The majority of the patients (68%) had been previously treated for prostate cancer by undergoing radical prostatectomy. The remainder had been treated by radiation (10%), brachytherapy (10%), a combination of surgery and radiation (7%), or cryotherapy (5%). (CX0815 at 0003).

1040. All 46 patients in the Pantuck Study drank eight ounces of pomegranate juice daily until meeting disease progression endpoints. Clinical endpoints were effect on serum prostate specific antigen (PSA), serum-induced proliferation and apoptosis of prostate cancer cells, serum lipid peroxidation, and serum nitric oxide levels. The primary endpoint was the effect on PSA variables, such as change in prostate specific antigen doubling time (PSADT). (CX0815 at 0002).

1041. The presence of detectable PSA after radical prostatectomy or other radical treatment usually indicates cancer is present. (deKernion, Tr. 3051).

1042. PSADT is a mathematical expression of the rapidity with which the prostate specific antigen is rising, and an expression of the rapidity of growth and number of prostate tumor cells. (deKernion, Tr. 3050).

1043. Patients in the Pantuck Study had their blood drawn every three months to have their PSA determined. Disease progression was defined as either a greater than 100% increase in PSA (with a minimum value of 1.0 ng/ml.) compared with the best response observed or any documentation of metastatic or recurrent disease. (CX0815 at 0002).

1044. Patients in the Pantuck Study who consumed POM Juice experienced a significant statistical increase in PSADT when compared to their own baseline pre-treatment PSADT. (CX0815 at 0001, 0004).

1045. In the Pantuck Study, the average pre-treatment PSADT before intervention was approximately 15 months, and after 33 months, the average post-treatment PSADT was approximately 54 months. Thus, mean PSA doubling time significantly increased from a mean of 15 months at baseline to 54 months post-treatment. (CX1080 at 0004).

1046. The Pantuck Study reported: *in vitro* assays comparing pre-treatment and post-treatment patient serum on the growth of the prostate cancer line LNCaP showed a 12% decrease in cell proliferation and a 17% increase in apoptosis, a 23% increase in serum NO, and significant reductions in oxidative state and sensitivity to oxidation of serum lipids after pomegranate juice consumption versus before pomegranate juice consumption. (CX0815 at 0001).

1047. The Pantuck Study concluded: the statistically significant prolongation of PSA doubling time, coupled with corresponding laboratory effects on prostate cancer *in vitro* cell proliferation and apoptosis, as well as oxidative stress, warrant further testing in a placebo-controlled study. (CX0815 at 0001).

iii. Follow up to the Pantuck Study

1048. In 2008, Dr. Pantuck released the following abstract: Pantuck, AJ, et al., "*Long term follow up of pomegranate juice for men with prostate cancer and rising PSA shows durable improvement in PSA doubling times*," American Society of Clinical Oncology ("Pantuck Phase II Follow-Up Results") which summarized follow-up results for the Pantuck Study. (PX0061).

1049. The Pantuck Phase II Follow-Up Results reported that fifteen (31%) active patients remained on the study. (PX0061). All of the men who had dropped out of the study did so because their PSA had increased. (CX0918 at 0001). As of June 2010, only 12 patients remained active in the study. (CX1128 at 0001).

1050. The Pantuck Phase II Follow-Up Results reported that those who continued on pomegranate juice maintained a lengthening of their PSA doubling time compared to men who did not continue on pomegranate juice. (PX0061; Eastham, Tr. 1305; CX1341 (Pantuck, Dep. at 136)).

1051. The Pantuck Phase II Follow-Up Results reported: mean PSA doubling time for the entire cohort continued to show a significant increase following treatment, from a mean of 15.4 at baseline to 60 months post-treatment, while the median PSA slope decreased 60% from 0.06 to 0.024. Patients remaining on study ("active") were compared to those no longer on study ("non-active"). At baseline, mean PSA doubling times were similar between Active and Non-Active patients. However, post-treatment PSADT prolongation was greater and the decline in median PSA slope was larger in active compared to non-active patients. (PX0061).

1052. The Pantuck Phase II Follow-Up Results concluded that long-term follow up of pomegranate juice consumption in men with prostate cancer and rising PSA following primary therapy demonstrates a durable increase in PSA doubling time and stated that a multi-center, randomized phase III study is ongoing to further evaluate the benefits of pomegranate in a placebo-controlled manner. (PX0061).

iv. Statements by Dr. Pantuck about the Pantuck Study

1053. Dr. Pantuck explained that the design of the study was for subjects to serve as their own control. Patients had a specific PSA doubling time prior to treatment; patients would then be treated and measured for any change in their doubling time after treatment. (CX1341 (Pantuck, Dep. at 78)).

1054. When the Pantuck Study report was released in 2006, Dr. Pantuck was quoted in an American Association for Cancer Research press release, as stating: "[w]e don't believe we are curing anyone from prostate cancer." He pointed out that "although a third of patients experienced a decrease in PSA during the study, nobody's PSA went to zero." Dr. Pantuck further explained: "The PSA doubling time, however, was longer. For many men, this may extend the years after surgery or radiation that they remain recurrence free and their life expectancy is extended. They may be able to prevent the need to undergo additional therapies, such as radiation, hormonal or chemotherapies." (CX0816 at 0002).

1055. Dr. Pantuck stated that the Pantuck Study did not prove that pomegranate juice prevents or reduces the risk of prostate cancer because all the patients in the study already had prostate cancer, thus his study did not address anything related to causation. (CX1341 (Pantuck, Dep. at 108)).

1056. Dr. Pantuck did not claim that the Pantuck Study proved that pomegranate juice can treat prostate cancer, but explained that the study showed that the doubling time for PSA was prolonged. (CX1341 (Pantuck, Dep. at 108)).

1057. Dr. Pantuck testified that the Pantuck Study showed evidence that the growth of the cancer had been altered by POM Juice. (CX1341 (Pantuck, Dep. at 118-19)).

1058. Dr. Pantuck stated that the feedback from the scientific community with regard to the peer-reviewed published Pantuck Study has primarily been favorable, and that some doctors have discussed the findings with patients. (CX1341 (Pantuck, Dep. at 268-69)).

1059. Dr. Pantuck also stated: "[i]t remains controversial whether modulation of PSA levels represents an equally valid clinical end point." (CX0815 at 0008). According to Dr. Pantuck, "PSA has not been validated prospectively as a surrogate endpoint for a meaningful prostate cancer outcome." (CX1080 at 0001). Dr. Pantuck has also stated that "although PSA changes are thought to be prognostically important, it is based on level 2 evidence, and nobody has ever shown conclusively that changes in PSA kinetics arising from therapeutic intervention is meaningful." (CX1080 at 0001).

1060. Dr. Pantuck testified that the greatest limitation of the Pantuck Study was the lack of a blinded control arm. (CX1341 (Pantuck, Dep. at 110)). In the published study report, Dr. Pantuck specifically pointed to the published study, *Rosiglitizone versus Placebo for Men with Prostate Carcinoma and a Rising Serum Prostate-Specific Antigen Level after Radical Prostatectomy and/or Radiation Therapy*, Cancer 2004: 101:1569-74 ("Rosiglitizone Study"). (CX0815 at 0008).

1061. The Rosiglitazone Study was a randomized, double-blind placebo-controlled study examining the effect of rosiglitazone in a population of men similar to the patients studied in the Pantuck Study, namely men who had been treated by radical prostatectomy or radiation with a rising PSA. (PX0172 at 0001; CX0815 at 0001; deKernion, Tr. 3069). The Rosiglitazone Study found that 40% of the placebo group and 38% of the treatment group experienced a prolongation in PSADT. (PX0172 at 0001; deKernion, Tr. 3071).

1062. The Rosiglitizone Study authors stated that "[t]he discordance between baseline and post-treatment PSADT in our placebo group suggests caution is required when using changes in PSADT as an outcome in uncontrolled trials and reinforces the value of randomized, placebo-controlled trials in this setting." The Rosiglitazone Study authors concluded that, "the current results do not diminish the potential value of changes in PSADT as an outcome variable for the early evaluation of novel therapeutic agents. In randomized studies of similar design, more active agents may demonstrate the value of PSA kinetics as a screen for biologic activity." (PX0172 at 0006).

1063. Dr. Pantuck stated that the Rosiglitazone Study "highlights the potential limitations of PSA variables in monitoring patients and the need for confirmatory prospective studies using a blinded control arm." (CX0815 at 0008).

b. Carducci Study

i. Background to the Carducci Study

1064. Respondents have also sponsored a human study looking at POMx use in men who have already been treated for prostate cancer. The study is completed and an abstract summarizing the results has been published. *See* M.A. Carducci, et al., *A Phase II Study of Pomegranate Extract for Men with Rising Prostate-Specific Antigen Following Primary Therapy* ("Carducci Study"), J Clin Oncol 29: 2011 (suppl 7; abstr 11). (PX0175; *see also* CX1174). A final, peer-reviewed study report had not been published at the start of trial in this matter. (*See* Nonparties Johns Hopkins University and Michael A. Carducci, M.D.'s Motion for *In Camera* Treatment, at 5).

1065. The Carducci Study was conducted by Dr. Michael A. Carducci, a professor of oncology and urology at the Johns Hopkins School of Medicine, in Baltimore, Maryland. Within the Cancer Center, he leads two programs, the prostate cancer/genitourinary cancer program and chemical therapeutics. (CX1340 (Carducci, Dep. at 14-15); CX1120).

1066. Dr. Carducci is a graduate of Georgetown University and Wayne State University Medical School. Dr. Carducci did a residency in internal medicine at the University of Colorado in Denver. After completing a year as chief resident at the University of Colorado, he accepted a fellowship in oncology at Johns Hopkins University. (CX1340 (Carducci, Dep. at 13-14)).

1067. Dr. Carducci has conducted 40 to 50 clinical trials relating to prostate cancer and has published approximately 80 articles related to prostate cancer. (CX1340 (Carducci, Dep. at 15-16)).

1068. In 2006, Dr. Carducci began working with Respondents to design the Carducci Study. (CX0806). Dr. Carducci submitted a proposed protocol for the Carducci Study to Respondents for a larger randomized three-arm study, with two treatment arms and one placebo arm. (CX1340 (Carducci, Dep. at 28-29; CX0064 at 0002, *in camera*).

1069. Respondents conducted a feasibility and cost analysis and decided that the study proposed by Dr. Carducci was too costly. The placebo arm was dropped from the study due to costs, and, in part, due to poor patient acceptance of a placebo. (CX1340 (Carducci, Dep. at 28-29)).

ii. About the Carducci Study

1070. The Carducci Study began in January 2008. (CX1138 at 0002). According to the protocol, the Carducci Study was an 18-month, multi-center, randomized, double-blind, dose-finding study of the effect of two different doses of POMx capsules (one or three

capsules) on PSADT in men who had received initial therapy for prostate cancer. (CX1110 at 0007).

1071. An interim analysis of the Carducci Study was conducted in 2009 and shared with Respondents in 2010. (*See* CX1088, *in camera*; CX1102, *in camera*). The final analysis was conducted in August 2010. (CX1146, *in camera*).

1072. In 2011, Dr. Michael Carducci presented the abstract of his clinical research study titled, "*A Phase II Study of Pomegranate Extract for Men with Rising Prostate-specific Antigen Following Primary Therapy*" at the disease specific meeting of the American Society of Clinical Oncology ("Carducci abstract"). (PX0175). Dr. Carducci's abstract was peer-reviewed prior to being selected for presentation. (CX1340 (Carducci, Dep. at 176)).

1073. The Carducci Study was a multi-center, double blind Phase II randomized trial that studied 104 men with rising PSA and without metastases. They were given either a high or low dose (one capsule or three capsules) of POMx, stratified by baseline PSADT and Gleason score, and with no restrictions for PSADT and no upper limit PSA value. (PX0175).

1074. In the Carducci Study, men were treated until progression or for 18 months. PSA levels were obtained every three months. (PX0175).

iii. Results of the Carducci Study

1075. According to the Carducci abstract, 104 men were enrolled and treated for up to six months (92%), 12 months (70%), and 18 months (36%). There was no significant treatment difference ($p = .920$) in PSADT between the one capsule and three capsule dose groups. (CX1174 at 0001).

1076. The Carducci abstract reported: median PSADT lengthened from 11.9 months at baseline to 18.5 months after treatment ($p < .001$), a within group measurement. Thus, it showed that POMx treatment significantly increased the PSA doubling time by over six months in both treatment arms. (CX1174 at 0001).

1077. The Carducci abstract also reported that 13 patients (13%) had declining PSA levels during the study. (CX1174 at 0001).

1078. The Carducci abstract concluded that POMx demonstrates "promising antitumor effects in prostate cancer." (CX1174 at 0001).

iv. Statements by Dr. Carducci about the Carducci Study

1079. Dr. Carducci testified that the use of PSA doubling time as a primary endpoint to determine if POMx has an effect on the disease state was a scientifically valid way to conduct the study. (CX1340 (Carducci, Dep. at 181-82)).

1080. Dr. Carducci also testified that the endpoint of PSA doubling time is not a standard for regulatory approval of drugs at the FDA level and PSA doubling time as a marker or surrogate has not been proven. (CX1340 (Carducci, Dep. at 89-90)).

1081. Dr. Carducci stated that the Carducci Study was not designed to use endpoints that were "drug-like," but was specifically designed for a natural product and that researchers were looking at safety and whether POMx had an effect on rising PSA. (CX1340 (Carducci, Dep. at 50-51)).

1082. Dr. Carducci testified that the Carducci Study results, as designed and planned, were statistically significant. (CX1340 (Carducci, Dep. at 183)).

1083. Dr. Carducci also testified that without a placebo, he cannot be sure that the effect on PSADT observed in the Carducci Study is attributable to POMx. (CX1340 (Carducci, Dep. at 95)).

1084. According to Dr. Carducci, the Carducci Study was never designed to prove, and did not prove, that POMx prevents or reduces the risk of prostate cancer. (CX1340 (Carducci, Dep. at 87-88)).

1085. According to Dr. Carducci, the Carducci Study was never designed to prove that POMx treats prostate cancer but the study showed that PSA doubling time increased by over six months in both arms of the study. (CX1340 (Carducci, Dep. at 87).

c. Expert opinion on the human clinical studies

i. Complaint Counsel's experts on the Pantuck Study

1086. Complaint Counsel's experts testified that the Pantuck Study fails to provide support for prostate cancer treatment claims for two major reasons: the lack of a placebo control group and the lack of an accepted endpoint marker. (Eastham, Tr. 1295-97; CX1287 (Eastham Expert Report at 0018-19); CX1293 (Stampfer Expert Report at 0024-25); Stampfer, Tr. 782-83).

1087. According to Dr. Stampfer, without a placebo control group in the Pantuck Study, it is not possible to know whether the same change in PSADT would have been observed in this patient group if they had never received POM Juice. (Stampfer, Tr. 869-70; CX1293 (Stampfer Expert Report at 0024)).

1088. According to Dr. Eastham, if the Pantuck Study had included a control group, it is possible that *no* statistical difference between groups would have been observed. Without a placebo, there is no way to eliminate confounding factors that may have impacted PSADT – such as changes in diet, exercise, or the reduction of stress. (Eastham, Tr. 1295-97; CX1287 (Eastham Expert Report at 0018)).

1089. The Pantuck Study used mean PSA doubling time as an endpoint. (PX0060). Complaint Counsel's experts testified that in a prostate cancer treatment trial, PSA doubling time is not a relevant surrogate marker for prostate cancer prevention. Instead, in a prostate cancer treatment trial, overall survival or prostate cancer-specific mortality is the endpoint generally accepted by experts in the field. (CX1293 (Stampfer Expert Report at 0025); Eastham, Tr. 1280; CX1287 (Eastham Expert Report at 0006-09, 0014) ("The primary endpoint in a prostate cancer prevention trial for measuring whether a product has been effective is the prevalence or incidence of prostate cancer between the treatment and placebo groups at the conclusion of the study.").

1090. Dr. Eastham criticized the Pantuck Study for the additional reason that the patients studied, with an average pre-treatment PSADT of 15 months, are considered to have a far lower risk of clinical progression, and because of this, it is unclear whether the increase in PSADT observed in the Pantuck Study is clinically significant. (Eastham, Tr. 1297-98).

1091. Complaint Counsel's experts also testified that the Pantuck Study was designed as a treatment study (*i.e.*, study was conducted in men with prostate cancer) and does not provide any evidence that POM Juice is a prostate cancer preventative. (CX1293 (Stampfer Expert Report at 0025); Eastham, Tr. 1294-99).

1092. Dr. Eastham opined that the appropriate sample population for a cancer prevention trial "would involve more than 10,000 healthy men, ages 50 to 65, having no sign of prostate cancer." (CX1287 (Eastham Expert Report at 0012)).

1093. Dr. Eastham further opined that a "prostate cancer prevention study must be conducted over a long enough period of time to see an effect over time." CX1287 (Eastham Expert Report at 0014)).

1094. Complaint Counsel's experts also state that the Pantuck Study on POM Juice cannot provide reliable evidence to support claims about POMx Pills' or POMx Liquid's benefit for prostate cancer. (Eastham, Tr. 1306; CX1293 (Stampfer Expert Report at 0025); CX1287 (Eastham Expert Report at 0020)). According to Dr. Eastham, POM Juice is not identical to POMx Pills and POMx Liquid. (CX1287 (Eastham Expert Report at 0020)). POM Juice has more than one active ingredient. Processing may result in eliminating a needed ingredient. (Eastham, Tr. 1306-07). Even if the active ingredient is known and the alternate compound contains the same amount of active ingredient, the alternate compound may contain some other as yet unknown compound that might counter-act the benefit of the active agent. (CX1287 (Eastham Expert Report at 0020)).

1095. Dr. Eastham is not an expert in bioavailability and did not review any of the equivalency studies or articles on POM Juice, POMx Pills or POMx Liquid. (PX0358 (Eastham, Dep. at 94)).

ii. Complaint Counsel's experts on the Carducci Study

1096. Complaint Counsel's experts testified that the Carducci Study cannot provide support for treatment claims because it lacked a placebo-control group and that without a placebo-control group, it is not possible to conclude that POMx caused the change in the patients' PSADT. (Eastham, Tr. 1310; CX1287 (Eastham Expert Report at 0022); Stampfer, Tr. 789-90; CX1293 (Stampfer Expert Report at 0028)).

1097. Complaint Counsel's experts testified also that the Carducci Study cannot provide support for treatment claims because the primary endpoint in the study is PSADT, which has not been accepted by experts in the field as a surrogate for overall survival. (Eastham, Tr. 1310; CX1287 (Eastham Expert Report at 0022); CX1293 (Stampfer Expert Report at 0028)).

1098. As found in F. 1075, the Carducci Study showed no difference between a one pill dose and a three pill dose. Complaint Counsel's expert testified that the lack of a dose response despite a three-fold difference in dosage does not support a causal relationship between POMx and change in PSADT. (Stampfer, Tr. 789-90; CX1293 (Stampfer Expert Report at 0028)).

1099. Complaint Counsel's experts also testified that the Carducci Study cannot provide support for prevention claims because it evaluated the effect of POMx in men who already had prostate cancer. (Eastham, Tr. 1309-10; *see also* CX1293 (Stampfer Expert Report at 27)).

iii. Complaint Counsel's experts on PSA doubling time

1100. Complaint Counsel's experts testified that in a prostate cancer treatment trial, PSA doubling time is not a relevant surrogate marker for prostate cancer prevention. (Eastham, Tr. 1280; CX1287 (Eastham Expert Report at 0006-09); CX1293 (Stampfer Expert Report at 0025)).

1101. In his testimony, Dr. Eastham stated: modulation of PSA doubling times has not been proven to be of any utility and that no one would propose that changes or modulation of PSA doubling time is a prognostic factor in men with biochemical recurrence after primary therapy for prostate cancer. (Eastham, Tr. 1342, 1345).

1102. Dr. Eastham has also written, in an article titled, "*Prostate-specific antigen doubling time as a prognostic marker in prostate cancer*," Nature Clinical Practice (2005): "PSA doubling time has emerged as an important factor in the evaluation of men with newly diagnosed prostate cancer or prostate cancer that recurs after treatment. PSA doubling time can also be used as a surrogate marker for prostate cancer-specific death." Dr. Eastham's article concluded "PSADT is an important prognostic marker in men with biochemical failure after local therapy for prostate cancer, and it predicts the probable

response to salvage radiotherapy, progression to metastatic disease and prostate cancer specific death." (PX0178 at 0001, 0009).

1103. In his expert report, Dr. Stampfer opined "it is unknown if PSADT predicts overall survival in prostate cancer patients throughout its range." (CX1293 (Stampfer Expert Report at 0026)).

1104. Dr. Stampfer also testified that PSA doubling time is a "predictor of disease and mortality" and that, if the extension of PSA doubling time is true, it would substantially prolong lives. (Stampfer, Tr. 869, 873).

iv. Respondents' experts on both clinical studies

(a) PSA doubling time

1105. Dr. deKernion testified that the presence of detectable PSA after radical prostatectomy or other radical treatment usually indicates cancer is present and that PSADT provides an expression of how those tumor cells are going to behave. The longer the PSADT, the less dangerous the growth of the cancer. (deKernion, Tr. 3051-52).

1106. Dr. deKernion testified that the Pantuck Study and the Carducci Study showed that POM Juice and POMx, respectively, slowed down the growth of the tumor cells as expressed by the longer time it took for those tumor cells to double. (deKernion, Tr. 3057).

1107. Dr. deKernion testified that the Pantuck Study and the Carducci Study both showed a dramatic lengthening of PSA doubling time. (deKernion, Tr. 3052-58).

1108. Dr. deKernion opined that PSA doubling time is used to determine success or failure of prostate cancer treatment and that multiple studies support that PSADT is correlated with the risk of clinical tumor and recurrence and, therefore, must have some association with longevity. (PX0161 (deKernion Expert Report-0004; deKernion, Tr. 3050-58).

1109. Dr. deKernion stated that PSA doubling time is clearly a useful marker in determining risk or outcome in patients following prostate cancer treatment. (deKernion, Tr. 3055).

1110. Dr. deKernion testified that given the understanding of PSA doubling time in predicting risk of clinical recurrence and to some extent survival, it is logical to use changes in PSADT as indicative of an intervention's effectiveness regarding prostate tumor behavior. (PX0161 (deKernion Expert Report at 0007, 0011-12)).

1111. Dr. deKernion also testified that the PSA doubling time is not accepted by experts in the field of prostate cancer as a surrogate endpoint for clinical benefit in chemotherapy trials. (deKernion, Tr. 3096).

1112. Dr. Heber testified that PSA doubling time is a "very important clinically utilized marker of clinical status." (CX1352 (Heber, Dep. at 314)).

1113. Dr. Heber testified that there is a lot of support from the urological community to get the FDA to accept PSA doubling time as a surrogate endpoint and that there is "a lot of feeling in the urological community and scientific agreement that [the] rate of rise of PSA is an important biomarker." (CX1352 (Heber, Dep. at 316-17)).

(b) Placebo control arm

1114. Dr. deKernion testified that a control arm is not necessary for an objective Phase II study that is exploratory in nature. Many studies on food and many other categories in science are observational type studies without use of a control—a control is important when there is a high risk that the observed effect could be attributed to something other than the substance being tested. (PX0161 (deKernion Expert Report at 0009); deKernion, Tr. 3059-60, 3066; PX0351 (deKernion, Dep. at 97-99)).

1115. Dr. deKernion testified that in both the Pantuck Study and the Carducci Study, the control was the previous doubling time prior to treatment. The researchers measured the doubling time before patients took POM Juice or POMx and then measured doubling time afterwards, comparing one to the other. This was done in lieu of a separate placebo group. (deKernion, Tr. 3059).

1116. Dr. deKernion testified that a control arm is often used to control for the placebo effect, that one purpose of a placebo control group is to limit confounding factors, and that the use of a placebo group is more important when you have a subjective reporting, as opposed to an objective reporting. (deKernion, Tr. 3059-60, 3066-67; PX0351 (deKernion, Dep. at 97-99)).

1117. Dr. deKernion specifically testified that a placebo control arm is not needed when PSADT is the study endpoint to assess the efficacy of the product or therapy being studied. In the Pantuck Study and the Carducci Study, the researchers were looking and testing objective blood results, and there is no evidence to suggest the placebo effect plays any role in modulating the PSADT of the subject. (deKernion, Tr. 3059-60, 3081; PX0351 (deKernion, Dep. at 97-99).

1118. Dr. deKernion also testified that without a placebo, one cannot be certain that the effect on PSA doubling time seen in the Carducci Study is attributable to POMx. (deKernion, Tr. 3103).

(c) Respondents' experts' conclusions

1119. Dr. Heber testified that in laboratory studies he conducted, he found no difference in the antioxidant effect between POM Juice and POMx products and that animal studies indicate that the effects of pomegranate juice and POMx Pills on prostate cancer are equivalent. (CX1352 (Heber, Dep. at 336); Heber, Tr. 2002; Heber, Tr. 2186-87).

1120. At trial, Dr. Heber testified that there is competent and reliable science showing that the POM Juice and POMx lengthen the PSA doubling time for men who have had prostate cancer and, thus, it is likely for those men to have a deferred recurrence or death from that disease; and that POM Juice and POMx are likely to lower the risk of prostate problems for men who have not yet been diagnosed with prostate cancer. (Heber, Tr. 2012-13).

1121. In his expert report, Dr. Heber opined: the statistically significant prolongation of PSA doubling time, corresponding laboratory effects on prostate cancer *in vitro* cell proliferation and apoptosis, as well as oxidative stress and inflammation, provide strong scientific rationale for the statement that pomegranate juice promotes prostate health. (PX0192 (Heber Expert Report at 0027)).

1122. Dr. deKernion testified that in order to show an effect of POM Products on prostate cancer, the best way to do that research is on patients whose prostate had been removed because the presence of PSA elevation is almost always an indication of remaining cancer. This is how the Pantuck Study and Carducci Study were conducted. (deKernion, Tr. 3057).

1123. Dr. deKernion opined that all "evidence supports that PSA changes including doubling time after failure of definitive therapy truly reflect a change in the tumor cell growth; no evidence exists to suggest that a biochemical effect on PSA measurement can account for changes; and no evidence exists that PSA doubling time significantly and spontaneously lengthens in a patient with known biochemical or clinical cancer." (PX0161 (deKernion Expert Report at 0008)). Therefore, in the Pantuck Study, it is only logical to conclude that the agent causing the change in PSA doubling time is POM Juice, especially given the pre-clinical evidence of the effect of the POM Products on prostate cancer, "and the results of these studies could not be explained otherwise." (PX0161 (deKernion Expert Report at 0011-12)).

1124. Dr. deKernion opined that POM Products are beneficial to prostate health and although there is not 100% proof that POM Products reduce the risk of prostate cancer, the same mechanism shown in the *in vitro* and animal studies and in the Pantuck and Carducci human studies showed, with a "high degree of probability," that POM Juice and POMx would inhibit the clinical development of prostate cancer in men who have not been diagnosed with that disease. (deKernion, Tr. 3119-20, 3126; PX0351 (deKernion, Dep. at 41-42)).

1125. Dr. deKernion testified that there is a high degree of probability that POM Products inhibit the clinical development of prostate cancer cells even in men not diagnosed with prostate cancer. (deKernion, Tr. 3126; PX0351 (deKernion, Dep. at 76-77) (in healthy men, who have never been diagnosed with prostate cancer, POM Juice and POMx could possibly play a role in preventing them from getting prostate cancer).

1126. Dr. deKernion testified that there is a high probability that the POM Products provide a special benefit to men with PSA after radical prostatectomy. (deKernion, Tr. 3126).

1127. Dr. deKernion also testified that the Carducci Study did not follow patients for a long enough time, especially for those with a long PSA doubling time, to prove that POMx will prolong their lives. (deKernion, Tr. 3103).

5. Determinations on the human clinical studies

a. PSA doubling time

1128. Clinicians use PSADT as a prognostic tool at the time of biochemical recurrence of prostate cancer to predict the odds of clinical progression of the disease in prostate cancer patients who have undergone initial treatment. (Eastham, Tr. 1260; PX0351 (deKernion, Dep. at 93)). *See also* PX0178 at 001 (Complaint Counsel's expert writing: "PSA doubling time has emerged as an important factor in the evaluation of men with newly diagnosed prostate cancer or prostate cancer that recurs after treatment. PSA doubling time can also be used as a surrogate marker for prostate cancer-specific death.").

1129. Clinicians accept PSADT as a useful marker in determining risk or outcome in patients following prostate cancer treatment and measuring the likelihood of recurrence of the tumor after a man has had his prostate removed. (deKernion, Tr. 3051, 3055); *see also* CX1341 (Pantuck Dep. at 254-55) (clinicians find PSADT to be clinically important for prostate cancer treatment and one of the most important variables that a doctor can discuss to characterize a prostate cancer patient).

1130. Some published studies demonstrate acceptance of PSA doubling time as a valid predictor of disease:

- In a study titled, "*Does PSADT After Radical Prostatectomy Correlate With Overall Survival?"* in the January 2011 edition of the Journal of Urology, Dr. Anna Teeter and her colleagues wrote of the "widespread acceptance" that PSADT after radical prostatectomy predicts prostate cancer mortality; that this has been "well established"; that PSADT is a "useful tool for identifying men at increased risk of all-cause mortality early in their disease course"; and that PSADT is "a powerful predictor of overall survival." (PX0167).

- In a study titled, "*Stratification of Patient Risk Based on Prostate-Specific Antigen Doubling Time after Radical Retropublic Prostatectomy*" in the April 2007 issue of Mayo Clinic Proceedings, Dr. Tollefson and colleagues wrote that PSADT was "a highly significant and reliable test" to determine the likelihood of disease recurrence and death, an "excellent indicator of clinical disease recurrence" and the only significant factor that predicts

clinical progression." The researchers concluded that, "prostate-specific antigen doubling time is an independent predictor of clinical disease recurrence and mortality after surgical biochemical failure." (PX0166).

- In a study titled, "*Risk of Prostate Cancer-Specific Mortality Following Biochemical Recurrence After Radical Prostatectomy*," Dr. Freedland and colleagues used PSADT to "define risk factors for prostate cancer death following radical prostatectomy and to develop tables to risk stratify for prostate cancer-specific survival." The researchers found that clinical parameters such as PSADT can help risk stratify patients for prostate cancer-specific mortality following biochemical recurrence after radical prostatectomy. (PX0165).

- In a study titled, "*Recurrence Patterns After Radical Retropubic Prostatectomy: Clinical Usefulness of Prostate Specific Antigen Doubling Times and Log Slope Prostate Specific Antigen*" published in the October 1997 edition of the Journal of Urology, Drs. Patel, deKernion, et al., studied the correlation between prostate specific antigen doubling time and clinical recurrence in patients with detectable PSA after radical retropubic prostatectomy and concluded that, after PSA became detectable, PSA doubling time was a better indicator of the risk and time to clinical recurrence after radical retropubic prostatectomy than other factors including preoperative PSA. (PX0162).

1131. There are no studies proving that modulating PSADT (*i.e.*, changing the rate of the PSA doubling time) changes the natural history of prostate cancer by delaying the development of metastases or death from the disease. (Eastham, Tr. 1261; CX1287 (Eastham Expert Report at 0011, 0019); PX0161 (deKernion Expert Report at 0004); PX0351 (deKernion, Dep. at 52-53)).

1132. The FDA has not accepted PSADT as a surrogate endpoint for clinical benefit in chemotherapy trials. (deKernion, Tr. 3096; CX1352 (Heber, Dep. at 316-17); CX1340 (Carducci, Dep. at 89-90)).

1133. Respondents acknowledged in a report on their expert panel on prostate cancer: "To date, all POM Wonderful clinical evaluations of pomegranate-derived products in prostate cancer have used PSADT as the primary endpoint. While data obtained using this approach has generated a high degree of interest from patients and urologists, it is unclear whether PSADT is acceptable as a registrational endpoint for a drug designed to prolong the time to disease progression after initial therapy for prostate cancer." (CX1104 at 0004).

1134. Experts in the field of prostate cancer agree that PSADT is not an accepted surrogate endpoint for survival or prostate cancer-specific mortality in prostate cancer treatment clinical trials. (Eastham, Tr. 1297; Stampfer, Tr. 782-83; deKernion, Tr. 3096; CX1287 (Eastham Expert Report at 0010); CX1293 (Stampfer Expert Report at 0025); CX1340

(Carducci, Dep. at 88-90); CX1341 (Pantuck, Dep. at 253-54)). Many men with increases in PSA after initial therapy do not die of prostate cancer. On the other hand, some men succumb to prostate cancer without an increase in PSA. (Stampfer, Tr. 783; Eastham, Tr. 1258; deKernion, Tr. 3088).

b. Research results

1135. There is no clinical study, research or trial that provides 100% proof that the POM Products prevent prostate cancer in humans. (deKernion, Tr. 3062, 3119).

1136. There is no clinical study, research or trial that provides 100% proof that the POM Products reduce the risk of prostate cancer in humans. (deKernion, Tr. 3062-63, 3119).

1137. There is clinical research demonstrating that patients who were given POM Products had their PSA go down, which is significant evidence that something is happening to those tumor cells. (deKernion, Tr. 3065).

1138. Although one cannot make a firm claim that the POM Products are absolutely preventative, given the data presented in the Pantuck Study and the Carducci Study, it is reasonable to state that POM Products have shown an effect on prostate cancer with little or minimal toxicity. (PX0161 (deKernion Expert Report at 0011)).

6. Conclusions

1139. Pomegranate consumption can potentially be used to prevent or delay clinical recurrence of prostate cancer once a patient experiences biochemical recurrences (PSA recurrences) after a radical prostatectomy. (PX0192 (Heber Expert Report at 0027)).

1140. No Phase III randomized trial has been completed to prove that POM Products prolong the life of patients who have recurrence of prostate cancer after supposedly curative therapy. Effective trials are ongoing. As reflected by changes in PSA doubling time, the POM Products are a reasonable adjunct for a patient who wishes to help their general health and possibly avoid a clinical recurrence of prostate cancer. (*See* PX0161 (deKernion Expert Report at 0011)).

1141. The statistically significant prolongation of PSA doubling time, coupled with corresponding laboratory effects on prostate cancer *in vitro* cell proliferation and apoptosis as well as oxidative stress, and inflammation provides strong scientific rationale for the statement that pomegranate juice promotes prostate health and has led to ongoing phase III clinical trials. (PX0192 (Heber Expert Report at 0027)).

1142. Competent and reliable scientific evidence supports the conclusion that the POM Products support prostate health, including by prolonging PSA doubling time in men with rising PSA after primary treatment for prostate cancer. (PX0161 (deKernion Expert Report); (PX0192 (Heber Expert Report at 0027); deKernion, Tr. 3126; PX0351 (deKernion, Dep. at 41-42); Heber, Tr. 2012).

1143. There is insufficient competent and reliable scientific evidence to support the conclusion that the POM Products treat, prevent, or reduce the risk of prostate cancer or that clinical studies, research and/or trials establish these effects. (CX1287 (Eastham Expert Report at 0024-26); Stampfer, Tr. 790-91; CX1293 (Stampfer Expert Report at 0029-30); *see also* Eastham, Tr. 1317-19)); *see also* deKernion, Tr. 3062-63; *see also* PX0161 (deKernion Expert Report at 0011)).

I. Substantiation for Respondents' Erectile Dysfunction Claims

1. Substantiation standard for erectile dysfunction claims

1144. Clinical evidence supported by basic scientific evidence is sufficient to support claims that pomegranate juice has a potential benefit for vascular blood flow and the vascular health of the penis. (PX0149 (Burnett Expert Report at 0006)).

1145. Experts in the field of erectile dysfunction would not require RCTs to substantiate health benefit claims for harmless pure fruit products like pomegranate juice. (PX0149 (Burnett Expert Report at 0006-07); Burnett, Tr. 2272, 2303; PX0189 (Goldstein Expert Report at 0003); Goldstein, Tr. 2600-02, 2611, 2620).

1146. Experts in the field of erectile dysfunction would not require that pomegranate juice or its derivatives be subjected to RCTs before concluding that pomegranate juice has a beneficial effect on preserving erectile function. (PX0149 (Burnett Expert Report at 0006-07); Burnett, Tr. 2272-74, 2303; PX0189 (Goldstein Expert Report at 0003); Goldstein, Tr. 2600-02, 2611, 2620).

1147. Experts in the field of erectile dysfunction would not require that pomegranate juice or derivatives be subjected to RCTs before concluding that pomegranate juice has a potential beneficial effect on erectile dysfunction. (Burnett, Tr. 2272-74, 2303).

1148. Experts in the field of erectile dysfunction would require that a product be scientifically evaluated through rigorous scientific and clinical studies, and believe that animal and *in vitro* studies alone are not sufficient, before concluding that pomegranate juice treats erectile dysfunction in a clinical sense. (Burnett, Tr. 2261-64; 2285-86; 2303).

2. Background facts on erectile health and dysfunction

a. Erectile health distinguished from erectile dysfunction

1149. Erectile health is having a healthy erectile mechanism. (PX0189 (Goldstein Expert Report at 0008)).

1150. Erectile health is promoted when the male practices strategies that encourage endothelial health, such as exercise, use of the Mediterranean diet, and use of endothelial-healthy medications (such as aspirin, statins, and PDE5-inhibitors).

(PX0189 (Goldstein Expert Report at 0008); PX0190; PX0352 (Goldstein, Dep. at 148)).

1151. Erectile health is distinguished from erectile dysfunction. (PX0189 (Goldstein Expert Report at 0008)).

1152. Erectile dysfunction is the consistent or persistent inability to obtain and/or sustain an erection adequate for sexual intercourse. (Burnett, Tr. 2257; PX0189 (Goldstein Expert Report (Goldstein Expert Report at 0008-09)).

1153. Improving ones erectile function may also help improving ones erectile dysfunction. (Burnett, Tr. 2303).

1154. A clinical treatment for erectile dysfunction is different than the concept of something having a potential beneficial effect on erectile tissue function and health. (PX0349 (Burnett, Dep. at 56-57)).

1155. Erectile dysfunction has been estimated to affect up to 30 million men in the United States. (PX0189 (Goldstein Expert Report at 0008-09)).

1156. The most common cause of erectile dysfunction is cardiovascular disease. (PX0189 (Goldstein Expert Report at 0009)).

1157. "Subjects with ED seem to have a vascular mechanism similar to that seen in atherosclerosis [. . .] and therefore, a diagnosis of ED may be seen as a sentinel event that should prompt investigation for coronary heart disease (CHD) in asymptomatic men." (PX0190 at 0002).

1158. Cardiovascular disease is strongly associated with endothelial cell dysfunction. (PX0189 (Goldstein Expert Report at 0009)).

1159. Endothelial cell dysfunction may act to adversely affect the structure and function of the critical arterial inflow mechanism, the critical expandability of the erectile tissue and the critical integrity of the veno-occlusive mechanism. (PX0189 (Goldstein Expert Report at 0009)).

1160. The erectile mechanism is largely dependent on the health, integrity, structure and function of the arterial vascular and corporal erectile tissue systems. (PX0189 (Goldstein Expert Report at 0008)).

b. Physiology of human penile erection

1161. The penis consists of two corpora cavernosa or erectile chambers and a corpus spongiosum or erectile tissue surrounding the urethra. The corpora cavernosa erectile tissue are contained by a thick and strong fibrous lining called the tunica albuginea that stretches to some extent during penile erection but also acts as a container to provide

axial rigidity to the erect penis. (PX0189 (Goldstein Expert Report at 0006); Burnett, Tr. 2245).

1162. The erectile tissue includes numerous interconnecting lacunar spaces that fill with blood during erection, and are lined by vascular endothelial cells. The lacunar spaces are surrounded by vascular smooth muscle and connective tissue such as collagen and elastin. (PX0189 (Goldstein Expert Report at 0006)).

1163. Arterial blood enters the corpora cavernosa via the right and left cavernosal arteries. There are numerous small regulatory arteries off the cavernosal artery called helicine arterioles that open into the lacunar spaces. At the peripheral edge of the erectile tissue, underneath the tunica albuginea, there are small veins called sub-tunical venules that drain blood from the peripheral lacunar spaces through the tunica into draining veins at the side of the penis to eventually return blood back to the heart. (PX0189 (Goldstein Expert Report at 0006); Burnett, Tr. 2245-46).

1164. In the flaccid state, smooth muscle in the helicine arterioles and surrounding the lacunar spaces are contracted allowing only small amounts of blood to enter the erectile chambers. Relaxation of the vascular smooth muscle of the corpora cavernosa leads to penile erection. Dilation of the helicine arterioles increases perfusion of high pressure arterial blood into the lacunar spaces. Relaxation of the smooth muscle surrounding the lacunar spaces results in engorgement of the erectile tissue and expansion of the erectile tissue against the tunca albuginea. This erectile tissue expansion results in compression of the sub-tunical venules that restricts blood outflow from the corporal erectile chambers. This venous trapping mechanism is the corporal veno-occlusive mechanism. Due to the hydraulic nature of increasing blood inflow and perfusion pressure and restricting blood outflow, there is an increase in intracavernosal pressure to a value approximating the mean systemic arterial blood pressure. The containment of pressure within the tunica albuginea leads to axial rigidity and penile hardness that enables functional penile penetration. (PX0189 (Goldstein Expert Report at 0006-07); Burnett, Tr. 2246-48).

c. The role of nitric oxide in human penile erection

1165. Nitric oxide ("NO") has a beneficial effect on blood flow. (Heber, Tr. 1969, 2140; Burnett, Tr. 2250).

1166. Blood vessels and the flow of blood to the penis are important to erectile function. (Melman, Tr. 1169).

1167. While many types of molecules participate in the erection process, NO "is the key molecule that governs penile erection," and is "known to be of paramount importance in the maintenance of good erectile function." (PX0149 (Burnett Expert Report at 0004); Burnett, Tr. 2249-50, 2276; PX0190 at 0006). Complaint Counsel's erectile dysfunction expert, Dr. Melman, agreed that NO employs a critical role in the erectile

process and that there are men whose erectile dysfunction is caused by the inadequate production of NO. (Melman, Tr. 1169; PX0360 (Melman, Dep. at 32)).

1168. The physiologic mechanism of penile erection involves release of NO in the corpus cavernsosum during sexual stimulation. (PX0149 (Burnett Expert Report at 0004-05); PX0189 (Goldstein Expert Report at 0007)).

1169. The NO is released from shear stress off the endothelial cells in the lacunar spaces within the corpora cavernosa and from autonomic nerves that innervate the erectile tissue and are activated during sexual stimulation. (PX0189 (Goldstein Expert Report at 0007); Burnett, Tr. 2248-49; PX0349 (Burnett, Dep. at 88-90)).

1170. Upon its synthesis and release from their cellular sources, NO diffuses to neighboring vascular and trabecular smooth muscle cells lining the lacunar spaces. (PX0149 (Burnett Expert Report at 0004-05); PX0189 (Goldstein Expert Report at 0007); PX0349 (Burnett, Dep. at 87-90)).

1171. The NO activates the enzyme guanylate cyclase within the vascular smooth muscle cells that results in increased levels of cyclic guanosine monophosphate (cGMP), an effector of smooth muscle relaxation via protein kinase G (PKG) actions. (PX0149 (Burnett Expert Report at 0004-05); PX0189 (Goldstein Expert Report at 0007); PX0349 (Burnett, Dep. at 87-90)).

1172. NO, cGMP and PKG mediate the relaxation of the cavernous smooth muscle and vasodilation of blood vessels. (PX0149 (Burnett Expert Report at 0004); PX0189 (Goldstein Expert Report at 0007)).

1173. Persistent smooth muscle relaxation leads to tissue engorgement within the corpora cavernosa and penile erection. (PX0189 (Goldstein Expert Report at 0007)).

1174. Cyclic guanosine monophosphate is hydrolyzed by the phosphodiesterases, predominantly type 5 ("PDE5"), to inactive 5'-GMP, terminating penile erection. (PX0149 (Burnett Expert Report at 0004-05); PX0349 (Burnett, Dep. at 92-93)).

1175. PDE5 inhibitors such as sildenafil (Viagra), vardenafil (Levitra) and tadalafil (Cialis) inhibit PDE5, thereby augmenting cGMP levels. (PX0149 (Burnett Expert Report at 0004-05); PX0349 (Burnett, Dep. at 93)).

1176. Endothelial NO function is fundamental to the vascular process of penile erection. (Burnett, Tr. 2290).

1177. The vascular function of vessels in various parts of the body behave similarly. (Burnett, Tr. 2290).

d. Antioxidant activity of pomegranate juice

1178. Oxidative stress molecules in the body, which are produced by various kinds of conditions of inflammatory change, disease states, etc., have deleterious effects throughout the body in the vasculature and in the penis that actually counter-effect the body's NO regulatory mechanism, not just for transient effects to bring about erection, but also to maintain the wellness of the erectile tissue. (PX0349 (Burnett, Dep. at 89-90); Burnett, Tr. 2250-51; Goldstein, Tr. 2604-05; PX0190 at 0006).

1179. Antioxidants are well known to enhance the biological actions of NO by virtue of their capacity to stabilize NO by protecting against the oxidative destruction of NO by oxidative stress molecules. (PX0056 at 0002; PX0059 at 0001, 0004; PX0190 at 0006; PX0149 (Burnett Expert Report at 0005-06); PX0189 (Goldstein Expert Report at 0004-05); Goldstein, Tr. 2604-05).

1180. The antioxidant effect described in F. 1179 results in much higher and more prolonged cellular concentrations of NO, leading to markedly increased biological actions of NO. (PX0056 at 0002; PX0059 at 0001, 0004; PX0149 (Burnett Expert Report at 0005-06)).

1181. Antioxidants play a potential role in preserving erectile tissue health and function. (Burnett, Tr. 2285-86; Goldstein, Tr. 2604-05).

1182. Pomegranate juice possesses potent flavonoid antioxidants. (PX0149 (Burnett Expert Report at 0005-06); Burnett, Tr. 2250-51; PX0189 (Goldstein Expert Report at 0011); PX0056; PX0058; PX0051; PX0004).

1183. Pomegranate juice enhances the production of endothelial NO formation by suppressing the oxidative stress molecules that oppose the endothelial NO synthase function. (PX0149 (Burnett Expert Report at 0005-06); PX0349 (Burnett, Dep. at 103, 119); Burnett, Tr. 2251-54).

1184. Pomegranate juice possesses anti-oxidative molecular effects and these effects activate endothelial NO mechanisms in vasculature which serve potential beneficial effects on vascular blood flow and promote vascular biologic health of the penis. (PX0149 (Burnett Expert Report at 0005-06)).

3. Erectile dysfunction studies

1185. Respondents have sponsored two human studies addressing erectile dysfunction-related endpoints and at least six *in vitro* and animal studies looking at NO metabolism in an effort to identify a potential erectile dysfunction benefit from pomegranate juice. (CX1193 at 0001; CX0716 at 0029; PX0051 at 0001; PX0056 at 0001; PX0057 at 0001; PX0059 at 0001; PX0004 at 0001; PX0058 at 0001).

a. Tools for human clinical studies evaluating erectile function

1186. Both Complaint Counsel's and Respondents' erectile dysfunction experts agree it is important to use a validated tool when conducting a human clinical trial investigating whether a product treats, prevents, or reduces the risk of erectile dysfunction. (Melman, Tr. 1099; CX1289 (Melman Expert Report at 0010); Burnett, Tr. 2266 (agreeing that experts would rely on a validated tool when conducting a human clinical trial investigating whether a product treats erectile dysfunction)).

1187. A validated tool is "established as measuring erectile dysfunction through rigorous assessments involving reliability testing, validity testing, construct validity, and other criteria." (Burnett, Tr. 2266; *see also* Melman, Tr. 1100 (stating that validation means that a measure has been shown to have statistical reliability)).

1188. Validation is important because "[r]igorous assessment of patient-reported outcomes is necessary to ensure reliability, responsiveness, and discriminant and predictive validity. These attributes ensure that the instrument measures what it states it measures, and that the results are reproducible and sensitive to change." (PX0352a02 at 0002; PX0352 (Goldstein, Dep. at 55-56)).

1189. Dr. Melman testified that a study to support a treatment for erectile dysfunction must show that a man can complete intercourse with sexual satisfaction and achieve orgasm. (Melman, Tr. 1141-43). *See also* Melman, Tr. 1146-47 (In the hypothetical case of "a man [that] hasn't been able to have an erection for five years, then he tries [a] product and he now has an erection and he can penetrate his wife and bring her to sexual satisfaction, but he doesn't have an orgasm himself," the maker of the product "can't tell the public about what [the product has] done.").

i. The IIEF

1190. The International Index of Erectile Function ("IIEF") is a validated measure for evaluating change in erectile function. (JX0003 ¶ A.9; Melman, Tr. 1099; CX1289 (Melman Expert Report at 0010); Burnett, Tr. 2293; PX0352 (Goldstein, Dep. at 65); CX1193 at 0002; *see also* CX1240 at 0003, *in camera* (stating in a pre-investigational new drug application for POMx that the FDA considered the "erectile function domain of the IIEF . . . as the most appropriate measure of the efficacy of the product for treating erectile dysfunction")).

1191. The IIEF is a 15 question psychometrically validated instrument designed to assess a man's overall erectile and sexual function via the individual domains of erectile function, orgasmic function, sexual desire, intercourse satisfaction and overall satisfaction. (PX0189 (Goldstein Expert Report at 0009); Melman, Tr. 1099-1101; CX0686 at 0026-29; CX1193 at 0002 (stating that the "IIEF is a validated questionnaire whose erectile function domain score has been demonstrated to correlate with ED [erectile dysfunction] intensity")).

1192. The erectile function domain relates only to erectile performance and does not evaluate orgasm or ejaculation. (Goldstein, Tr. 2604).

1193. The IIEF was designed for evaluating pharmaceuticals, not natural botanical products. (Goldstein, Tr. 2603-04).

1194. Dr. Goldstein, who was at the Pfizer Drug Company meeting where the IIEF was developed for its pharmaceutical product Viagra, testified that the IIEF was originally intended for pharmaceutical products in patients with IIEF scores consistent with erectile dysfunction. (PX0352 (Goldstein, Dep. at 67-69)).

1195. The IIEF has some ambiguous questions. For example, one question asks how often do you get an erection, but does not qualify as to what type of erection, *i.e.*, mild erection; moderate erection, etc. (Goldstein, Tr. 2603). Also, IIEF has deficiencies as it requires patient recall and involves patients' subjective interpretation of their erection physiology. (Burnett, Tr. 2293-94).

ii. The GAQ

1196. The Global Assessment Questionnaire ("GAQ") is not a validated measure for assessing erectile function. (Melman, Tr. 1118; Burnett, Tr. 2294; PX0352 (Goldstein, Dep. at 73)).

1197. By itself, experts would not consider the GAQ to be a sufficient endpoint in a clinical study evaluating a treatment for erectile dysfunction. (Burnett, Tr. 2294-95) (agreeing that the GAQ was more vague and nonspecific than a validated tool in measuring whether a therapy had an effect on the ability to achieve and maintain erections).

1198. The GAQ is commonly accepted as a standardized instrument among those conducting erectile dysfunction research. The GAQ's "clinical meaningfulness based on its simplicity makes it extremely widely used and very important in assessing erectile function." (Goldstein, Tr. 2602-03, 2634; Burnett, Tr. 2304; PX0349 (Burnett, Dep. at 127); CX1337 (Forest, Dep. at 79)).

1199. In the development of pharmaceutical products for sexual medicine, the FDA widely approves of non-validated, patient-reported outcomes, such as the GAQ. (PX0352 (Goldstein, Dep. at 57)).

1200. The GAQ does not measure the degree of improvement, indicate how often a study participant experienced improved erections, or show whether he was able to complete sexual intercourse. (Melman, Tr. 1120, 1122; CX1289 (Melman Expert Report at 0014)).

1201. The GAQ is a single yes/no question designed to assess the individual self-evaluation of the study treatment (*e.g.*, pomegranate juice consumption versus placebo consumption)

effect on the patient's sexual health concern. (PX0189 (Goldstein Expert Report at 0009); Goldstein, Tr. 2603).

1202. The GAQ is a very easy evaluation and written for a high school educated person to understand. (Goldstein, Tr. 2603; CX1337 (Forest, Dep. at 151-52)).

1203. The GAQ is used in all sexual medicine trials. (Goldstein, Tr. 2603; PX0352 (Goldstein, Dep. at 57)).

1204. The GAQ was used by Pfizer in testing sildenafil (Viagra) and in every vardenafil (Levitra) and tadalafil (Cialis) trial. (Burnett, Tr. 2304; Goldstein, Tr. 2602; PX0352 (Goldstein, Dep. at 57)).

1205. The GAQ is a very "acceptable," informative," and "valuable" tool to use for testing pomegranate juice. (Burnett, Tr. 2294, 2304).

b. The Forest/Padma-Nathan Study

i. About the Forest/Padma-Nathan Study

1206. POM sponsored a study by Mr. Christopher Forest, Dr. Harin Padma-Nathan, and Dr. Harley Liker, titled, *Efficacy and Safety of Pomegranate Juice on Improvement of Erectile Dysfunction in Male Patients with Mild to Moderate Erectile Dysfunction: A Randomized, Placebo-Controlled, Double-Blind, Crossover Study* ("Forest/Padma-Nathan Study"). (CX1147 at 0004; CX1193 at 0001, 0004). The clinical trial was conducted in 2004 to 2005, and the results were later published in the *International Journal of Impotence Research* in 2007. (CX1193 at 0001; CX1147 at 0004).

1207. Dr. Padma-Nathan, the principal investigator of the Forest/Padma-Nathan Study, received the first fellowship from the American Foundation for Urologic Disease that was awarded in the area of erectile dysfunction. The prestigious fellowship is awarded to two urologists annually. His work involved two years of basic lab and *in vitro* scientific research in smooth muscle pharmacology cosponsored by the Department of Urology and the Department of Cardiology at Boston University. (CX1338 (Padma-Nathan, Dep. at 23, 32-33)). Dr. Padma-Nathan is a man of repute in the field of urology. (Heber, Tr. 2000).

1208. Mr. Forest, at the time of the Forest/Padma-Nathan Study, was Physician Assistant and Director of Clinical Trials, working for Dr. Padma-Nathan. (CX1337 (Forest Dep. at 20)).

1209. Dr. Liker, POM's medical director, was involved with the design and conduct of the Forest/Padma-Nathan Study. (*See* CX 1350 (Liker, Dep. at 191); CX0637 at 0001; CX0622 at 0001; CX0704 at 0001; CX0644 at 0001-02; CX0834 at 0001-02). Dr. Liker also reviewed and approved changes to the article prior to publication.

(CX0881 at 0001-02; *see also* CX0856 at 0001) (sending revised draft of manuscript to Dr. Liker)).

1210. The Forest/Padma-Nathan Study was a randomized, double-blinded, placebo-controlled pilot study that examined the efficacy of POM Juice versus placebo in improving erections in 53 men with mild to moderate erectile dysfunction. (CX1193 at 0001; CX1289 (Melman Expert Report at 0012-13)).

1211. The Forest/Padma-Nathan Study used a crossover design, and the 53 participants who completed the study received a different beverage during the two 28-day treatment periods. (CX1289 (Melman Expert Report at 0012-13); CX1193 at 0002-03). Participants in cohort one consumed POM Juice in period one and then switched to the placebo beverage in period two. (CX1193 at 0002-03). Participants in cohort two consumed the placebo beverage in period one and POM Juice in period two. (CX1193 at 0002-03).

1212. The Forest/Padma-Nathan Study used the GAQ as the primary outcome measure and the IIEF as the secondary outcome measure. (CX1337 (Forest, Dep. at 84); CX1193 at 0002; Melman, Tr. 1120; CX0686 at 0008).

1213. The Forest/Padma-Nathan Study hypothesized that treatment of the participants with POM Juice would produce: 1) statistically significant positive GAQ scores when compared to placebo-controlled patients, and 2) changes in the erectile function domain of the IIEF when the values are compared with the baseline and between the two groups. (CX0686 at 0008).

1214. The Forest/Padma-Nathan Study's GAQ asked participants the following yes or no question: "While using the study beverage, did you feel that your erections improved?" (CX0686 at 0025).

1215. Dr. Padma-Nathan, the lead researcher, testified that while the GAQ is not a validated measure for measuring erectile function, "it's not unreasonable to have it as a single question, to try to capture a signal for any evidence of [erectile] treatment effect." (CX1338 (Padma-Nathan Dep. at 90-91, 94)).

1216. The erectile function domain questions of the IIEF have graded response scales and ask specific questions relating to erectile function, such as "Over the last month, when you attempted sexual intercourse, how often were you able to penetrate (enter) your partner?" and "Over the last month, during sexual intercourse, how often were you able to maintain your erection after you had penetrated (entered) your partner?" (CX0686 at 0026-27; *see also* Melman, Tr. 1123).

1217. Dr. Padma-Nathan testified that the IIEF was a validated measure and the "gold standard." (CX1338 (Padma-Nathan, Dep. at 90)).

1218. Dr. Padma-Nathan considered the Forest/Padma-Nathan RCT Study "a scientifically rigorous study." (CX1338 (Padma-Nathan Dep. at 196-97)).

1219. A study as scientifically rigorous as the Forest/Padma-Nathan RCT Study is almost unheard of in the food industry. (Goldstein, Tr. 2601-02, 2613-14).

1220. Dr. Goldstein, indicated that as editor in chief of the *International Journal of Impotence Research*, the Forest/Padma-Nathan Study "is the first and only nutraceutical clinical trial that is randomized and double-blind that [he has] ever come across in [the] field." (Goldstein, Tr. 2598).

ii. Results of the Forest/Padma-Nathan Study

1221. Of the 53 participants who completed the Forest/Padma-Nathan Study, a total of 42 subjects demonstrated improved GAQ scores, 25 after drinking pomegranate juice. (PX0189 (Goldstein Expert Report at 0012-13); CX0908).

1222. In the pomegranate juice–placebo sequence, 56% demonstrated improvement of GAQ score versus 33% in the placebo-pomegranate juice sequence. (PX0189 (Goldstein Expert Report at 0012-13); CX0908).

1223. In the placebo–pomegranate juice sequence, 38% versus 29% reported improvement in GAQ score. (PX0189 (Goldstein Expert Report at 0012-13); CX0908).

1224. Overall, the GAQ scores demonstrated that pomegranate juice drinkers enjoyed a nearly 50% better improvement in erections over the placebo drinkers. (CX0908 at 0003; PX0352 (Goldstein, Dep. at 109, 144); CX1338 (Padma-Nathan, Dep. at 191-92)).

1225. The Forest/Padma-Nathan Study's GAQ results achieved a probability value ("*p*-value") of 0.058, which is not statistically significant, as it is slightly above the statistical significance measure of 0.050. (PX0189 (Goldstein Expert Report at 0012-13); CX0908; Heber, Tr. 1978; Goldstein, Tr. 2598). This means the study had a 94%, rather than 95%, probability of being valid and not the result of chance. (Heber, Tr. 1978; Goldstein, Tr. 2599; Burnett, Tr. 2305).

1226. The Forest/Padma-Nathan RCT Study's IIEF erectile function domain results achieved a *p*-value of 0.72, which is not statistically significant. (Melman, Tr. 1120-21; Burnett, Tr. 2297 (agreeing that a *p*-value of 0.72 is "nowhere near approaching statistical significance"); PX0352 (Goldstein, Dep. at 65); CX1193 at 0003; CX1213 at 0001 (comparing the change from baseline for the treatment group versus the control group)).

1227. The Forest/Padma-Nathan Study report noted the treatment period was a limitation because it might not have been long enough to allow for a clinical response. (CX1193 at 0004). *See also* Melman, Tr. 1125, 1127; CX1289 (Melman Expert Report at 0014) (the study not conducted over a sufficient duration to show a sustained clinically significant effect on erectile function).

1228. Dr. Padma-Nathan also testified that the Forest/Padma-Nathan RCT Study was "[u]nder-powered to achieve statistical significance . . . [but] that shouldn't be misconstrued to mean that the study was a deficient one." (CX1338 (Padma-Nathan, Dep. at 106, 108)). Dr. Padma-Nathan further testified that he did not think they were "trying to achieve [statistical significance] and didn't believe [they would] get statistical significance." (CX1338 (Padma-Nathan, Dep. at 106)).

1229. Dr. Padma-Nathan testified that the study concluded that there was a potential for pomegranate juice to have beneficial effects on erectile dysfunction, with the caveat of the need for further studies to confirm. (CX1338 (Padma-Nathan, Dep. at 184)).

1230. Dr. Padma-Nathan and Mr. Forest testified that the study did not conclude that POM Juice treats, prevents, or reduces the risk of erectile dysfunction. (CX1338 (Padma-Nathan, Dep. at 157-58); CX1337 (Forest, Dep. at 165-66)).

1231. After the Forest/Padma-Nathan Study was submitted for publication, a peer reviewer for the *International Journal of Impotence Research* stated that it was "a negative study, not a positive study, and should be presented that way." (CX0856 at 0001).

1232. A published review by Dr. Jacob Rajfer, Professor of Urology at UCLA, *Pomegranate Juice: Is It the New, All-Natural Phosphodiesterase Type 5 Inhibitor?*, 10 Rev. Urol. 168-69 (2008), also stated that the Forest/Padma-Nathan Study had negative results. (CX1290 at Ex. C; Melman, Tr. 1128-29; CX1289 (Melman Expert Report at 0016)).

iii. Expert opinion on the Forest/Padma-Nathan Study

1233. Dr. Melman testified that the GAQ is not a validated measure for assessing erectile function; has not been tested for statistical reliability; and does not measure the degree of improvement, indicate how often a study participant experienced improved erections, or show whether he was able to complete sexual intercourse. (Melman, Tr. 1118-22; CX1289 (Melman Expert Report at 0014)). Dr. Melman further testified that without the ability to show meaningful change of erectile function, the GAQ does not provide clinically significant information. (Melman, Tr. 1118-22; CX1289 (Melman Expert Report at 0014)).

1234. Dr. Melman had not heard of the term GAQ until being involved as an expert in this case and he formed his opinions about the GAQ after being involved in this case. (Melman, Tr. 1180-81).

1235. Dr. Melman testified that the Forest/Padma-Nathan Study was not conducted over a sufficient duration to show a sustained clinically significant effect on erectile function. (Melman, Tr. 1125, 1127; CX1289 (Melman Expert Report at 0014)). Dr. Melman further opined that experts in the erectile dysfunction field would require that a study be conducted over an appropriate duration because, even if there is improvement in the

quality of erection, a treatment is not efficacious when the participant is still unable to complete intercourse. (CX1289 (Melman Expert Report at 0011-12)).

1236. Dr. Melman testified that the Forest/Padma-Nathan Study's IIEF erectile function domain results achieved a *p*-value of 0.72 and GAQ results achieved a *p*-value of 0.058, which are not statistically significant. (Melman, Tr. 1120-21). Dr. Melman further testified that nearly achieving statistical significance is insufficient to prove a product's efficacy in treating, preventing, or reducing the risk of erectile dysfunction in humans. (Melman, Tr. 1103, 1121).

1237. Dr. Melman also testified that based on the results of an animal study and one study on 11 men, Dr. Melman has made public statements that a gene-transfer therapy for erectile dysfunction called hMaxi-K would help erectile dysfunction. (Melman, Tr. 1148, 1150, 1155).

1238. Respondents' experts testified that even though the statistical significance was not reached, the Forest/Padma-Nathan Study "provides very valuable information" regarding erectile health and function and is absolutely "clinically significant" because "it supports the conclusion that the positive results in the basic science are borne out in human function." (Goldstein, Tr. 2598-99, 2605, 2608; PX0352 (Goldstein, Dep. at 34-47, 105-09)).

1239. Dr. Goldstein testified that the results of the Forest/Padma-Nathan Study showed that "there were 50 percent more people than the placebo who thought that there was erectile benefit from using this drug. And I will call that clinically significant in conjunction with the fact that there are no deaths, no priapisms, no heart attacks, no strokes, no flushing, no nasal congestion, none of the traditional side effects seen by PDE5 inhibitors. No need for stents, drug-eluting stints, no need for surgery. No need for penile prosthetic procedures." (PX0352 (Goldstein, Dep. at 109)).

1240. Dr. Goldstein also testified that the Forest/Padma-Nathan Study "is of extreme relevance to the clinician and consumer" and is "suggestive evidence that use of pomegranate juice would benefit [a] patient with erectile dysfunction." (PX0189 (Goldstein Expert Report at 0014); Goldstein, Tr. 2605; PX0352 (Goldstein, Dep. at 34, 105-06)).

1241. Dr. Goldstein opined that the short treatment period in the Forest/Padma-Nathan Study "actually resulted in less favorable findings such that one would anticipate that a more robustly designed study would certainly have obtained statistically significant results." (PX0189 (Goldstein Expert Report at 0013); PX0352 (Goldstein, Dep. at 80)).

1242. Dr. Burnett testified that the results of the Forest/Padma-Nathan Study provide support that pomegranate juice "may be an intervention that would complement conventional ED treatment, and [he] would support its use by patients." (Burnett, Tr. 2298).

1243. Dr. Burnett opined that the Forest/Padma-Nathan Study supports the conclusion that pomegranate juice has a beneficial effect on erectile tissue physiology, health, and function, and is "a potential treatment for ED." (PX0149 (Burnett Expert Report at 0006); Burnett, Tr. 2255-56, 2270; PX0349 (Burnett, Dep. at 103, 112, 116-18, 138-39, 142)).

1244. Dr. Heber opined that the Forest/Padma-Nathan Study showed that consumption of POM juice created a marked improvement in erectile function among men who had experienced erectile dysfunction, and it had major clinical significance in showing a benefit from pomegranate juice despite barely missing statistical significance. (Heber, Tr. 1830-31, 1979).

1245. Dr. Heber testified that the Forest/Padma-Nathan Study "could [not] be disregarded" and that "it is a positive in providing important scientific information consistent with the basic science that pomegranate juice may be helpful for men with erectile dysfunction." (Heber, Tr. 2001).

iv. Determinations on the Forest/Padma-Nathan Study

1246. The GAQ is an adequate tool for testing a product like pomegranate juice. (Burnett, Tr. 2303-04).

1247. The Forest/Padma-Nathan Study's IIEF erectile function results of a *p*-value of 0.72 is not statistically significant. (Melman, Tr. 1120-21; Burnett, Tr. 2297).

1248. The Forest/Padma-Nathan Study's GAQ results of a *p*-value of 0.058 was a few thousandths of a percentage point short of the 95% threshold, and thus not "statistically significant." (PX0189 (Goldstein Expert Report at 0012-13); CX0908; Heber, Tr. 1978; Goldstein, Tr. 2598-99; Burnett, Tr. 2305).

1249. As noted in the Forest/Padma-Nathan Study itself, the treatment period was a limitation because it might not have been long enough to allow for a clinical response. (CX1193 at 0004).

1250. Despite the limitations stated in F. 1247-1249, the Forest/Padma-Nathan Study has clinical significance in showing a benefit from pomegranate juice on erectile tissue physiology and health. (PX0189 (Goldstein Expert Report at 0013); PX0149 (Burnett Expert Report at 0006); CX0908; Heber, Tr. 1979, 2001; Goldstein, Tr. 2598-99; PX0352 (Goldstein, Dep. at 108-09); Burnett, Tr. 2256; PX0349 (Burnett, Dep. at 138-39)).

1251. The Forest/Padma-Nathan Study supports the conclusion that pomegranate juice has a beneficial effect on erectile tissue physiology, health, and function. (PX0149 (Burnett Expert Report at 0006); Burnett, Tr. 2255-56; PX0349 (Burnett, Dep. at 103, 112, 116-18, 138-39, 142)).

1252. The Forest/Padma-Nathan Study supports the conclusion that pomegranate juice is a potential treatment for erectile dysfunction. (PX0349 (Burnett, Dep. at 142); CX1338 (Padma-Nathan, Dep. at 184)).

1253. The Forest/Padma-Nathan Study does not support the conclusion that POM Juice treats, prevents, or reduces the risk of erectile dysfunction. (CX1338 (Padma-Nathan, Dep. at 157-58); CX1337 (Forest, Dep. at 165-66); PX0349 (Burnett, Dep. at 142)).

c. Davidson BART/FMD Study

1254. A subset of 27 participants from the Davidson BART/FMD Study, a randomized, double blind, and placebo-controlled cardiovascular study funded by Roll (discussed in F. 903), also completed the IIEF questionnaire. (CX1065 at 0001; CX0716 at 0029; CX0684 at 0001, 0014). This analysis was planned for in the protocol for the Davidson BART/FMD Study. (CX0716 at 0029).

1255. The Davidson BART/FMD Study was primarily a cardiovascular study and therefore its protocols did not include any of the type of inclusion or exclusion criteria one would expect to see in a basic erectile dysfunction clinical trial. (CX0716; PX0019; Melman, Tr. 1092).

1256. The unpublished IIEF results from the Davidson BART/FMD Study were not statistically significant for the intent to treat population. (Melman, Tr. 1130-31; CX1289 (Melman Expert Report at 0017); CX1336 (Davidson, Dep. at 88-89)). The *p*-value was 0.7887 when comparing the intent to treat population's change in IIEF erectile function domain scores for the treatment group versus the control group. (CX0684 at 0014).

1257. The erectile dysfunction findings in the Davidson BART/FMD Study were flawed since one of the two study sites was unable to collect any data for the baseline IIEF measurement. (CX0654 at 0001 ("IIEF data not collected on most subjects at site 2; Mary Sue was aware of this and site staff reported that subjects are uncomfortable completing this questionnaire in the office (close quarters) so they tried to send it to them prior to their visit for them to bring in completed, yet it still was incomplete. Unfortunately, this baseline data will be missing.")).

1258. Neither Dr. Burnett nor Dr. Goldstein reviewed the IIEF data from the Davidson BART/FMD Study. (PX0352 (Goldstein, Dep. at 142); PX0349 (Burnett, Dep. at 170)).

1259. The IIEF results from Davidson BART/FMD study do not support the conclusion that drinking eight ounces of POM Juice daily treats, prevents, or reduces the risk of erectile dysfunction. (Melman, Tr. 1130-31; CX1289 (Melman Expert Report at 0017)).

d. Nitric oxide studies

i. Studies sponsored by Respondents

1260. Respondents have sponsored at least six *in vitro* and/or *in vivo* studies investigating the effects of pomegranate juice on NO levels, including:

- *Pomegranate Juice Consumption Reduces Oxidative Stress, Atherogenic Modifications to LDL, and Platelet Aggregation: Studies in Humans and in Atherosclerotic Apolipoprotein E-Deficient Mice*, by Dr. Aviram;
- *Oxidative Stress in Arteriogenic Erectile Dysfunction: Prophylactic Role of Antioxidants*, by Dr. Azadzoi;
- *Effects of a Pomegranate Fruit Extract Rich in Punicalagin on Oxidation-Sensitive Genes and eNOS Activity at sites of Perturbed Shear Stress and Atherogenesis*, by Dr. de Nigris;
- *The Influence of Pomegranate Fruit Extract in Comparison to Regular Pomegranate Juice and Seed Oil on Nitric Oxide and Arterial Function in Obese Zucker Rats*, by Dr. de Nigris;
- *Beneficial Effects of Pomegranate Juice on Oxidation-Sensitive Genes and Endothelial Nitric Oxide Synthase Activity at Sites of Perturbed Shear Stress*, by Dr. de Nigris; and
- *Pomegranate Juice Protects Nitric Oxide Against Oxidative Destruction and Enhances the Biological Actions of Nitric Oxide*, by Dr. Ignarro.

(PX0051at 0001; PX0056 at 0001; PX0057at 0001; PX005 9at 0001; PX0004 at 0001; PX0058 at 0001).

1261. Respondents' *in vitro* and *in vivo* studies are "basic science" or "pre-clinical." (PX0149 (Burnett Expert Report at 0005-06); PX0189 (Goldstein Expert Report at 0010-13) (describing the de Nigris, Aviram, Ignarro, and Azadzoi studies as *in vitro* or *in vivo*); CX0982 at 0011-14 (describing the de Nigris, Aviram, Ignarro, and Azadzoi studies as "pre-clinical" studies)).

(a) Dr. Aviram's Study

1262. Dr. Aviram is a distinguished professor of biochemistry and researcher at the Technion Faculty of Medicine and the Rambam Medical Center in Haifa, Israel, and head of the Lipid Research Laboratory. (PX0004; CX1358 (Aviram, Dep. at 7-8)).

1263. Dr. Melman, described Technion Institute in Haifa, Israel as a "terrific" institution. (Melman, Tr. 1168).

1264. For over 30 years, Dr. Aviram's major research focused on antioxidants in general, and on its dietary role in cardiovascular disease. (CX1358 (Aviram, Dep. at 5)).

1265. Dr. Aviram has concluded, based on his medical research, that pomegranate juice had greater antioxidant potencies than red wine, which he believed at the time possessed the most potent antioxidant. (CX1358 (Aviram, Dep. at 5-6)).

1266. Dr. Aviram's Study, titled, *Pomegranate juice consumption reduces oxidative stress, atherogenic modifications to LDL, and platelet aggregation: studies in humans and in atherosclerotic apolipoprotein E-deficient mice,* reported that dietary supplementation with nutrients rich in antioxidants was associated with inhibition of atherosclerosis. (PX0189 (Goldstein Expert Report at 0012); PX0004).

1267. Dr. Aviram and his colleagues studied, in healthy male volunteers and in atherosclerotic apolipoprotein E-deficient mice, the effect of consumption of pomegranate juice on such outcomes as lipoprotein oxidation, aggregation and retention, macrophage atherogenicity, platelet aggregation and atherosclerosis. (PX0189 (Goldstein Expert Report at 0012); PX0004).

1268. Dr. Aviram and colleagues found that in humans, pomegranate juice consumption decreased low-density lipoprotein ("LDL") susceptibility to aggregation and retention and increased an high-density lipoprotein ("HDL") associated esterase that can protect against lipid peroxidation. (PX0189 (Goldstein Expert Report at 0012); PX0004).

1269. Similar positive anti-atherosclerosis effects were seen in the E-deficient mice. (PX0189 (Goldstein Expert Report at 0012); PX0004).

1270. Dr. Aviram and colleagues concluded that pomegranate juice had potent antiatherogenic effects in humans (and atherosclerotic mice) that may be attributable to its antioxidative properties. (PX0189 (Goldstein Expert Report at 0012); PX0004).

1271. Dr. Goldstein noted that Dr. Aviram's Study is "a very fascinating and very important piece of information." (PX0352 (Goldstein, Dep. at 127)).

(b) Dr. Azadzoi's Study

1272. Dr. Azadzoi is a distinguished research professor of urology and pathology at the Boston University School of Medicine and Director of Urology Research at the Veterans Affairs Boston Healthcare System. (PX0051).

1273. Dr. Azadzoi, along with Dr. Goldstein, developed an atherosclerotic animal model for erectile dysfunction. (Goldstein, Tr. 2595).

1274. Dr. Azadzoi has published extensively on studies using atherosclerotic animal models with erectile dysfunction. (Goldstein, Tr. 2595).

1275. Dr. Azadzoi's Study, titled, *Oxidative Stress in Arteriogenic Erectile Dysfunction: ProphylacticRrole of Antioxidants,* studied the antioxidant properties of various fruit juices, such as orange juice, blueberry juice, and cranberry juice, and other known antioxidant beverages such as green tea and red wine, and reported that pomegranate juice possessed the highest free radical scavenging capacity. (PX0189 (Goldstein Expert Report at 0011-12); PX0051; PX0352 (Goldstein, Dep. at 123-24); Goldstein, Tr. 2595).

1276. Dr. Azadzoi and colleagues examined that effect of various antioxidant beverages on arteriogenic erectile dysfunction in rabbits that demonstrated decreased intracavernous blood flow, erectile dysfunction, loss of smooth muscle relaxation, decreased endothelial NO synthase, and neuronal NO synthase, diffuse cavernosal fibrosis and increased cavernous levels of the oxidative product isoprostane 8 – epi – prostaglandin F 2 alpha. (PX0189 (Goldstein Expert Report at 0011-12); PX0051).

1277. Dr. Azadzoi and colleagues found that long term pomegranate juice intake increased intracavernosal blood flow, improved erectile responses, improved smooth muscle relaxation, and decreased erectile tissue fibrosis. (PX0189 (Goldstein Expert Report at 0011-12); PX0051; PX0352 (Goldstein, Dep. at 123); Goldstein, Tr. 2595-97).

1278. Dr. Azadzoi and colleagues concluded that arteriogenic erectile dysfunction accumulates oxidative products in erectile tissues and that oxidative stress may be of great importance in the pathophysiology of erectile dysfunction. (PX0189 (Goldstein Expert Report at 0011-12); PX0051).

1279. Dr. Azadzoi and colleagues found that antioxidant therapy may be useful as a prophylactic for preventing smooth muscle dysfunction and fibrosis in erectile dysfunction. (PX0189 (Goldstein Expert Report at 0011-12); PX0051).

(c) Dr. de Nigris Study One

1280. Dr. de Nigris, of the Department of General Pathology and Excellence Research Center on Cardiovascular Diseases of the 1st School of Medicine at the II University of Naples, Italy, and colleagues, including Dr. Louis Ignarro, evaluated the effects of intervention with pomegranate juice on oxidation-sensitive genes and endothelial NO synthase expression induced by high shear stress *in vitro* and *in vivo*. (PX0059). The study was titled, *Beneficial effects of pomegranate juice on oxidation-sensitive genes and endothelial nitric oxide synthase activity at sites of perturbed shear stress,* and is referred to herein as "de Nigris Study One." (PX0059).

1281. Cultured human coronary artery endothelial cells exposed to high shear stress *in vitro* and hypercholesterolemic mice were used in the de Nigris Study One. (PX0059).

1282. Dr. de Nigris and colleagues found that pomegranate juice concentrate reduced the activation of redox-sensitive genes and increased endothelial NO synthase expression in

cultured human coronary artery endothelial cells and hypercholesterolemic mice. (PX0059; Burnett, Tr. 2290).

1283. Dr. de Nigris and colleagues also found that oral administration of pomegranate juice to hypercholesterolemic mice at various stages of disease reduced significantly the progression of atherosclerosis. (PX0059).

1284. The de Nigris Study One indicates that polyphenolic antioxidants contained in pomegranate juice can contribute to the reduction of oxidative stress and atherogenesis. (PX0059; Burnett, Tr. 2290).

(d) Dr. de Nigris Study Two

1285. In a study titled, *Effects of a Pomegranate Fruit Extract rich in punicalagin on oxidation-sensitive genes and eNOS activity at sites of perturbed shear stress and atherogenesis*, (referred to herein as de Negris Study Two), Dr. de Nigris and colleagues showed that atherosclerosis is enhanced in arterial segments exposed to perturbed shear stress as a result of increased expression of oxidation-sensitive responsive genes. (PX0189 (Goldstein Expert Report at 0010-11); PX0056).

1286. The authors of the de Nigris Study Two studied the effect of pomegranate fruit extract and pomegranate juice antioxidant activity on reduction of oxidative stress and atherogenesis during disturbed shear stress flow using cultured human coronary artery endothelial cells. (PX0189 (Goldstein Expert Report at 0010-11); PX0056).

1287. The de Nigris Study Two showed that pomegranate fruit extract and pomegranate juice reduced the activation of oxidation-sensitive genes and increased endothelial NO synthase expression. (PX0189 (Goldstein Expert Report at 0010-11); PX0056).

1288. The de Nigris Study Two also showed that pomegranate fruit extract and pomegranate juice increased cyclic GMP levels. (PX0189 (Goldstein Expert Report at 0010-11); PX0056).

1289. The de Nigris Study Two further showed that administration of pomegranate juice reduced the progression of atherosclerosis in hypercholesterolemic mice. (PX0189 (Goldstein Expert Report at 0010-11); PX0056).

1290. The authors of the de Nigris Study Two concluded that the proatherogenic effects of perturbed shear stress can be reversed with chronic administration of pomegranate fruit extract. (PX0189 (Goldstein Expert Report at 0010-11); PX0056).

1291. The authors of the de Nigris Study Two also stated that some large clinical trials for different antioxidants have failed to show any beneficial effect in terms of preventing major cardiovascular events. (PX0056 at 0008).

(e) Dr. Ignarro's Study

1292. Dr. Louis Ignarro has won a Nobel prize for his discoveries concerning NO. Dr. Ignarro conducted an *in vitro* study, titled, *Pomegranate juice protects nitric oxide against oxidative destruction and enhances the biological actions of nitric oxide, to evaluate pomegranate juice's capacity to protect nitric oxide against oxidative destruction*. (PX0189 (Goldstein Expert Report at 0011); PX0058; Goldstein, Tr. 2593-95; Heber, Tr. 1995-96; Burnett, Tr. 2252-53).

1293. Dr. Ignarro has tested pomegranate juice for its capacity to protect NO against oxidative destruction and found that pomegranate juice was around 5,000 times more potent than the other antioxidants he has tested and possesses more antioxidant activity than grape juice, blueberry juice, red wine and ascorbic acid. (PX0189 (Goldstein Expert Report at 0011); Goldstein, Tr. 2594-95; Heber, Tr. 1967; Burnett, Tr. 2253; PX0058).

1294. Based on a series of studies that were performed on vascular endothelial cells, Dr. Ignarro concluded that pomegranate juice possesses potent antioxidant activity that results in marked protection of NO against oxidative destruction, thereby augmenting the biologic actions of NO. (PX0189 (Goldstein Expert Report at 0011); PX0058).

1295. Dr. Goldstein testified that the "Ignarro study is another part of the sequence of evidence that supports that a nutraceutical, specifically pomegranate juice, has incredible vascular-sparing properties that ultimately, when you follow this path leads to the improvement of erectile function in men with erectile health issues." (PX0352 (Goldstein, Dep. at 133)).

1296. Dr. Goldstein testified also that "you have to study humans to make statements about humans." (PX0352 (Goldstein, Dep. at 124)).

1297. Complaint Counsel's expert, Dr. Melman, recognizes that Dr. Ignarro is highly respected and that UCLA School of Medicine, where Dr. Ignarro is a professor in molecular and medical pharmacology, has a good reputation. (Melman, Tr. 1167-68).

ii. Expert opinions on the basic science relied upon by Respondents

1298. Dr. Burnett, offered the following expert opinions regarding the basic science relied upon by Respondents:

- "basic scientific evidence exists that establishes that pomegranate juice possesses potent antioxidative molecular effects and these effects operate by activating endothelial NO mechanisms in vasculature [structures involved in human penile erection]." (PX0149 (Burnett Expert Report at 0005-06));

- basic science alone "support[s] the potential benefit at the human level to improve the physiology of erectile tissue preserving erect tissue health."

(PX0149 (Burnett Expert Report at 0004-05); PX0349 (Burnett, Dep. at 103, 112, 116-18)); and

- on the basis of animal studies or *in vitro* studies, pomegranate juice has a "potential benefit . . . to likely improve one's erection physiology." (Burnett, Tr. 2262-63).

1299. Dr. Goldstein provided the following expert opinions regarding the basic science relied upon by Respondents:

- "pomegranate juice has excellent basic science both in animal tissue and human tissue and excellent animal model data." (PX0352 (Goldstein, Dep. at 51-52)); and
- POM's "strong *in vitro* and *in vivo* studies . . . suggest a probable benefit of pomegranate juice on erectile health," and that "in and of itself it has shown huge pieces of information that will be helpful in understanding how it would work in humans . . . ." (PX0189 (Goldstein Expert Report at 0013); Goldstein, Tr. 2644).

1300. Dr. Goldstein also provided the following expert opinions:

- competent and reliable scientific evidences shows that pomegranate juice provides a benefit to erectile function. (Goldstein, Tr. 2605); and
- competent and reliable scientific evidence exists upon which clinicians who treat men with erectile health concerns would rely in concluding that pomegranate juice promotes erectile health. (PX0189 (Goldstein Expert Report at 0014)).

1301. Dr. Melman provided the following expert opinions regarding the basic science relied upon by Respondents:

- basic research studies about antioxidants' effects on NO levels may relate to the biochemical process for erectile function. (CX1289 (Melman Expert Report at 0017-18)); and
- basic research studies do not directly involve erectile function in humans and cannot alone prove that POM Juice treats, prevents, or reduces the risk of erectile dysfunction in humans. (CX1289 (Melman Expert Report at 0017-18)).

1302. Notwithstanding Dr. Melman's opinion in F. 1301, Dr. Melman also testified that based on the results in an animal model testing gene therapy erectile dysfunction product (*see* F. 653), he was "personally satisfied" that it would also work in humans. (PX0360 (Melman, Dep. at 56-57)).

4. Determinations

1303. There is no true preventative intervention for erectile dysfunction. There are a wide variety of interventions believed to have some potential benefit, anything from dietary changes to weight loss and perhaps things that are still being evaluated, although the role played is not sure. Because these interventions seem to be potentially beneficial and do not necessarily have harms, physicians feel comfortable in promoting them. (PX0349 (Burnett Dep. at 79); Burnett, Tr. 2301, 2272-73).

1304. "[T]reatment can have different meanings . . . . [T]reatment in the context of a pharmaceutical drug that is approved by the FDA as an intervention for a disease may have a different meaning . . . than the broad term of treatment, which is to intervene for a condition." (Burnett, Tr. 2312).

1305. Pomegranate juice "could be a treatment [to erectile dysfunction] in the sense that it offers some potential health benefits." (Burnett, Tr. 2312).

1306. Urologists would recommend pomegranate juice as a management tool to promote erectile health in men who are aware that their erectile function is declining but who do not yet meet the clinical definition of erectile dysfunction under the IIEF and therefore do not qualify for pharmacologic treatment. (PX0189 (Goldstein Expert Report at 0014-0015); PX0352 (Goldstein, Dep. at 42-45); Goldstein, Tr. 2609).

1307. Urologists would recommend pomegranate juice as a complement to conventional erectile dysfunction treatment. (Burnett, Tr. 2298, 2313; PX0349 (Burnett, Dep. at 78-79)) ("To the extent that any intervention out there has some potential benefit of a better benefit than harm that meets some level of safety, I would support that intervention, at least as a complimentary intervention and not a mainstay of ED treatment.") (PX0352 (Goldstein, Dep. at 80) (there are patients in whom there are erectile dysfunction and/or erectile health problems related to inflammatory endothelial dysfunctions, and . . . pomegranate juice has a logical context in the treatment of those patients.").

1308. Dr. Goldstein "would strongly suggest and encourage" use of pomegranate juice to treat erectile dysfunction in a subpopulation of men who have had an insufficient response to PDE5 inhibitors (like Viagra, Levitra and Cialis) and who wish to reestablish erectile function without invasive or mechanical technology or therapies. (PX0352 (Goldstein, Dep. at 37-42, 46)). Dr. Goldstein opined that the consumption of pomegranate juice is a logical option for men who are not responsive to conventional drugs designed to treat erectile dysfunction and who are unwilling to consider invasive or mechanical therapies for treatment of their erectile dysfunction. (PX0189 (Goldstein Expert Report at 0005); PX0352 (Goldstein, Dep. at 37-42); Goldstein, Tr. 2605, 2641).

1309. Pomegranate juice costs far less than Viagra and there are no side effects to drinking pomegranate juice. (PX0352 (Goldstein, Dep. at 44).

5. Conclusions

1310. The available body of scientific literature – including *in vitro, in vivo,* and preliminary clinical trials – suggests that consuming pomegranate juice promotes erectile health. (PX0189 (Goldstein Expert Report at 0003)).

1311. The use of pomegranate juice to promote erectile *health* is a separate and distinct concept from the use of this neutraceutical as a safe and effective treatment for the medical condition of erectile *dysfunction* such as with a PDE5 inhibitor. (PX0189 (Goldstein Expert Report at 0004) (emphasis in original)).

1312. Competent and reliable scientific evidence shows that pomegranate juice provides a benefit to promoting erectile health and erectile function. (Goldstein, Tr. 2605, 2608; PX0189 (Goldstein Expert Report at 0014); PX0149 (Burnett Expert Report at 0006); Burnett, Tr. 2255-56).

1313. There is insufficient competent and reliable scientific evidence to show that pomegranate juice prevents or reduces the risk of erectile dysfunction or has been clinically proven to do so. (Burnett, Tr. 2274, 2300-01; CX1289 (Melman Expert Report at 0018)).

1314. There is insufficient competent and reliable scientific evidence to show that pomegranate juice treats erectile dysfunction in a clinical sense or has been clinically proven to do so. (Burnett Tr. 2285, 2300; Goldstein, Tr. 2611; CX1289 (Melman Expert Report at 0018). *See also* Burnett, Tr. 2261-64).

J. Materiality

1. Overview

1315. Mrs. Resnick believes that part of the intrinsic value of pomegranate juice is that it has been shown to reduce arterial plaque and factors leading to atherosclerosis and was shown to have a "powerful effect against prostate cancer." (L. Resnick, Tr. 75-76).

1316. Mr. Resnick testified that POM communicates to consumers the "[company's] belief that pomegranate juice is beneficial in treating some causes of impotence, for the purpose of promoting sales of its product." (CX1372 (S. Resnick, Tropicana Dep. at 45)).

1317. Mr. Resnick acknowledged that the kinds of benefits revealed by POM's research results are the primary reason people buy pomegranate juice. (CX1372 (S. Resnick, Tropicana Dep. at 31)). Mr. Resnick also acknowledged that consumers buy pomegranate juice "because they believe and in fact it does postpone the onset of prostate cancer, which postpones the onset of death." (CX1376 (S. Resnick, Ocean Spray Dep. at 217)).

1318. Mr. Resnick expressed his belief that a great deal of consumers are buying POM Juice because they believe "that we've proven that . . . [POM Juice] really does prolong people's lives if they are getting the onset of prostate cancer." (CX1376 (S. Resnick, Ocean Spray Dep. at 218-19)).

1319. According to a draft creative brief for POMx dated October 12, 2006, the concept behind communicating the amount of money the company spent on research is: "We don't just say our product is great, we have clinical studies that prove its efficacy." (CX0409 at 0057).

1320. POM was aware that among those purchasing the POM products were "people that have heart disease or prostate cancer in their family, or have a fear of having it themselves." (CX1368 at 17 (L. Resnick, Welch Dep. at 67)).

1321. According to a September 2006 press article, Ms. Posell, POM's then vice president of corporate communications, said "every time new research is released touting" a health benefit of pomegranate juice, "there is a spike in sales. The study . . . linking the consumption of pomegranate juice to a reduction in prostate cancer was especially helpful, she said. . . Pom Wonderful can see the results in increased sales every time a new study surfaces." (CX0433 at 0004).

1322. According to a July 2004 e-mail from John Regal, POM's head of marketing at the time, with the subject line "POM Medical research timing and advertising", POM's goal for its 2-page *Prevention* "advertorial" (CX0029, F. 297-305, *supra*) was to convey "how POM is particularly good for clean & healthy arteries. We also wanted to highlight the new Aviram study regarding plaque reduction in humans." (Leow, Tr. 437; CX0667 at 0001).

1323. In evaluating how copy dense or medically oriented to make a planned POMx Pill advertisement, Ms. Kuyoomjian, Senior Vice President of Marketing for POM from 2008 to 2009, reminded Mrs. Resnick in a January 2009 e-mail: "you'll recall that a previous ad test with less copy did not generate as many orders. That would suggest we keep the research info in the new ad, which would make it information dense as well." (CX1357 (Kuyoomjian Dep. at 22); CX0266 at 0002).

1324. Mr. Perdigao, the head of Fire Station, Roll's in-house advertising agency used by POM (F. 134, 138), noted in an e-mail dated June 11, 2009, that the "consumer benefit" of proposed advertisements that did not reference prostate health or heart health was less compelling than more general references to POM being good for you because it offers antioxidants that reduce free radicals. As Mr. Perdigao explained, less specific advertising is generally less provocative. (CX0320 at 0002; L. Resnick, Tr. 90; *see also* Perdigao, Tr. 670-73).

1325. A creative brief (*see* F. 145-151) for the POM Wonderful website, from June 2008, stated the objective for the assignment was to "tell the story (health benefits, research & how POM fits)." For the "Health Benefits" section of the POM Wonderful website, the

creative brief further stated that, to engage viewers, the page should identify "What are the health benefits?", including "heart health," "prostate health," and "E.D."; "How does it work?", including antioxidant and anti-inflammatory properties, the "commitment" to research; "What the experts say," on such matters as heart and prostate, and a "comprehensive research database," searchable by subject matter, including heart and prostate, and by results. The directed tone and manner included "authoritative." (CX0200 at 0001-02).

1326. Ms. Leow, a creative director for Roll, stated that scientific information in advertising and marketing material helps sell the products, because the scientific information provided the consumer with a "reason to believe." (Leow, Tr. 512-13; CX0095).

1327. A creative brief for POMx Pills, dated September 1, 2006, included the sentence in an opening narrative paragraph, as a bullet point: "main creative focus is prostate cancer." (CX0409 at 0023).

1328. A creative brief for POMx Pills, dated September 5, 2006, stated under "benefit," in bold type, "Main creative focus for 1st round is prostate cancer. (The benefits are from the studies – which showed a decrease in the doubling time of PSA levels)." The "benefit" section continued: "The other versions of the creative [brief] should definitely focus on the other benefits of POM – antioxidant, anti-aging, heart health, etc." (CX0409 at 028).

1329. Respondents' marketing expert, Dr. David Reibstein, stated that it was indeed possible, and he would expect that, consumers in POM's target audience who were concerned about heart disease would find a claim that drinking a bottle of POM Juice a day prevents or treats heart disease to be important, that those concerned about prostate cancer would find a prostate cancer prevention or treatment claim important, and that those concerned about erectile dysfunction would find an erectile dysfunction prevention or treatment claim important. (PX0356 (Reibstein, Dep. at 117-19)).

2. OTX A&U Study and Zoomerang survey

1330. In the ordinary course of business, POM conducted consumer research to understand the characteristics, attitudes and usage habits of their customers and to identify barriers and opportunities for increasing consumption, particularly *vis-à-vis* other brands of pomegranate juice. (CX0370 at 0002; CX0292; CX0136; CX0453 at 0004).

1331. In June 2009, OTX, a consumer research firm, conducted an Attitudes and Usage consumer survey ("OTX A&U Study") on POM's behalf. (CX0370 at 0002, 0004; PX0227). The A&U Study's sample included current and former POM Juice drinkers, other pomegranate juice drinkers and users of other antioxidant fruit juices. (CX0370 at 0003).

1332. In the OTX A&U Study, among other things, current pomegranate juice users, including users of POM Juice, were asked why they drink pomegranate juice, and were

given a list of options, including: "It's healthy/good for my health," "I like the taste," "I like pomegranates," "it's all natural," or "Other (specify"), and were directed to select all that applied. (PX0227 at 0006). Among the POM Juice drinkers, 85% said they drank pomegranate juice because "it's healthy good for my health," 75% said "I like the taste," 59% said "I like pomegranates," 50% said "it's all natural," 29% said "it's new/interesting food trend," and 4% said "other." (CX0370 at 0011).

1333. Those in the OTX A&U Study that responded, "It's healthy/good for my health," were asked a follow-up question, "Which specific health reasons below describe why you personally drink pomegranate juice?" and were presented with a list of reasons, depending on whether they were male or female. (CX0370 at 0012; PX0227 at 0006; Reibstein, Tr. 2558-59; Mazis, Tr. 2682-84).

1334. The choices given to the survey respondents identified in F. 1333 were: helps promote heart health; helps protect against prostate cancer [for males only]; helps protect against other cancers (besides prostate); contains naturally occurring antioxidants; will help me live longer; helps improve thinking and memory; good for bone and joint health; helps protect against urinary tract infections; provides immunity from colds and flu; promotes healthy pregnancy [for females only]; promotes menstrual health [for females only] and "[o]ther (specify)." (PX0227 at 0006).

1335. Among the POM Juice drinkers responding to the question in F. 1334, 91% said "contains naturally occurring antioxidants," 57% said "helps promote heart health," 47% of men said "helps protect against prostate cancer," 45% said "provides immunity from colds and flu," 43% said "helps protect against other cancers (besides prostate); 38% said "helps protect against urinary tract infections," 28% said "will help me live longer," 28% said "good for bone and joint health," 25% said "helps improve thinking and memory," 14% said "promotes menopausal/post-menopausal health," 6% said "promotes healthy pregnancy," and 2% said "other." The percentages attributed for the different responses attributable to non-POM Juice and other antioxidant beverage drinkers were slightly less. (CX0370 at 0012).

1336. POM's Senior Vice President of Marketing, Ms. Kuyoomjian, was not surprised by the OTX A&U Study result that, for 47% of male POM users, part of the reason they drink POM Juice is because they believe it helps protect against prostate cancer. (CX1357 (Kuyoomjian, Dep. at 259-60)).

1337. Dr. Reibstein reviewed the OTX A&U Study and concluded that although it presented some information contradictory to the conclusions he drew from his own survey (*see* F. 1344-1372), the OTX A&U Study had methodological flaws, cannot be relied upon, and does not invalidate the results of Dr. Reibstein's survey. (PX0223 (Reibstein Expert Report at 0021)).

1338. In rebuttal to the opinion of Respondents' expert Dr. Reibstein, that the OTX A&U Study was not reliable or relevant (F. 1337), Complaint Counsel's expert, Dr. Mazis, reviewed the OTX A&U Study and expressed his opinion that the OTX A&U Study

was highly relevant and demonstrated that the heart disease and prostate cancer claims are important to consumers, and are reasons that POM Juice users choose to purchase POM Juice. (Mazis, Tr. 2688-89, 2760; CX1297 (Mazis Expert Report at 0012-13)).

1339. Dr. Mazis testified that, with respect to the likely importance that the challenged claims would have on consumers' purchase or use decisions, he finds the OTX A&U Study more reliable than the Reibstein Survey (*see* F. 1344-1372; Mazis, Tr. 2689).

1340. In Dr. Reibstein's opinion, the OTX A&U Study used closed-ended questions, in that it provided respondents with a list of five choices as to why they drink pomegranate juice, and that this method "cues" the survey respondent to certain answers, excludes other potential answers that were not included on the list of choices, and inflates results. (PX0227 at 0006; Reibstein, Tr. at 2518-20).

1341. Dr. Mazis opined that, when studying purchase motivations, the use of closed-ended questions have an advantage because it allows the researcher to get some specificity, and, therefore, closed-ended questions tend to be used in most of these types of studies. Although close-ended questions have a disadvantage in that they may lead to some upward bias, in a study like the OTX A&U Study, one accounts for this by giving a long list of choices, as was done in the OTX A&U Study, and examining the relative ranking of responses. (Mazis Tr. 2662-63).

1342. In August 2007, Respondents commissioned a Zoomerang online survey of the general public, "to better understand pomegranate and non-pomegranate juice consumers," with respect to, among other things, "importance of certain health benefits." The survey included 287 heavy pomegranate juice drinkers. Six health benefits were listed and these respondents were asked to rank which health benefit was the most important to them personally. For heavy pomegranate juice drinkers, the number one response, for both males and females was "cardiovascular," and the number two choice for men was "prostate." (*See* CX0292 at 0025; CX0136 at 0001, 0003, 0006).

1343. For members of the general public responding to the Zoomerang survey question regarding ranking of health benefits (F. 1342), 60% ranked cardiovascular health as the first or second most important benefit, 40% of males ranked prostate health as the first or second most important benefit, and approximately 18% of males did so for erectile dysfunction. (CX0136 at 0002, 07-08; CX0453 at 0004).

3. Reibstein Survey

1344. The Reibstein Survey was conducted on behalf of POM Wonderful in connection with this litigation, by an independent market research company, Horizon Consumer Science ("HCS") under the direction of Dr. David J. Reibstein. (PX0223 (Reibstein Expert Report at 0001, 0003); F. 266-275).

1345. HCS maintains an online panel of over one million subjects. From this population, a stratified sample of 2,164 was drawn from the United States population. (PX0223 (Reibstein Expert Report at 0004)).

1346. The Reibstein Survey sought to reveal (i) a buyer's motivation for purchasing pomegranate juice; (ii) whether having previously seen POM Juice advertisements in the normal sequence of viewing advertisements and not in an artificial setting, the advertisements affected the buyer's motivations for buying pomegranate juice; and (iii) whether the buyer's awareness of the legal issues around the case might have affected their motivation for buying pomegranate juice. (PX0223 (Reibstein Expert Report at 0005); Reibstein, Tr. 2487; PX0356 (Reibstein Dep. at 11, 38-39, 51)).

1347. The Reibstein Survey was conducted in October 2010. (Reibstein, Tr. 2541).

1348. Dr. Reibstein's Survey did not address POMx or the purchase motivations of POMx purchasers, and Dr. Reibstein did not undertake to extrapolate the results of his survey to POMx purchasers. (Reibstein, Tr. 2565-66).

1349. To qualify for the Reibstein Survey, respondents had to meet the following criteria: (i) purchased pomegranate juice in the six months prior to the survey; (ii) had not completed any online survey within the 3 months prior to the survey for any beverage products; (iii) did not work in any of the following industries: advertising, public relations, beverages, marketing or market research; and (iv) was over 18 years old. This was accomplished through a series of screening questions. (PX0223 (Reibstein Expert Report at 0004); PX0237 at 0001-02; PX0356 (Reibstein, Dep. at 50-51, 57-58)).

1350. Of the 2,164 panelists that completed the online Reibstein Survey, 750 of them met the qualification criteria, and actually completed the survey. (PX0223 (Reibstein Expert Report at 0004)).

1351. The Reibstein Survey surveyed two groups, 406 respondents who purchased POM Juice in the past six months ("POM Juice consumers") and 344 respondents who purchased brands of pomegranate juice other than POM in the past six months. (PX0223 (Reibstein Expert Report at 0004); Reibstein, Tr. 2493-94).

1352. The Reibstein Survey employed two types of controls. The first control was to draw a sample of non-POM Juice buyers and ask them the same questions as the POM Juice buyers to see if these buyers had different motivations for purchasing pomegranate juice. The second control was to compare the responses of people who had seen POM advertisements against those who had not seen any POM advertisements. (PX0223 (Reibstein Expert Report at 0004-05); Reibstein, Tr. 2488-89, 2493; PX0356 (Reibstein, Dep. at 73-74)).

1353. For the sample of 406 POM Juice consumers, the Reibstein Survey asked three primary open-ended questions in Questions E through G, set forth below in F. 1354-1356. (PX0223 (Reibstein Expert Report at 0005)).

1354. Question E asked "Why did you purchase POM Wonderful 100% Pomegranate Juice? *Please include as many specific details*." (PX0237 at 0002 (italics in original); PX0223 (Reibstein Expert Report at 0006)).

1355. Question F asked "Would you consider purchasing POM Wonderful 100% Pomegranate Juice again?

(SELECT ONE ONLY)

1. Yes a. Why? *Please include as many specific details as to why you would?*
2. No a. Why not? *Please include as many specific details as to why you would not?* 3. Don't know."

(PX0237 at 0002 (emphases in original); PX0223 (Reibstein Expert Report at 0007)).

1356. Question G asked "Would you recommend POM Wonderful 100% Pomegranate Juice to a friend?

(SELECT ONE ONLY)

1. Yes a. Why? *Please include as many specific details as to why you would?*
2. No a. Why not? *Please include as many specific details as to why you would not?*
3. Don't know."

(PX0237 at 0002 (emphases in original); PX0223 (Reibstein Expert Report at 0008)).

1357. For the 344 non-POM Juice pomegranate juice consumers, the Reibstein Survey asked three primary open-ended questions in Questions H through J, set forth below in F. 1358-1360. (PX0223 (Reibstein Expert Report at 0005)).

1358. Question H asked "You indicated that you have purchased pomegranate juice. *Please include as many specific details* as to why you purchased it. *Please* be *as detailed as possible.*" (PX0237 at 0002 (emphases in original); PX0223 (Reibstein Expert Report at 0006)).

1359. Question I asked "Would you consider purchasing pomegranate juice again?

(SELECT ONE ONLY)
1. Yes a. Why? *Please include as many specific details as to why you would again*?
2. No. a. Why not? *Please include as many specific details as to why you* would *not again*?
3. Don't know."

(PX0237 at 0003 (emphases in original)).

1360. Question J asked "Would you recommend pomegranate juice to a friend?

(SELECT ONE ONLY)
1. Yes a. Why? *Please include as many specific details as to why* you *would?*
2. No. a. Why not? *Please include as many specific details as to why you would not?*
3. Don't know."

(PX0237 at 0003 (emphases in original)).

1361. A summary of the results of the responses to Questions E-J was set forth by Dr. Reibstein in Figure 5 in his expert report. Figure 5 is set forth below:

Question	**Percentage of POM Wonderful Juice Buyers whose response mentions a specific disease reference n=406**	**Percentage of Pomegranate Juice Buyers whose response mentions a specific disease reference n=344**
E/H (Why did you purchase?)	1.0% (4/406)	.9% (3/344)
F/I (Why would you purchase/not purchase again?)	.5% (2/406)	0% (0/344)
G/J (Why would/would not recommend?)	.3% (1/406)	.9% (3/344)
NET	**1.48% (6/406)**	**1.74% (6/344)**

(PX0223 (Reibstien Expert Report at 0020)).

1362. The "specific disease" references, as reported by respondents to the Reibstein Survey (F. 1361) included: heart disease, getting rid of plaque, cancer, urinary tract infections, bowel movements, diabetes, kidney stones, and arthritis pain. (PX0223 (Reibstein Expert Report at 0011-12)).

1363. The above findings (F. 1361-1362) reflect 12 unique survey respondents, because one participant responded to both Question E and Question F with a disease reference. This respondent is counted only once in the "net" results. (PX0223 (Reibstein Expert Report at 0011, 0020 n.1-6)).

1364. Questions E through J of the Reibstein Survey were in open-ended format, to reduce any biasing of the survey respondents. (PX0223 (Reibstein Expert Report at 0005); PX0356 (Reibstein Dep. at 84-85)).

1365. In response to questions E and H of the Reibstein Survey, respectively, 35.2% of POM Juice purchasers stated that they purchased or would repurchase POM Juice because it was "healthy" and 46.8% stated that they would recommend it to a friend because it was "healthy." In addition, 43.6% of POM Juice purchasers stated they purchased because of the taste, and 74% stated they would repurchase because of the taste. (PX0223 (Reibstein Expert Report at 0006-07)).

1366. Question K asked respondents: "Have you ever seen a POM Wonderful 100% Pomegranate Juice advertisement?

(SELECT ONE ONLY)

1. Yes a. Please include as many specific details as to what you remember about the ad. *Please be as detailed as possible*.
2. No
3. Don't know."

(PX0237 at 0003 (emphases in original); PX0223 (Reibstein Expert Report at 0016); Reibstein, Tr. 2507, 2567).

1367. In response to Question K of the Reibstein Survey, 39.6% of people (297 out of 750) who consumed pomegranate juice in the prior six months had seen a POM advertisement. (PX0223 (Reibstein Expert Report at 0009, 0016); PX0233 at 0028; Reibstein, Tr. 2536).

1368. In response to Question K of the Reibstein Survey, while 20% of the respondents reported "healthy," none of the respondents who saw a POM advertisement responded that they remember the advertisement making a specific disease claim. Other common details reported by POM Juice purchasers were bottle appearance (22.4%); people or objects in the advertisement (20.6%); and "don't know/no response" (20%). (PX0223 (Reibstein Expert Report at 0009); PX0233 at 0029).

1369. In the Reibstein Survey, among the 12 unique respondents out of 750 total respondents, including non-POM Juice buyers, who mentioned a specific disease as a reason for purchasing or recommending pomegranate juice, 4 reported having seen a POM advertisement at some point and 8 reported not ever having seen an advertisement. (PX0223 (Reibstein Expert Report 0009, 0016-19)).

1370. Based on the Reibstein Survey findings, Dr. Reibstein, expressed the opinion that POM advertisements had no impact on buyers' purchase motivations. (PX0223 (Reibstein Expert Report at 0020)).

1371. Dr. Reibstein did not expose consumers to the Challenged Advertisements. (Reibstein, Tr. 2494).

1372. Based on the Reibstein Survey results, Dr. Reibstein, expressed the opinion that there is a very small percentage of people that bought, would buy again, or would recommend POM Juice to a friend because they believe that it cures or prevents a specific disease. (PX0223 (Reibstein Expert Report at 0020)).

1373. In rebutting the opinions of Dr. Reibstein, Dr. Mazis opined that the Reibstein Survey did not employ a valid measure of materiality of the challenged claims in this case because the survey was a general assessment of consumer motivations but did not assess whether any one of the challenged claims in the complaint would be important in the decision to purchase or to use POM Juice. According to Dr. Mazis, what a consumer might identify as a motivation for purchasing a product is not the same thing as assessing whether, if a consumer knew of a claim, that claim would be important in his or her decision to purchase the product. (CX1297 (Mazis Expert Report at 0008); Mazis, Tr. 2673).

1374. According to Dr. Mazis, in order to do a survey on materiality, "you don't have to show them the ad, but you have to give them a statement about what the claim was and you have to ask them how important they think that claim would be in their potential purchase decision." (Mazis, Tr. 2728).

1375. Dr. Mazis further opined that Dr. Reibstein's methodology was flawed because he asked only open-ended questions but did not follow-up with questions probing further what the respondents meant when referring to POM Juice being "healthy" or having "health benefits" as their motivation for purchasing. According to Dr. Mazis, the Reibstein Survey should have explored what survey respondents meant by their "healthy" response and whether there were specific reasons or benefits that underlay "healthy" responses. (Mazis, Tr. 2756-57, 2707-09; PX0296 (Mazis Expert Report at 0009-10)).

1376. Dr. Mazis agreed that open-ended questions make it "significantly less likely that the respondents will be led into giving a particular answer." (Mazis, Tr. 2732).

1377. Dr. Mazis expressed the opinion that "the impact of advertising on beliefs about a product is not an appropriate measure of materiality or ad claim communication." (CX1297 (Mazis Expert Report at 0009)).

K. Remedy

1. Roll Global and POM entities

1378. Roll Global ("Roll") is an approximately $2 billion corporation that includes under its umbrella the companies Teleflora, Fiji Water, Paramount Farms (which sells Wonderful Pistachios and Wonderful Almonds), Paramount Citrus (which sells Cuties), Justin

Vineyards and Winery, and Suterra. (JX0003 ¶ B.3; S. Resnick, Tr. 1629-30; Perdigao, Tr. 593-94).

1379. POM manufactures, advertises, and sells other products containing pomegranate, including various POM Juice blends, Lite POM Juice, POMx bars, POMx iced tea and iced coffee, and a POMx sports recovery beverage. (JX0003 ¶ B.8).

1380. POM is headquartered in the same building as Roll, in many cases with employees of both companies occupying the same floor. For example, Mr. Perdigao, the president of Roll's in-house advertising agency, Fire Station and Roll's Corporate Communications department (F. 134, 138), and Ms. Leow, Fire Station's Creative Director, are located on the same floor as the offices of Mrs. Resnick, Mr. Resnick, and Mr. Tupper, among other POM employees. (Tupper, Tr. 888; Leow, Tr. 418; PX0277 at 0002-03).

1381. Mrs. Resnick describes Roll as "the umbrella company for all of our businesses" and others that work for Respondents describe Roll similarly and consider POM to be part of Roll. (CX0001 at 00011; Posell, Tr. 298, 305; Tupper, Tr. 894; Perdigao, Tr. 593).

1382. Mr. and Mrs. Resnick each maintain a business address at 11444 West Olympic Blvd., 10th Floor, Los Angeles, CA 90064, which is also the business address for POM and Roll. (PX0277 at 0002-03; *see also* PX0276 at 0002).

1383. Mrs. Resnick does not have a specific corporate title at POM. (L. Resnick, Tr. 287-88; CX1359 (L. Resnick, Dep. at 37)).

1384. Although Roll's affiliated companies' pay Roll for certain provided services, including advertising (F. 13-14), not all expenses, such as advertising and marketing services, provided to POM were reimbursed. Roll has provided various services over the years to POM relating to POM Juice, POMx Pills, and POMx Liquid "with some portion charged back to POM . . . ." (CX1383 at 0014; CX1357 (Kuyoomjian, Dep. at 235)). For example, the former Vice President of Corporate Communications at Roll testified she was not required to keep track of her time based on whether she was working on a POM project or a project for another Roll company. (Posell, Tr. 325). In addition, Roll provides risk management, human resources, consulting, and travel services to POM without any reimbursement. (CX1354 (Bryant, Dep. at 41-42, 48-50, 55-64)).

1385. When Fire Station acts as Roll's in-house advertising agency, Fire Station bills POM and other Roll entities separately, and each client pays for advertising and marketing expenses incurred. (CX1376 (S. Resnick, Ocean Spray Dep. at 24-25); L. Resnick, Tr. 88-89; CX1359 (L. Resnick, Dep. at 26); Perdigao Tr. 616-17).

1386. The Resnicks have had ultimate say over all business functions of Roll and POM. They have set policy and supervised the senior executives of both companies, disregarding corporate formalities. For example, Mrs. Resnick has had complete oversight over POM's business, despite lacking any formal position with the company. (CX1368 at

0002-03 (L. Resnick, Welch Dep. at 8-9); CX1362 at 0012 (L. Resnick, Coke Dep. at 45-46); CX1374 (Tupper, Ocean Spray Dep. at 18-19); S. Resnick, Tr. 1631 (stating that Mrs. Resnick is very involved in setting POM's marketing and advertising budget); L. Resnick, Tr. 184 (stating that she has interviewed candidates for the chief marketing officer or other senior vice president positions at POM); JX0001 ¶ 18 (showing overlapping officers between POM and Roll); Posell, Tr. 321, 325 (stating that while Vice President of Corporate Communications, Ms. Posell reported to Mr. Tupper and Mrs. Resnick)).

1387. For accounting purposes, Roll and its affiliated companies, including POM, were represented as being under common control or ownership and have been included together on consolidated financial and tax statements. (CX1354 (Bryant, Dep. at 23, 27, 52-53), *in camera*; *see also* CX1355 (Hemmati, Dep. at 52-54) (stating that Roll provided information about the Resnick Trust's payments for medical research to POM); CX1276 at 0003).

1388. POM's Consumer Affairs representative would typically respond to consumer complaints; however, "if necessary, [they] might get escalated" to others at POM or Roll, such as Roll's Corporate Communications, which may respond directly to the consumer. (CX1357 (Kuyoomjian, Dep. at 204-10)

1389. Roll also interacts with POM for the purposes of joint cash management, as noted by Roll's Chief Financial Officer, Robert Bryant, who stated that Roll "pool[s] together the cash from each one of [its] operating companies and will invest that cash . . . overnight for purposes of investments . . . [o]r if [Roll has] debt outstanding on [its] working capital lines, then [Roll] will use that cash to pay down those working capital . . . lines." (CX1354 (Bryant, Dep. at 67)).

1390. POM's medical research program was sponsored and funded by various Resnick entities (*e.g.*, Roll, POM, and the Resnick Trust). (CX1118 at 0001; CX0604 at 0022 (stating that "Roll Int'l will reimburse Technion [Institute] directly," even though POM was listed as the research sponsor); CX0628 at 0001 (describing a study on pomegranate juice as the "Roll Beverage Study"); *see also* F. 1391).

2. The Resnicks

1391. The Stewart and Lynda Resnick Revocable Trust entered into contracts to fund research; however, regardless of which Resnick-controlled organization has paid for pomegranate research, the money ultimately comes from the Resnicks. (CX0610; S. Resnick, Tr. 1657, 1675-76, 1722-23; CX1363 at 0016 (S. Resnick, Coke Dep. at 61) (whether a study is sponsored by Roll or POM, "[t]he money comes out of the same pockets"); *see also* CX1376 (S. Resnick, Ocean Spray Dep. at 229-30 (the $34 million referenced in a POM advertisement is ultimately "our money, however it comes")); L. Resnick, Tr. 198-99).

1392. Mr. Resnick has been directly involved in the development of POM's scientific research program by engaging and communicating with scientific consultants, participating in scientific advisory board meetings, and convening company-sponsored research summits. (CX1360 (S. Resnick, Dep. at 85, 110-12); Tupper, Tr. 1027-28; Liker, Tr. 1880, 1889, 1891; CX0589).

1393. With regard to the medical research budget, Mr. Resnick reviews and approves the POM research budget annually, and when necessary if any changes occur during the year. (CX1376 (S. Resnick, Ocean Spray Dep. at 227)).

1394. Mr. Resnick reviews the results of the scientific research he sponsors, and has seen the results of all the important tests and also some of the draft manuscripts before they were published. (S. Resnick, Tr. 1656-57).

1395. Mr. Resnick meets with POM and its scientific advisors about POM-sponsored research ten to twelve times a year "officially" and three to four additional times to review what has been learned and where the company's research may go. (CX1376 (S. Resnick, Ocean Spray Dep. at 223-24).

1396. Mrs. Resnick participated in POM's business on almost a daily basis in the company's early years, and on a weekly or biweekly basis thereafter and through 2010. (L. Resnick, Tr. 93, 157-58; *see also* CX1375 (L. Resnick, Tropicana Dep. at 19-22, 78); CX1359 (L. Resnick, Dep. at 108)).

1397. If there were disputes or issues to resolve regarding advertising decisions, the final authority was either Mr. or Mrs. Resnick. As the overseer of all branding and marketing, Mrs. Resnick had the "final word" on advertising content and concepts. (CX1365 (Perdigao, Coke Dep. at 36-37)); CX1368 at 0003 (L. Resnick, Welch's Dep. at 9); L. Resnick, Tr. 93; CX1347 (Glovsky, Dep. at 36); CX1357 (Kuyoomjian, Dep. at 84)).

1398. Mrs. Resnick has participated in the hiring and firing of heads of marketing at POM. (L. Resnick, Tr. 183-84, 227-28).

1399. Mrs. Resnick has had a principal role in approving advertising content since POM's inception. For example, Mrs. Resnick requested that copies of all advertising campaigns be submitted to her for final approval including the headlines used in POM's advertisements. (CX1368 at 0003 (L. Resnick, Welch Dep. at 9); *see also* CX1357 (Kuyoomjian, Dep. at 56-57, 77, 127); CX1346 (Rushton, Dep. at 42 (approval of website designs)); CX0147).

1400. At LRR Meetings (F. 141) and during other interactions with POM Marketing and Fire Station, Mrs. Resnick would approve a general direction for POM's advertising and also approved the lion's share of POM's advertising concepts. (*see* F. 143).

1401. Mrs. Resnick was "very involved" in developing the POMx brochure, identified as CX1426, Exhibit I "Antioxidant Superpill" package insert, when it was first produced. (L. Resnick, Tr. 246; *see* F. 328-342).

1402. Mrs. Resnick was involved in the approval of the print advertisement identified as CX0029 ("10 OUT OF 10 PEOPLE DON'T WANT TO DIE") (CX0471 at 0007-08; L. Resnick, Tr. 158; CX0029; *see* F. 299-305).

1403. Mrs. Resnick approved the headline for the POMx print advertisement headlined "The Only Antioxidant Supplement Rated X." (L. Resnick, Tr. 266; *see* CX0351 and CX0355; *see* F. 321-327)).

1404. Mrs. Resnick approved the print advertisement identified as CX0031 ("Floss your arteries" print advertisement); CX0471 at 0010; L. Resnick, Tr. 158-59; CX0031; *see* F. 440-448).

3. Matthew Tupper

1405. Mr. Tupper has never had any ownership interest in POM Wonderful and has no expectation of ever having such an interest. (CX1353 (Tupper, Dep. at 14-15); Tupper, Tr. 2973).

1406. Mr. Tupper had no more authority at POM than was delegated to him by Mr. Resnick. Mr. Resnick delegated to Mr. Tupper the authority to decide which advertisements should run. (S. Resnick, Tr. 1870).

1407. When Mrs. Resnick reduced her day-to-day involvement in POM's business beginning in 2007, Mrs. Resnick felt confident that Mr. Tupper would be able to take care of the marketing aspects of the business, as she had previously done. (L. Resnick, Tr. 229).

1408. Mr. Tupper reviewed work on each of POM's large advertising campaigns at the concept stage, before they were shown to Mrs. Resnick. (Leow, Tr. 459-60).

1409. With respect to health benefit advertising, Mr. Tupper was the "connecting piece" or "liaison" between the marketing vision and the communication of the science. (Tupper, Tr. 2975-76).

1410. Mr. Tupper led meetings to review advertising copy from a scientific perspective prior to its dissemination. (Dreher, Tr. 530).

1411. Mr. Tupper was engaged in the medical research aspect of POM's business from the time he first joined POM full-time in 2003. Beginning in late 2006 or early in 2007, he became more engaged as the "connecting piece" between research and marketing. (Tupper, Tr. 2975-77; *see* F. 1409).

1412. As POM's president, Mr. Tupper attended most of the marketing review meetings with Mrs. Resnick, which included discussions of POM's scientific research. (Tupper, Tr. 929-30; CX1351 (McLaws, Dep. at 33-34); CX1347 (Glovsky, Dep. at 149-50)).

1413. Mr. Tupper was significantly involved in the research aspects of POM's business, the internal decision-making as to what research to fund, and overseeing for POM the clinical trials on POM's products that were conducted by research institutions. (Tupper, Tr. 895-96, 906; *see also* CX0770; CX0779; CX0800; CX0919; CX0920).

1414. POM's former Senior Vice President of Marketing, Ms. Diane Kuyoomjian, relied on her conversations with Mr. Tupper to understand the content in POM's advertising regarding the relationship between POM advertisements and the scientific support for these advertisements. She relied on Mr. Tupper to be the "arbiter" of whether people felt POM's advertising was accurate. (CX1378 (Kuyoomjian, Ocean Spray Dep. at 71-72)).

1415. Ms. Kuyoomjian, "would never do something [Mr. Tupper] wasn't involved in. He was [her] boss." (CX1357 (Kuyoomjian, Dep. at 51)).

1416. As one of the senior leaders at POM, Mr. Tupper organized meetings to review advertising copy from a scientific perspective. (Dreher, Tr. 530).

1417. Mr. Tupper reviewed and gave direction to POM's marketing staff on parts or elements of creative briefs. (Tupper, Tr. 924).

1418. According to POM's former Senior Vice President of Marketing, Ms. Kuyoomjian, Mr. Tupper was the primary person from whom she received information on POM's medical research, including information that would appear in consumer advertising copy, and Mr. Tupper in general would provide input as to how to describe the medical research used in advertisement copy. (CX1357 (Kuyoomjian, Dep. at 164-66); *see also* CX0906 at 0001-02 (providing guidance on what types of studies should be used in newsletters and websites)).

1419. Mr. Tupper participated in meetings in which Fire Station and POM personnel presented and reviewed advertising concepts and advertising. (L. Resnick, Tr. 91-92; Tupper, Tr. 929).

1420. Mr. Tupper reviewed advertising copy (including headlines), made changes to copy, and, depending on the project, had final say over POM advertising content and which advertisements should or should not run. (L. Resnick, Tr. 87; Leow, Tr. 423-24, 464-66; Tupper, Tr. 925-27; S. Resnick, Tr. 1870; CX1357 (Kuyoomjian, Dep. at 141-42)).

1421. Sometimes, Mr. Tupper would provide the specific words to use when presenting medical research facts, and in other instances, POM Marketing or Fire Station employees would "take a stab at writing [this information] and send it to [Mr. Tupper] to approve." (CX1357 (Kuyoomjian, Dep. at 169-70)).

1422. On average, Mr. Tupper has interacted with Mr. Perdigao, head of Fire Station creative agency, once a week. (Perdigao, Tr. 613).

1423. During periods when the position of head of marketing at POM was vacant, Mr. Tupper would step in to some extent, and if the subject matter required a high level person, Mr. Tupper would take the lead in communicating with Fire Station. (L. Resnick, Tr. 185; Perdigao, Tr. 611-12).

1424. Mr. Tupper had direct contact with research scientists who were working on POM's products, including substantive discussions of the underlying science. (Tupper, Tr. 899, 914).

1425. Mr. Tupper worked with Dr. Dreher in preparing summaries of POM's research portfolio. Mr. Tupper offered the business perspective by drafting the "where do we go from here" sections of POM's medical research summaries. He also edited the research summaries. (Dreher, Tr. 555-56, 558; CX1015 at 0001; CX1029).

1426. Mr. Tupper, along with Mr. Resnick, would meet on occasion with Dr. Liker, POM's Medical Director, to communicate the scientific research areas that POM was interested in exploring. (Liker, Tr. 1880).

1427. Mr. Tupper's responsibilities included keeping up to date on the status of medical research on POM's products, as well as reviewing the unpublished and published data that resulted from studies on POM's products. (Tupper, Tr. 913-14, 941; S. Resnick, Tr. 1720-21).

1428. Mr. Tupper, along with Mr. Resnick, participated in meetings with POM's scientific advisors to review research summaries, discuss research results, and come up with future plans for additional research. (Liker, Tr. 1889, 1915, 1925; Dreher, Tr. 555-56). Some of these scientific research meetings also included POM's scientific director at the time (either Risa Schulman, Dr. Dreher, or Dr. Gillespie), Dr. Liker, Dr. Heber, or Dr. David Kessler ("Dr. Kessler"), an advisor to POM. (Liker, Tr. 1889; Heber, Tr. 2068, 2072; Heber, Tr. 2072; S. Resnick, Tr. 1859).

1429. Mr. Tupper participated in regular research summits, which were meetings with scientists that helped POM interpret the results of scientific research and facilitated discussions about future research. (Liker, Tr. 1890-92).

1430. Mr. Tupper reviewed press releases prior to issuance. (Posell, Tr. 368; CX0062; CX0127).

1431. Mr. Tupper participated in drafting the *Time* magazine cover wraps found herein to have made the claims alleged in the Complaint (*see* F. 308-320, 581; CX1378 (Kuyoomjian, Ocean Spray Dep. at 88-90)).

III. ANALYSIS

A. Burden of Proof

The parties' burdens of proof are governed by Rule 3.43(a) of the Federal Trade Commission's Rules of Practice, Section 556(d) of the Administrative Procedure Act ("APA"), and case law. Pursuant to Commission Rule 3.43(a), "[c]ounsel representing the Commission . . . shall have the burden of proof, but the proponent of any factual proposition shall be required to sustain the burden of proof with respect thereto." 16 C.F.R. § 3.43(a). Under the APA, "[e]xcept as otherwise provided by statute, the proponent of a rule or order has the burden of proof." 5 U.S.C. § 556(d).

It is well established that the preponderance of the evidence standard governs Federal Trade Commission ("FTC") enforcement actions. *In re Telebrands Corp.*, No. 9313, 140 F.T.C. 278, 426, 2004 FTC LEXIS 154, at *76 (Sept. 15, 2004) (Initial Decision), *aff'd*, 140 F.T.C. 278, 2005 FTC LEXIS 178 (Sept. 19, 2005), *aff'd*, 457 F.3d 354 (4th Cir. 2006); *In re Automotive Breakthrough Sciences, Inc.*, No. 9275, 1998 FTC LEXIS 112, at *38 n.45 (Sept. 9, 1998) (holding that each finding must be "supported by a preponderance of the evidence in the record"); *In re Adventist Health System/West*, No. 9234, 117 F.T.C. 224, 1994 FTC LEXIS 54, at *28 (Apr. 1, 1994) ("[e]ach element of the case must be established by a preponderance of the evidence"); *In re Bristol-Meyers Co.*, No. 8917, 102 F.T.C. 21, 1983 FTC LEXIS 64, at *143 (Sept. 28, 1979) (Initial Decision) (stating that complaint counsel has "the burden of proving by a preponderance of credible evidence that the challenged advertising claims have not been established or did not have a reasonable basis"), *aff'd*, 1983 FTC LEXIS 21, at *242 (July 5, 1983), *aff'd*, 738 F.2d 554 (2d Cir. 1984). *See also Steadman v. SEC*, 450 U.S. 91, 102 (1981) (holding that the APA establishes preponderance of the evidence standard of proof for formal administrative adjudicatory proceedings).

The Complaint in this case alleges that Respondents disseminated advertising and promotional materials representing that the consumption of eight ounces of POM Juice, one POMx Pill, or one teaspoon of POMx Liquid (the "POM Products") daily "prevents or reduces the risk of" or "treats" heart disease, prostate cancer or erectile dysfunction. Complaint ¶¶ 9,

10, 19. The Complaint further alleges that Respondents represented that they possessed and relied upon, but in fact did not possess or rely upon, a reasonable basis substantiating such claims, and thus, Respondents' representations were false or misleading. Complaint ¶¶ 19-21. In addition, the Complaint alleges that Respondents have disseminated advertising and promotional materials representing that "clinical studies, research, and/or trials prove" that consuming the POM Products "prevents or reduces the risk of" or "treats" heart disease, prostate cancer or erectile dysfunction, Complaint ¶¶ 9, 10, 12, 14, 16, but that these representations were false or misleading because clinical studies, research, and/or trials do not in fact prove that consuming the POM Products, "prevents or reduces the risk of" or "treats" heart disease, prostate cancer or erectile dysfunction. Complaint ¶¶ 13, 15, 17, 18. Complaint Counsel has the burden of proving each of the foregoing factual issues by a preponderance of credible evidence. *In re Bristol-Myers Co.*, 1983 FTC LEXIS 64, at *143-44. *See also FTC v. QT, Inc.*, 448 F. Supp. 2d 908, 959 (N.D. Ill. 2006), *aff'd*, 512 F.3d 858 (7th Cir. 2008).

B. Jurisdiction

Section 5 of the Federal Trade Commission Act ("FTC Act") grants the Federal Trade Commission the authority to "prevent unfair or deceptive acts or practices in or affecting commerce" by "persons, partnerships, or corporations." 15 U.S.C. § 45(a)(1)-(2) (2012). Section 4 of the FTC Act defines "corporation," in part, as "any company, trust, so-called Massachusetts trust, or association, incorporated or unincorporated, which is organized to carry on business for its own profit or that of its members, and has shares of capital or capital stock or certificates of interest . . . ." 15 U.S.C. § 44.

POM Wonderful ("POM Wonderful" or "POM") is a limited liability company. F. 1. Roll International Corporation, which was reorganized at the end of 2010 and is currently known as Roll Global ("Roll"), is a separate corporation. F. 7-8. POM Wonderful is one of several separate operating businesses under Roll's ownership umbrella. F. 11. Mr. Stewart Resnick ("Mr. Resnick") and Mrs. Lynda Resnick ("Mrs. Resnick") are the sole owners of Roll and its affiliated companies, including POM Wonderful. F. 12. Mr. Resnick is the Chairman and President of Roll and the Chairman and Chief Executive Officer of POM Wonderful. F. 19-21. Mrs. Resnick is Vice Chairman of Roll. F. 27-28. She is the chief marketing person

at POM, with responsibilities for marketing, branding, public relations, and product development. F. 29-31. Mr. Matthew Tupper was the President of POM and managed the day-to-day operations of POM Wonderful, including the POM marketing team, prior to his retirement in 2011. F. 37-38, 40, 44. Thus, POM Wonderful and Roll Global are partnerships or corporations and Mr. and Mrs. Resnick and Mr. Tupper are individuals over which the FTC has jurisdiction.

POM Wonderful is currently in the business of selling fresh pomegranates and pomegranate-related products, including 100% pomegranate juice ("POM Juice") and pomegranate extract products known as POMx Pills and POMx Liquid ("POMx"). F. 6. Respondents began selling POM Juice in 2002. F. 5, 95. POM Juice is sold in supermarkets nationally and is a major seller in the premium juice category. F. 95. POM's U.S. Sales of 100% POM Juice, from September 2002 to November 2010, totaled approximately $247,739,776. F. 96. Respondents admit that "[t]he acts and practices of respondents alleged in this complaint have been in or affecting commerce, as 'commerce' is defined in Section 4 of the Federal Trade Commission Act." Answer ¶ 8. In addition, Respondents promoted the POM Products through various methods, including print advertisements in magazines, freestanding inserts in newspapers, out of home media such as billboards and bus shelters, posters in health clubs and doctors' offices, Internet websites, online banner advertisements, press releases, and television advertisements. F. 171. The acts and practices charged in the Complaint in this matter are in or affecting commerce within the meaning of the FTC Act, as amended. 15 U.S.C. § 41 *et seq*. Accordingly, the Commission has jurisdiction over the conduct challenged in the Complaint, pursuant to Sections 4 and 5 of the FTC Act. 15 U.S.C. §§ 44, 45.

C. Scope of Challenged Advertisements in this Case

1. "Advertisements"

The Complaint charges Respondents with violating Sections 5 and 12 of the FTC Act. Complaint ¶ 22. Section 5(a) of the FTC Act provides that "unfair or deceptive acts or practices in or affecting commerce are hereby declared unlawful." 15 U.S.C. § 45(a)(1). Section 12 of the FTC Act prohibits the dissemination of "any false advertisement" in order to

induce the purchase of "food, drugs, devices, services, or cosmetics." 15 U.S.C. § 52(a)(2). For the purposes of Section 12, "false advertisement" is defined as "an advertisement, other than labeling, which is misleading in a material respect[.]" 15 U.S.C. § 55(a).

The interrelation between Section 5(a) and Section 12 of the FTC Act was recently described by the Court of Appeals for the First Circuit as follows:

> [T]he FTC statute . . . provides that both "unfair or deceptive acts or practices in or affecting commerce" (15 U.S.C. § 45(a)(1)) and "disseminat[ing], or caus[ing] to be disseminated, any false advertisement . . . in or having an effect upon commerce" (15 U.S.C. § 52(a)) are "unlawful." 15 U.S.C. § 55 defines the term "false advertisement" as "an advertisement, other than labeling, which is misleading in a material respect . . . ." Given the strong similarity between the terms "deceptive" and "misleading," it is no surprise that sections 45 and 52 are sometimes applied in tandem as the basis for an FTC action against an alleged false advertiser; indeed, such a tandem reading is expressly allowed by 15 U.S.C. § 52(b).

FTC v. Direct Marketing Concepts, Inc., 624 F.3d 1, 7-8 (1st Cir. 2010).

Complaint Counsel in this case has challenged 43 items, which Complaint Counsel describes as "Respondents' ads and promotional pieces," as violating Sections 5 and 12 of the FTC Act. CCB at 19; CCB Appendix A, Tables 1 and 2 (hereafter, "CCB Appendix A"). Specifically, Complaint Counsel challenges print advertisements, newsletters, website advertising, and "public relations" promotional pieces, including press releases and press interviews. CCB Appendix A; *see also* CCB at 13. Complaint Counsel asserts that all of the challenged promotional pieces constitute "advertisements" within the scope of Section 12 of the FTC Act, 15 U.S.C. § 52, and deceptive acts or practices within the scope of Section 5 of the FTC Act, 15 U.S.C. § 45. CCB at 14.

Respondents contend that the following four challenged items do not constitute "advertisements" in violation of Sections 5 and 12 of the FTC Act[5]:

[5] Respondents also assert that an April 2009 discussion by Mrs. Resnick at USC's Annenberg School of Communication with Dean Ernest J. Wilson III, on "How to Uncover the Hidden Gems in Your Business," (CX0472 at 0002), does not constitute "advertising." RB at 92-95. Complaint Counsel responds that it does not challenge CX0472 at 0002 as deceptive under the FTC Act. CCRB at 43, n.41; CCRRFF ¶ 2546. Accordingly, an analysis of that exhibit is not undertaken. Except as described in this section, Respondents do not dispute that the other advertisements and promotional materials challenged in this case are "advertisements" for purposes of Sections 5 and 12 of the FTC Act.

1. Mrs. Resnick's November 2008 television appearance on *The Martha Stewart Show*, during which she shared personal recipes for a POMtini cocktail and Thanksgiving stuffing, (CX1426 (Compl. Ex. E-6));

2. Mrs. Resnick's February 2009 television appearance on *The Early Show*, during which she shared some marketing ideas for POM and FIJI Water, (CX0472 at 0003);

3. an interview of Mrs. Resnick in *Newsweek* magazine, dated March 20, 2009, discussing the economy, her business acumen, and promoting the sale of her book, *Rubies in the Orchard*, (CX1426 (Compl. Ex. F)); and

4. a June 2008 television interview of Mr. Tupper on FOX Business discussing the newest "hot" wave in foods – the pomegranate – and the pomegranate juice industry, (CX1426 (Compl. Ex. E-7)).

Respondents assert that these four interviews are not actionable under the FTC Act because they do not constitute "advertising." RB at 92. Complaint Counsel charges that these media appearances constitute "advertisements" within the scope of Section 12, CCB at 14, and contends that neither Section 5 nor Section 12 limits the FTC's reach to paid for advertising. CCRB at 44. Complaint Counsel further argues that the Commission's authority to regulate advertising is circumscribed only by its statutory authority and the limits of the commercial speech doctrine. CCRB at 44 (citing *In re R.J. Reynolds Tobacco Co.*, No. 9206, 111 F.T.C. 539, 542 (Mar. 4, 1988)).

The term "advertisement" is not defined in the FTC Act. However, in *R.J. Reynolds Tobacco*, the Commission made clear that it "understands[] [the term advertisement] to mean a notice or announcement that is publicly published or broadcast and is paid-for." *R.J. Reynolds Tobacco Co.*, 1988 FTC LEXIS 9, at *20. Complaint Counsel does not contend and has not pointed to any evidence to support a conclusion that Respondents paid anyone for their participation in the interviews or to allow them to speak about their products. *See* CCFF 570-577. Moreover, these media interviews were conducted by individuals working with *The Martha Stewart Show*, *The Early Show*, *Newsweek*, and FOX Business – entities other than the Respondents – and were not sponsored by Respondents. *See* F. 575-578. By contrast, the radio program that was found to constitute an "advertisement" in *Daniel Chapter One* ran on a radio network founded and funded by respondents, was titled "Daniel Chapter One HealthWatch,"

and was co-hosted by the individual respondents who were responsible for its content. *In re Daniel Chapter One*, No. 9329, 2009 FTC LEXIS 157, *21-22, 48, 163, 169-70 (Aug. 5, 2009) (Initial Decision), *aff'd*, 2009 FTC LEXIS 259 (Dec. 24, 2009).[6] *See also In re Witkower Press, Inc.*, 57 F.T.C. 145, 1960 FTC LEXIS 186, *157 (July 19, 1960) (finding "respondents' newspaper advertisements, book jackets and the television shows *sponsored by them* unquestionably constitute commercial advertising") (emphasis added).

Complaint Counsel has cited no cases where the Commission charged a respondent with violating Section 12 of the FTC Act based on public statements that were not paid for or sponsored by the respondent. *E.g.*, *In re R. J. Reynolds Tobacco Co.*, 1988 FTC LEXIS 9, *1 ("This case involves an advertisement, entitled 'Of Cigarettes and Science,' allegedly disseminated by Reynolds in the course of its business of manufacturing, advertising and selling cigarettes."); *FTC v. Nat'l Comm'n on Egg Nutrition*, 517 F.2d 485, 487-88 (7th Cir. 1975) ("[P]ublished and broadcast statements, in the form of paid advertisements, representing in substance that there is no scientific evidence that eating eggs increases the risk of heart disease or a heart attack . . . were advertisements within the meaning of that term as used in the [FTC] Act, because they were representations concerning the qualities of a product and promoting its purchase and use."); *Nat'l Comm'n on Egg Nutrition v. FTC*, 570 F.2d 157, 159 (7th Cir. 1977) (enforcing, in part, order imposed on industry association which "mounted an advertising and public relations campaign to convey the message that eggs are harmless and are needed in human nutrition").

The only case found involving statements made in a public speaking engagement, cited by Respondents and addressed by Complaint Counsel, is *FTC v. Koch*, 206 F.2d 311 (6th Cir. 1953). The court there, without addressing whether promotional materials must be paid for to constitute advertising, found that a challenged book, which "set forth primarily matter of opinion," did "not fall within the provisions of the statutes involved here." *Id.* at 317. The court explained:

[6] In a case it brought against a telemarketer, the FTC, as prosecutor, acknowledged the distinction between "an independent television program," and an infomercial, which was a "paid advertisement." *FTC v. Direct Marketing Concepts, Inc.*, 569 F. Supp. 2d 285, 304-05 (D. Mass. 2008).

> We also think that if these provisions of the statutes were construed so as to prohibit dissemination of such a book they would violate the First Amendment to the Constitution of the United States. It was not error for the Commission to consider this book and to quote extracts from it as throwing light upon the existence or non-existence of facts supporting the charge in the complaint, for the book was introduced by the respondents. However, we hold that it is not an advertisement covered by Sections 5, 12, or 15(a). We make a similar conclusion with reference to Dr. Koch's address before the College of Physicians and Surgeons of Quebec in 1939. If the record contained only these two exhibits, the Commission would not have jurisdiction in this proceeding.

Id.

Complaint Counsel has offered no authority to support a conclusion that publicly disseminated information that is not paid for or sponsored by Respondents constitutes "advertisements" within the scope of Section 12 of the FTC Act. Under the Commission's precedent regarding the statutory term "advertisement," the media appearances and interviews by Respondents in this case do not constitute "advertisements" within the scope of Section 12 of the FTC Act because they were not paid for or sponsored by Respondents. Therefore, the issue of whether the media interviews constitute constitutionally protected speech need not be, and is not, decided. Because the following exhibits – CX1426 (Compl. Ex. E-6) (Mrs. Resnick's November 2008 television appearance on *The Martha Stewart Show*); CX0472 at 0003 (Mrs. Resnick's February 2009 television appearance on *The Early Show*); CX1426 (Compl. Ex. F) (interview of Mrs. Resnick in *Newsweek* magazine); and CX1426 (Compl. Ex. E-7) (television interview of Mr. Tupper on FOX Business) – do not constitute "advertisements," this Initial Decision does not evaluate whether Respondents made any of the alleged claims in those exhibits. Moreover, the term, "Challenged Advertisements," as used herein, does not include these four media appearances and interviews.

2. "Food" or "drug"

The FTC Act defines the words "food" and "drug" broadly for purposes of Section 12. 15 U.S.C. § 55(b), (c) (defining "food" as, among other things, "articles used for food or drink for man," and defining "drug" as, among other things, "articles intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease in man"). Courts have

repeatedly held that these definitions of "food" or "drug" cover dietary supplements. *In re Daniel Chapter One*, 2009 FTC LEXIS 157, at *171-73 (Initial Decision) (citing *FTC v. Natural Solution, Inc.*, 2007 U.S. Dist. LEXIS 60783, at *11-12 (C.D. Cal. 2007); *FTC v. Nat'l Urological Group*, 645 F. Supp. 2d 1167, 1190 (N.D. Ga. 2008); *Direct Marketing*, 569 F. Supp. 2d at 300-03). POM Juice is a juice derived from pomegranate fruits. F. 57-58. POMx Pills and Liquid are extracts derived from the pomegranate. F. 67, 70-71, 89-90. Accordingly, each of the POM Products are a "food" or "drug" (F. 60, 61, 67, 70-71, 89-90) as defined in Section 12 of the FTC Act.

D. Overview of Applicable Law

An "advertisement is deceptive under the [FTC] Act if it is likely to mislead consumers, acting reasonably under the circumstances, in a material respect." *Kraft, Inc. v. FTC*, 970 F.2d 311, 314 (7th Cir. 1992) (citing *In re Thompson Medical Co.*, No. 9149, 104 F.T.C. 648, 788, 1984 FTC LEXIS 6, at *311 (Nov. 23, 1984), *aff'd*, 791 F.2d 189 (D.C. Cir. 1986)); *In re Cliffdale Assocs.*, No. 9156, 103 F.T.C. 110, 164-66, 1984 FTC LEXIS 71, at *104 (Mar. 23, 1984)). The determination of whether Respondents disseminated false advertisements in violation of the FTC Act requires a three-part inquiry: (1) whether Respondents disseminated advertisements conveying the claims alleged in the Complaint; (2) whether those claims were false or misleading; and (3) whether those claims are material to prospective consumers. *Kraft*, 970 F.2d at 314; *FTC v. Pantron I Corp.*, 33 F.3d 1088, 1095 (9th Cir. 1994); *Direct Marketing*, 569 F. Supp. 2d at 297. Each of these elements is addressed below.

E. Whether Respondents Disseminated Advertisements Conveying the Alleged Claims

1. General principles

"The Commission will deem an advertisement to convey a claim if consumers, acting reasonably under the circumstances, would interpret the advertisement to contain that message." *Thompson Medical*, 104 F.T.C. at 788; *Cliffdale Associates, Inc.*, 103 F.T.C. at 164-66; *Federal Trade Commission Policy Statement on Deception*, appended to *Cliffdale Associates, Inc.*, 103 F.T.C. 110, 1984 FTC LEXIS 71, at *176-77 (1984) (the "*Deception Statement*"); *In re Kraft, Inc.*, 114 F.T.C. 40, 1991 FTC LEXIS 38, at *10 (1991).

Advertising claims may be conveyed either expressly or impliedly. Express claims directly state the representation at issue. *Kraft*, 970 F.2d at 319 n.4; *Thompson Medical*, 104 F.T.C. at 788, 1984 FTC LEXIS 6, at *311; *Cliffdale*, 1984 FTC LEXIS 71, at *108 (1984). Because the claim is stated unequivocally, the statement itself establishes its meaning, and it is, therefore, reasonable to interpret such advertisement as making the alleged claim. *Thompson Medical*, 104 F.T.C. at 788, 1984 FTC LEXIS 6, at *311-12. Implied claims are made in an oblique or indirect way. *Kraft*, 970 F.2d at 319 n.4.

An interpretation of an advertisement may be reasonable even though it is not shared by a majority of consumers. *Kraft*, 1991 FTC LEXIS 38, at *14; *Deception Statement*, 1984 FTC LEXIS 71, at *177 n.20. A reasonable interpretation is one that would be shared by a "significant minority" of reasonable consumers. *Id.*; *In re Novartis Corporation*, No. 9279, 127 F.T.C. 580, 1999 FTC LEXIS 63, at *22-23 (May 13, 1999); *Kraft*, 1991 FTC LEXIS 38, at *14; *see also Telebrands Corp.*, 140 F.T.C. at 291 ("An ad is misleading if at least a significant minority of reasonable consumers are likely to take away the misleading claim.").

"[F]indings with respect to what representations are made in advertisements are factual. *See, e.g., Thompson Medical v. FTC*, 791 F.2d 189, 197 (D.C. Cir, 1986) (quoting from the FTC's brief); *AHP* [*American Home Products*], 695 F.2d [681,] 686 [(3rd Cir. 1982)]; *Beneficial Corp. v. FTC*, 542 F.2d 611, 617 (3d Cir. 1976)." *Removatron Int'l Corp. v. FTC*, 884 F.2d 1489, 1496 (1st Cir. 1989). In the instant case, it has been found as a fact that none of the Challenged Advertisements expressly (*i.e.*, unequivocally and directly) states that "drinking eight ounces of POM Juice daily" or "taking one POMx Pill daily," or "taking one teaspoon of POMx Liquid daily" (1) "treats," "prevents," or "reduces the risk" of "heart disease," including by reducing arterial plaque, lowering blood pressure, and/or improving blood flow to the heart, or that these effects are "clinically proven"; (2) "treats," "prevents," or "reduces the risk" of "prostate cancer," including by prolonging prostate-specific antigen doubling time, or that these effects are "clinically proven"; or (3) "treats," "prevents," or "reduces the risk" of erectile dysfunction, or that these effects are "clinically proven." F. 586. Thus, the issue is whether any of the Challenged Advertisements made the alleged claims implicitly; that is, whether a significant minority of consumers, acting reasonably in the circumstances, would interpret any

of the Challenged Advertisements to convey the claims alleged in the Complaint. The methodology used in making this factual determination is further explained in below.

a. Facial analysis

To determine whether an advertisement conveys an alleged claim, the first step is to examine the advertisement itself (a "facial analysis"). *Thompson Medical*, 1984 FTC LEXIS 6, at *313; *Cliffdale*, 1984 FTC LEXIS 71, at *108. A proper facial analysis requires "an evaluation of such factors as the entire document, the juxtaposition of various phrases in the document, the nature of the claim, and the nature of the transaction." *Deception Statement*, 103 F.T.C. 110, 1984 FTC LEXIS 71, at *172. The advertisement must be viewed as a whole "without emphasizing isolated words or phrases apart from their context." *Removatron*, 884 F.2d at 1496 (quoting *AHP*), 695 F.2d at 687; *see also FTC v. Sterling Drug, Inc.*, 317 F.2d 669, 674 (2d Cir. 1963) ("The entire mosaic should be viewed rather than each tile separately."). "But the Commission may not inject novel meanings into ads and then strike them down as unsupported; ads must be judged by the impression they make on reasonable members of the public." *In re Bristol-Meyers Co.*, No. 8917, 102 F.T.C. 21, 1983 FTC LEXIS 64, *249 (July 5, 1983), *aff'd*, 738 F.2d 554 (2d Cir. 1984).

"If, after examining the interaction of all the different elements in the ad, the Commission can conclude with confidence that an advertisement can reasonably be read to contain a particular claim, a facial analysis is sufficient basis to conclude that the advertisement conveys the claim. *See Kraft*, 114 F.T.C. at 121; *Thompson Medical*, 104 F.T.C. at 789." *In re Stouffer Foods Corp*, No. 9250, 118 F.T.C. 746, 1994 FTC LEXIS 196, at *9 (Sept. 26, 1994). However, the alleged claim must be reasonably clear or conspicuous from the face of the advertisement. *Kraft*, 970 F.2d at 319 (holding that the Commission can rely on its own reasoned analysis to determine what claims, including implied ones, are conveyed in a challenged advertisement "so long as those claims are reasonably clear from the face of the advertisement"); *accord Nat'l Urological Group*, 645 F. Supp. 2d at 1189 (holding that facial analysis is sufficient basis to find alleged claim was made if claims are "clear and conspicuous" or "apparent" on the face of the advertisement); *QT, Inc.*, 448 F. Supp. 2d at 958 ("Where

implied claims are conspicuous and reasonably clear from the face of the advertisements, extrinsic evidence is not required.").

If, after a facial analysis, it cannot be concluded with confidence that a particular advertisement can reasonably be read to contain a particular implied message, "the Commission will not find the ad to have made the claim unless extrinsic evidence allows the conclusion that such a reading of the ad is reasonable. *Kraft*, 114 F.T.C. at 121; *Thompson Medical*, 104 F.T.C. at 789." *Stouffer*, 1994 FTC LEXIS 196, at *10. In all cases, however, if extrinsic evidence has been introduced, that evidence "must be considered by the Commission in reaching its conclusion on the meaning of the advertisement." *Bristol-Meyers*, 1983 FTC LEXIS 64, at *247-48; *see Deception Statement*, 1984 FTC LEXIS 71, at *172-73; *Thompson Medical*, 1984 FTC LEXIS 6, at *324-25 (holding that because Thompson offered extrinsic evidence, the Commission was "obliged to consider it"). The Commission will carefully consider any extrinsic evidence that is introduced, taking into account the quality and reliability of the evidence. *See Kraft*, 114 F.T.C. at 122, 1991 FTC LEXIS 38, at *14; *Stouffer*, 1994 FTC LEXIS 196, at *10.

b. Extrinsic evidence

Extrinsic evidence includes, but is not limited to, "reliable results from methodologically sound consumer surveys." *Kraft*, 114 F.T.C. at 121, 1991 FTC LEXIS 38, at *13; *Cliffdale*, 103 F.T.C. at 164-66, 1984 FTC LEXIS 71, at *108-09. In determining whether a consumer survey is methodologically sound, the Commission will look to whether it "draws[s] valid samples from the appropriate population, ask[s] appropriate questions in ways that minimize bias, and analyze[s] results correctly." *Thompson Medical*, 104 F.T.C. at 790, 1984 FTC LEXIS 6, at *315. "The Commission does not require methodological perfection before it will rely on a copy test or other type of consumer survey, but looks to whether such evidence is reasonably reliable and probative. *See Bristol-Myers Co.*, 85 F.T.C. 688, 743-44 (1975). Flaws in the methodology may affect the weight that is given to the results of the copy test or other consumer survey." *Stouffer*, 1994 FTC LEXIS 196, at *10-11.

In addition to consumer surveys, another type of extrinsic evidence the Commission will look at is:

> evidence not specifically showing how consumers understood the advertisements at issue before us, but showing how consumers might ordinarily be expected to perceive or understand representations like those contained in the ads we are reviewing. For example, we might look at the dictionary definition of a word to identify the word's common usages. Or we might look at principles derived from market research, as expressed by marketing experts, which show that consumers generally respond in a certain manner to ads that are presented in a particular way, and presume that consumer reactions to a particular ad before us would be consistent with the general response pattern. Where we apply such marketing principles, we will derive them from research presented in references generally accepted as reliable in the field of marketing. Such references may be cited by marketing experts called to testify in the proceeding.

Thompson Medical, 1984 FTC LEXIS 6, at *315-16.

A third type of evidence the Commission "will consider if offered is the opinion of expert witnesses in the proceeding as to how an advertisement might reasonably be interpreted. For example, we might consider the opinion of a marketing expert who stated his or her view that consumers would interpret an advertisement in a particular manner. However, where the opinions voiced by experts are not adequately supported we ordinarily give them little weight." *Thompson Medical*, 1984 FTC LEXIS 6, at *316-17.

Whether examining the advertisement itself, extrinsic evidence, or both, the Commission considers the overall, common-sense, net impression made by the advertisement in determining whether the alleged claim may reasonably be ascribed to it. *FTC v. Tashman*, 318 F.3d 1273, 1283 (11th Cir. 2003); *Kraft*, 114 F.T.C. at 122; *Thompson Medical*, 104 F.T.C. at 790; *Stouffer* 118 F.T.C. 746, 1994 FTC LEXIS 196, at *11. Ultimately, "[t]he meaning of an advertisement, the claims or net impressions communicated to reasonable consumers, is fundamentally a question of fact. . . . This question of fact may be resolved by the terms of the advertisement itself or by evidence of what consumers interpreted the advertisement to convey." *Nat'l Urological Group*, 645 F. Supp. 2d at 1189; *QT*, 448 F. Supp. 2d at 957-58; *see also Removatron*, 884 F.2d at 1497 (holding that findings with respect to what representations are made in advertisements are factual).

c. Intent of the advertiser

Complaint Counsel urges that the evidence shows that Respondents intended to make the claims alleged in the Complaint. Citing *Telebrands Corp.*, 140 F.T.C. at 304 and *Novartis Corp.*, 127 F.T.C. at 683, Complaint Counsel argues that such intent constitutes extrinsic evidence that the Challenged Advertisements in fact conveyed the claims alleged. Respondents deny any intent to make the disease claims alleged in the Complaint. This Initial Decision need not, and does not, determine whether or not Respondents intended to make the disease claims alleged in the Complaint because the evidence is sufficient to conclude that Respondents disseminated advertisements containing the alleged claims, without regard to Respondents' alleged intent. *See* Section III.E.2, *infra.* Moreover, to the extent Complaint Counsel is arguing that advertiser intent alone can support interpreting an advertisement to contain an alleged claim, absent a facial analysis and/or other extrinsic evidence demonstrating that such claim was made, that argument is rejected, as more fully explained below.

It is well established that liability under Section 5 of the FTC Act does not require proof of intent to deceive. *FTC v. World Travel Vacation Brokers, Inc.*, 861 F.2d 1020, 1029 (7th Cir. Ill. 1988); *Chrysler Corp. v. FTC*, 561 F.2d 357, 363 & n.5 (D.C. Cir. 1977); *Kraft*, 114 F.T.C. at 121. Similarly, it is no defense to an action for deceptive advertising that the advertiser did not intend to make the claim alleged. *World Travel Vacation Brokers*, 861 F.2d at 1029; *FTC v. Sabal*, 32 F. Supp. 2d 1004, 1007 (N.D. Ill. 1998). It would be incongruous, at best, if intent could be used as a sword but not a shield.

Moreover, the law is clear that the goal of advertising interpretation is to determine whether reasonable consumers would interpret an advertisement to convey an alleged claim. *See, e.g., Thompson Medical*, 104 F.T.C. at 788, 1984 FTC LEXIS 6, at *311 (holding that an advertisement conveys a claim if consumers, acting reasonably under the circumstances, would interpret the advertisement to contain that message); *Nat'l Urological Group*, 645 F. Supp. 2d at 1189 (question of advertisement's meaning "may be resolved by the terms of the advertisement itself or by evidence of what consumers interpreted the advertisement to convey"). Complaint Counsel's suggested approach is contrary to law because it would have the analysis of the Challenged Advertisements focus on the perspective of the advertiser, based

on the intent of a respondent, rather than focus on the perspective of the audience, *i.e.*, the consumer who sees or hears the advertisement. It is also noteworthy that, while extrinsic evidence of consumer interpretation is appropriate to consider, advertiser "intent" is not mentioned among the types of extrinsic evidence that is considered in determining how consumers would interpret an advertisement. As the Commission explained in the *Deception Statement*, extrinsic evidence "can consist of expert opinion, consumer testimony (particularly in cases involving oral representations), copy tests, surveys, *or any other reliable evidence of consumer interpretation*." 1984 FTC LEXIS 71, at *173 n.8 (emphasis added); *see also Thompson Medical*, 1984 FTC LEXIS 6, at *315-16.

In *Telebrands*, upon which Complaint Counsel relies, the Commission held: "Based on our own review of the challenged advertising, we conclude that consumers would reasonably interpret respondents' Ab Force ads to mean that the device (1) causes loss of weight, inches, or fat; (2) creates well-defined abdominal muscles; and (3) is an effective alternative to regular exercise . . . ." 140 F.T.C. at 301. The Commission further held that "other considerations," including "ample evidence that respondents intended to convey the challenged claims," provided further support for the conclusions of the facial analysis. *Telebrands Corp.*, 140 F.T.C. at 304. Similarly, in *Novartis*, 127 F.T.C. at 683, also cited by Complaint Counsel, the Commission stated that "evidence of intent to make a claim may support a finding that the claims were indeed made." The Commission held, however, similar to *Telebrands*, that the challenged claim was "plain from a facial analysis of the challenged ads alone" and that the "extrinsic evidence" indicating respondent intended to make the challenged claim "provide[d] additional support for [the] finding that the superiority claims" were made. *Novartis*, 127 F.T.C. at 683-84. Indeed, in *Novartis*, "the issue of whether the claim was made [was] not a close one." *Id.* at 683.

Thus, while *Telebrands* and *Novartis* indicate that evidence of an advertiser's intent to make a claim can bolster or confirm a finding that a claim was in fact made, the law does not indicate that advertiser intent alone is a valid basis for finding that a claim was made, absent a facial analysis and/or other extrinsic evidence demonstrating that such claim was made. In the instant case, the evidence is sufficient to conclude that Respondents disseminated

advertisements containing the alleged claims, and it is, therefore, not necessary to determine, or rely upon, Respondents' alleged intent.

d. Target audience

Complaint Counsel argues that the Challenged Advertisements must be interpreted from the perspective of the target audience for POM Product advertising which, according to Complaint Counsel, consists of "consumers concerned about preventing or reducing their risk of illness." CCB at 18. *See Telebrands*, 140 F.T.C. at 291 (stating that "[i]f an ad is targeted at a particular audience, the Commission analyzes ads from the perspective of that audience" (citing *Deception Statement*, 1984 FTC LEXIS 71, at *178-79)); *Thompson Medical*, 1984 FTC LEXIS 6, *321 n.15 (recognizing precedent that persons with health-related problems can be a target audience). In support of the argument that consumers concerned about preventing or reducing their risk of illness constitute a "target audience" for purposes of interpreting the Challenged Advertisements, Complaint Counsel relies principally on certain "creative briefs" prepared by POM Marketing and provided to the in-house advertising agency, Fire Station, which served to guide Fire Station's work in developing advertising for POM Juice, POMx Pills and Pomwonderful.com. CCFF 299-308; CX0409; F. 145-152. These creative briefs include a section titled, "target audience," which, for the purpose of these documents, meant the audience to whom the advertisement would appeal. F. 148, 175. Complaint Counsel also notes that Respondents placed advertising in health-oriented magazines, such as *Prevention* and *Men's Fitness*, in health clubs, on prescription drug bags, and on medical-oriented websites (*e.g.*,WebMD). CCB at 19.

Respondents dispute that the creative briefs or POM's alleged focus on health-conscious consumers are probative in this matter, and further note that the POM Products were advertised in a wide variety of local and national publications that are not devoted to health. RRB at 49-50. Respondents do not appear to dispute, however, that health-conscious consumers are among POM's target consumers.

The creative briefs, as well as the fact that Respondents sought to reach health-conscious consumers by placing advertising in such magazines as *Health Magazine*, *Men's Health*, and *Men's Fitness*, and in health clubs, on prescription drug bags, and on medical-

oriented websites (*e.g.*,WebMD), show that Respondents endeavored to reach educated, affluent, and health-conscious individuals. F. 171, 179, 181.[7] Although at least one creative brief for POM Pills specifically included within the "target audience," among others, middle-aged men or seniors who are concerned or "scared" about prostate cancer, *e.g.*, F. 178, Complaint Counsel's extrapolation from such evidence that POM's target group was "consumers concerned about preventing or reducing their risk of illness" in general is unpersuasive and is, therefore, rejected. Moreover, the evidence shows that Respondents' advertising was also directed to a more general audience. F. 169-171. In particular, the evidence shows that the Challenged Advertisements were disseminated in a wide variety of locally and nationally distributed publications, well beyond health-oriented publications, including the *Chicago Tribune*, *Details*, *Rolling Stone*, I*nStyle*, *Town and Country*, *Fortune*, the *New York Times*, *Discover*, *Popular Science*, and *Time*. F. 169-170.

In any event, even if Respondents' advertising sought to appeal to educated, affluent, and health-conscious individuals, this conclusion has no practical utility in the instant case. As the Commission stated in *Thompson Medical*, with respect to "target audiences": "[A]lmost all advertising is targeted at some demographic group, such as farmers, housewives, or residents of a particular area. This alone does not mean that we apply a standard different from our customary one." *Thompson Medical*¸1984 FTC LEXIS 6, *321 n.15. The term, "target audiences," for purposes of interpreting advertising, refers to "special audiences who as a group have a greater or lesser capability to recognize deceptive advertising than ordinary members of the adult population or a distinctive reaction to particular advertising claims[.]" *Id.* Complaint Counsel does not cite to any evidence in the record indicating how, if at all, "educated, affluent, health-conscious consumers" would be more capable or more likely than ordinary consumers to infer the alleged disease claims from the Challenged Advertisements. *See* CCB at 18-19. In fact, what little evidence there is on the characteristics of this group indicates, if anything, that educated, affluent, health-conscious consumers are more likely to be more discerning and careful readers of an advertisement, and more likely to better understand an advertisement, F. 521-522, all of which weigh against a conclusion that such consumers would be more susceptible to inferring disease claims.

[7] Complaint Counsel's assertion that advertisements were distributed in the reception area of urologists' offices is not supported by the evidence cited by Complaint Counsel. *See* CCFF 226.

In addition, the only evidence of a "distinctive reaction to particular advertising claims" among educated, affluent, health-conscious consumers is the opinion of Complaint Counsel's rebuttal expert on, *inter alia*¸ advertising and consumer behavior, Dr. David Stewart (*see* F. 285, 288), that such consumers are more likely to be "more attentive to health claims" and more likely to "draw pragmatic inferences" about the benefits of the POM Products. F. 517. However, Dr. Stewart defined such "pragmatic inferences" as meanings that are neither expressed in the advertisements, nor implied by the advertisements, and may or may not even follow, logically. F. 517. Finally, as Dr. Stewart also noted, consumers are not simply passive recipients of messages, but are active processors, and in determining how a consumer would interpret an advertisement, it is critical to consider prior beliefs, prior knowledge, what the consumer may regard as relevant, how the consumer will process the information, and generally what the consumer brings to the viewing situation. F. 542-543. Complaint Counsel introduced no evidence on these considerations cited by Dr. Stewart.

In summary, while the evidence shows that Respondents' advertising may have been geared, at least in part, toward educated, affluent, health-conscious consumers, Complaint Counsel has failed to prove that this group would be more likely to interpret, or in fact did interpret, the Challenged Advertisements differently than ordinary consumers, or in what manner that group would do so. Accordingly, to meaningfully analyze the Challenged Advertisements from the perspective of the asserted target group would require unacceptable speculation, because what constitutes such perspective, or how such perspective would be applied to the group's interpretation of advertising, has not been proven.

2. Respondents disseminated advertisements making the claims alleged in the Complaint

a. Summary of findings

As noted above, the determination of what claims are made in an advertisement is a factual one. *Removatron Int'l Corp.*, 884 F.2d at 1496; *AHP*, 695 F.2d at 686; *Nat'l Urological Group*, 645 F. Supp. 2d at 1189; *QT*, 448 F. Supp. 2d at 957-58. In *Thompson Medical*, the Administrative Law Judge ("ALJ") described the approach that he employed in making such determination as follows:

> In determining the meaning of individual advertisements, I have primarily relied on my knowledge and experience to determine what impression or impressions an advertisement as a whole is reasonably likely to convey to a consumer. When my initial determination is confirmed by the expert testimony of complaint counsel or respondent, I rested. When my initial determination disagreed with that of expert testimony, which was often conflicting, I reexamined the advertisement in question, and further considered other record evidence such as copy tests and other consumer research before reaching a final determination. I have not relied on such extrinsic evidence when, after careful study and reflection, I found it to be unpersuasive and contrary to the weight of evidence.

Thompson Medical, 1984 FTC LEXIS 6, *82-83 (Initial Decision).

Employing and applying the above methodology, based upon a facial analysis and having considered all applicable extrinsic evidence, this Initial Decision finds that certain Challenged Advertisements disseminated by Respondents made the claims alleged in the Complaint. F. 579-584. Therefore, Complaint Counsel has satisfied the first element of its deceptive advertising claim. *See Kraft*, 970 F.2d at 314. Detailed findings of fact are set forth in Section II.D, *supra* and summarized, as applicable, in the following analysis. *See also* Initial Decision Appendix (containing advertisements found to have made the alleged claims). The reasoning for these findings is further explained below. The evidence upon which Respondents rely to argue that none of the Challenged Advertisements should be interpreted as making the challenged claims, including the opinions of their linguistics expert, Dr. Ronald Butters (F. 259-263), have been fully considered. F. 579. With respect to those Challenged Advertisements found to have made the alleged claims, such evidence fails to outweigh the evidence demonstrating that the claims were in fact made, including the overall net impression of the advertisements themselves. F. 584. Respondents' arguments are further addressed in Section III.E.2.f, *infra*.

As to those of the Challenged Advertisements that were not found to have made the challenged claims, this Initial Decision finds that such claims were not reasonably clear or conspicuous on the face of the advertisements, and that considering the interplay of all the elements of such advertisements, it could not be concluded with confidence, on the face of the advertisements alone, that a significant minority of reasonable consumers would interpret the

advertisements to make the claims alleged in the Complaint. F. 585, 587. Among other reasons, these advertisements: do not mention heart disease, prostate cancer, or erectile dysfunction; use vague, non-specific, substantially qualified, and/or otherwise non-definitive language; use language and/or images that, in the context of the advertisement, are inconsistent with the alleged claim; and/or do not draw a connection for the reader, such as through associated explanatory text, between health benefits, or study results, and effectiveness for heart disease, prostate cancer, or erectile dysfunction. F. 588; *see also* F. 585. *See In re Sterling Drug, Inc.*, No. 8919, 102 F.T.C. 395, 1983 FTC LEXIS 66, at *477-78 (July 5, 1983) (holding that claim that Bayer aspirin relieved tension was not apparent in advertisement depicting Bayer relieving a headache caused by tension). In the context of these advertisements, the nature of the transaction, *i.e.*, the purchase of a food product, or a supplement derived therefrom, as opposed to the purchase of a drug (F. 57, 65-68, 70-72), further weighs against interpreting such advertisements as making the alleged claims. *See Deception Statement*, 103 F.T.C. 110, 1984 FTC LEXIS 71, at *172 (noting that in evaluating whether implied claim was made, the Commission will consider, among other factors, the nature of the transaction). To this extent, the facial analysis is confirmed by the opinion of Respondents' expert, Dr. Butters, that an advertisement promoting the consumption of food is far less likely to be interpreted by a reasonable consumer as conveying a treatment claim, than an advertisement promoting a drug. F. 491-492.

Furthermore, as to those of the Challenged Advertisements, described above, for which the alleged claims are not reasonably clear from a facial analysis, the weight of the applicable extrinsic evidence also fails to demonstrate that such advertisements would be reasonably interpreted to make the claims alleged in the Complaint. F. 589; *see also* F. 585. For example, Complaint Counsel relies on the Bovitz Survey, a 2009 study of billboard headlines, commissioned by Respondents to assess the impact of their advertising campaigns. F. 544-548; *see* CCFF 588. In particular, Complaint Counsel relies on the fact that forty-three percent of survey respondents in POM's general target audience and forty-eight percent of those survey respondents that were POM Juice users, when shown an advertisement picturing a POM Juice bottle saying, "I'm off to save PROSTATES!" and a sub-headline "The Antioxidant Superpower," said the advertisement's main idea was "good for prostates." F. 557. However,

this vague and general interpretation is not persuasive evidence that a significant minority of reasonable consumers would draw the further inference, when viewing an advertisement containing such language and imagery, that the POM Products treat, prevent, or reduce the risk of "prostate cancer." *See also* F. 524 (In linguistic terms, "I'm off to save prostates" would not imply that a product will protect or rescue one from disease). Similarly, Complaint Counsel relies on the fact that fourteen percent of survey respondents in POM's general target audience, when shown an advertisement picturing a POM Juice bottle inside a blood pressure cuff, with the headline "Decompress" and a sub-headline "POM Wonderful Pomegranate Juice[ ] The Antioxidant Superpower," said the advertisement's main idea was "helps/lowers blood pressure." F. 555. This vague and ambiguous conclusion is not enough to support a finding that a significant minority of reasonable consumers would draw the further inference, when viewing an advertisement containing this language and imagery, that the POM Products treat, prevent, or reduce the risk of "heart disease." None of the survey respondents in the Bovitz Survey answered that the main idea of these billboard advertisements was prevention, risk reduction, or treatment of any specific disease. F. 555-558, 572. The most common "main idea" communicated (at least 90%) was that POM Juice had general health benefits. F. 572. Moreover, the Bovitz Survey examined only advertisement headlines and images, as shown on the billboard advertisements. F. 547. Thus, the Bovitz Survey did not examine the headlines, images and text, as shown on any of the Challenged Advertisements. F. 547. As Complaint Counsel's rebuttal expert, Dr. Stewart, acknowledged, other text that is added in a lengthier print advertisement might modify a message communicated by the image and headline of a billboard. F. 561. For this reason as well, the findings of the Bovitz Survey are entitled to little weight.

Complaint Counsel also places too much weight on opinions that Complaint Counsel obtained from Dr. Butters on cross-examination that phrases such as "prostate health" and "heart health" would be interpreted to mean the absence of disease. F. 538-539. While the meaning of "health" may well include the absence of disease, the meaning of "health" is surely not so limited as to include only treatment, prevention or reduction of the risk of disease, and to the extent Dr. Butters opined as such, that opinion is rejected.

Accordingly, because, as to certain Challenged Advertisements, the alleged claims are not reasonably clear or conspicuous on the face of the advertisements themselves, and because the applicable extrinsic evidence of the meaning of those advertisements is insufficient or unpersuasive, this Initial Decision finds that the evidence fails to demonstrate that such advertisements made the claims alleged in the Complaint. F. 587-590; *see also* F. 585. *See Sterling Drug*, 1983 FTC LEXIS 66, at *477-78 (stating Commission was "unwilling in the absence of extrinsic evidence to find that consumers infer from these ads that Bayer will relieve tension" where such claim was "not apparent . . . from a careful examination of the ads"); *Thompson Medical*, 104 F.T.C. at 339-40 (holding that Commission "cannot find the ad to convey" implied claim that Aspercreme contained aspirin where Commission was unable to "conclude with adequate confidence" based on the advertisement itself "whether or not one message conveyed to consumers" was that Aspercreme contained aspirin and where extrinsic evidence was insufficient to find such claim). It is worth emphasizing that this is not a finding that the advertisements *do not* convey the alleged claims, but merely that the evidence was insufficient to conclude that they do. As the Commission stated in *Thompson Medical*:

> Here we merely say that complaint counsel failed to provide extrinsic evidence demonstrating that [the advertisements] created a net impression which did [make the challenged claim]. We do not attempt to use our judgment to reach any substantive conclusion. Where the implied meanings of an advertisement are unclear absent extrinsic evidence, our expertise is no more reliable in permitting conclusions that an interpretation is unreasonable than that it is reasonable.

Thompson Medical, 1984 FTC LEXIS 6, at *371.

To be clear, Complaint Counsel has demonstrated, based on a number of the Challenged Advertisements, that Respondents *did*, in fact, disseminate some advertisements making the claims alleged in the Complaint. It is not necessary to find that all the Challenged Advertisements made the alleged claims in order to warrant injunctive relief for deceptive advertising. *Bristol-Meyers*, 1983 FTC LEXIS 64, at *250-51 (disagreeing with ALJ findings that certain advertisements made the challenged claims, and stating: "Although we find a smaller number of violative ads than did the ALJ, there is certainly an adequate number to support the order . . . "); *Fedders Corp.*, No. 8932, 85 F.T.C. 38, 71-72, 1975 FTC LEXIS 282,

*72 (Jan. 14, 1975) ("The Commission has previously issued orders in cases involving no more than one or a few deceptive advertisements.").

b. "Establishment" claims vs. "efficacy" claims

Advertisements that claim a certain type or level of support are considered "establishment claims." *Thompson Medical*, 791 F.2d at 194. An establishment claim includes a claim that the effectiveness of a product has been shown by clinical proof. *Removatron*, 884 F.2d at 1492 n.3. As the Commission stated in *Thompson Medical*: "There is no conceptual or practical reason to single out such claims [ ] for special treatment. They are but one example of an express or implied claim that an advertiser possesses a particular level of substantiation." 1984 FTC LEXIS 6, at *387 n.59; *see also Bristol-Meyers*, 1983 FTC LEXIS 64, at *253 (noting that a claim of clinical proof can be express or implied). A claim that a product is effective, without expressly or impliedly representing a particular level of support, is not an establishment claim, but is an efficacy claim. *Removatron*, 884 F.2d at 1491 n.3.

The majority of the Challenged Advertisements that have been found herein to have made the claims alleged in the Complaint represented that clinical studies supported the claimed effectiveness of the POM Products, and, therefore, are referred to herein as "establishment claims." The remainder of the Challenged Advertisements found to have made the claims alleged in the Complaint made non-establishment, "efficacy" claims.

c. Heart disease claims

The evidence shows that Respondents disseminated advertisements that impliedly represented that the POM Products treat, prevent, or reduce the risk of heart disease and, in many of these same advertisements, are clinically proven to do so, by lowering blood pressure, reducing arterial plaque, and/or increasing blood flow to the heart. F. 580, 583. Respondents made these claims indirectly and obliquely, typically by presenting, through words and images, a logical syllogism that: free radicals cause or contribute to heart disease; the POM Products contain antioxidants that neutralize free radicals; and, therefore, the POM Products are effective for heart disease. F. 294-295, 301-303, 348, 374, 394-396, 398, 407, 414, 444, 452-453, 460-462. Against this background, many of the advertisements further state or represent that the

POM Products have been shown in one or more clinical, medical, or scientific studies, to reduce plaque, lower blood pressure, and/or improve blood flow to the heart, in a context where it is readily inferable that the referenced study results involve heart disease risk factors and, therefore, constitute clinical support for the effectiveness claim. F. 295, 301, 303, 349, 373, 376, 379, 395-397, 400, 407, 414, 420.

For example, in April 2009, the "Cardiovascular" section of the health benefits webpage of pomwonderful.com had a "read more" link that took the viewer to text stating that "heart disease" is a leading killer of men and women in the United States, that "atherosclerosis," which is defined for the reader as too much "plaque," is a leading factor in "heart attacks," and further describes the role of antioxidants in reducing LDL (defined as "bad" cholesterol) oxidation. F. 373-374. The "read more" links from this page connect to a 2005 study on the effect of pomegranate juice on myocardial perfusion published in the *American Journal of Cardiology*; a 2004 study on reduction of carotid intima-media thickness, blood pressure (CIMT-BP) and LDL oxidation; and a 2001 study on reduction of systolic blood pressure. F. 374. The "Cardiovascular" section of the health benefits webpage of pomwonderful.com also advised the reader that POM Juice was shown in one study to improve blood flow to the heart in "coronary heart disease" "patients"; and, in another study, to reduce arterial plaque. F. 373. In this context, asserting clinical proof of a beneficial effect on the underlying conditions of the body (blood flow, arterial plaque, CIMT-BP, and LDL) would reasonably be interpreted as representing clinical proof of effectiveness for heart disease. F. 373-375, 381.

Another example is the Heart Newsletter (CX1426 (Compl. Ex. M); F. 346-350), which states or represents that (1) "58.8 million Americans suffer from some form of heart disease"; (2) supplementation with antioxidants is "your ally" in fighting "heart disease"; (3) antioxidants fight free radicals and help prevent cell and tissue damage that lead to "disease"; (4) POM Juice and POMx have polyphenol antioxidants, which are unique and superior; and (5) POMx provides antioxidant supplementation without adding the calories of POM Juice. F. 348. The Heart Newsletter further states that POM's "scientists have found" that POM Juice "may help counteract factors leading to arterial plaque buildup, as well as inhibit a number of factors associated with heart disease." F. 349. The text then proceeds to describe these findings, from

"new research," including (1) a "pilot" study involving 19 "patients" with "clogged arteries" which found a "30% decrease in arterial plaque" among those drinking eight ounces of POM Juice daily; and (2) a study involving 45 "patients" with "impaired blood flow to the heart," showing "17% improved blood flow" among those who consumed eight ounces of POM Juice daily. F. 349. By connecting POM-provided antioxidants to benefits for "heart disease," and by further connecting the study results to heart disease risk factors, the advertisement implies that the POM Products are effective for heart disease, and that such effectiveness is based upon clinical testing. F. 350. *See also* F. 301 (CX0029 print advertisement representing, *inter alia*, that "heart attacks are due to . . . plaque in the arteries" and "scientific research shows" that POM Juice prevents LDL oxidation and reduces plaque); F. 414 (CX0473 Ex. E-1 (pomegranatetruth.com)), representing that "atherosclerosis," which is defined for the reader as too much "plaque," is a leading factor in "heart attacks" and linking to research studies on the effects of pomegranate juice on myocardial perfusion, reduction of carotid intima-media thickness, blood pressure, and LDL oxidation); F. 339-340, 419-420.

The Challenged Advertisements that were not found to have made establishment claims, as alleged by Complaint Counsel, but which were found to have made heart disease efficacy claims only, either do not reference any clinical testing or refer to clinical testing in such a way, and in such context, that it cannot be concluded with confidence that a significant minority of reasonable consumers would take away the message that the efficacy claim is "clinically proven." *See* F. 440-448 (CX0031 ("Floss your arteries")); F. 456-468 (CX0034 ("Amaze your cardiologist")). For example, CX0031 represents that "clogged arteries lead to heart trouble," free radicals cause "artery clogging plaque," and that drinking eight ounces of POM Juice a day "can reduce plaque up to 30%!*" F. 444. While this advertisement makes an efficacy claim, the only reference to any scientific support is in very small print, at an asterisk at the bottom of the page, which states: "Aviram, M. Clinical Nutrition, 2004. Based on a clinical pilot study." F. 447. CX0034 is a similar advertisement. F. 466.

As the Commission stated in *Bristol Meyers*, not "every reference to a test necessarily gives rise to an establishment claim. The key, of course, is the overall impression created by the ad." 1983 FTC LEXIS 64, at *253. In CX0031 and CX0034, this small print, single reference to a study, particularly in the context of a qualified assertion that POM Juice "can"

reduce plaque, is insufficient to conclude with confidence that a significant minority of reasonable consumers would interpret these advertisements to be claiming that POM Juice is "clinically proven" to be effective for heart disease. F. 446-447, 466-467. Moreover, the applicable extrinsic evidence does not support a conclusion that consumers would interpret these advertisements to be making a "clinically proven" claim. F. 579, 585. Accordingly, the evidence fails to demonstrate that these advertisements, which do make efficacy claims, convey the additional message that POM Juice's efficacy is demonstrated by clinical proof. F. 448, 468, 585.

d. Prostate cancer claims

The evidence shows that Respondents disseminated advertisements that impliedly represented that the POM Products are clinically proven to treat, prevent, or reduce the risk of prostate cancer, by prolonging prostate-specific antigen ("PSA") doubling time. F. 581. These advertisements typically communicate the claim by juxtaposing statements and representations that prostate cancer is a leading cause of death in men; antioxidants, such as those provided by the POM Products, may help prevent cancer; that PSA is an indicator of prostate cancer; that PSA doubling time is an indicator of prostate cancer progression; and that the POM Products have been shown in clinical testing to slow PSA doubling time. F. 310-318, 332, 334-336, 352-353, 371, 381, 389-392, 398, 400-405, 409, 429-430. Thus, similar to those advertisements found herein to have made heart disease claims, these advertisements specifically refer to prostate cancer, and connect both POM-provided antioxidants, and the study results, to effectiveness for prostate cancer. *Id.*

For example, CX1426 (Compl. Ex. I) (POMx Pill package insert) juxtaposes statements and representations that: (1) antioxidants fight free radicals, which may be linked to "serious health threats like cancer . . ."; (2) "Prostate cancer is the most commonly diagnosed cancer . . . and the second-leading cause of cancer death" among men in the United States; (3) POMx is a "time pill" because "stable levels of PSA," which is defined for the reader as "prostate-specific antigens," "are critical for men with prostate cancer," and "[p]atients with quick PSA doubling times are more likely to die from their cancer"; (4) "[a]ccording to a UCLA study of 46 men age 65 to 70 with advanced prostate cancer, drinking an 8oz glass of POM Wonderful 100%

Pomegranate Juice every day slowed their PSA doubling time by nearly 350%. 83% of those who participated in the study showed a significant decrease in their cancer regrowth rate"; and (5) "basic studies" indicate POMx may have the same effects as POM Juice. F. 332, 334.

Similarly, the Prostate Newsletter (CX1426 (Compl. Ex. N)) states and represents that: (1) "Prostate cancer is the second leading cause of cancer related death in men in the United States . . . "; (2) "risk factors" for prostate cancer include "diet," and advises a diet that includes, among other things, "fruits rich in antioxidants"; (3) a "preliminary UCLA medical study" on 46 men treated for prostate cancer, showed that a majority of those consuming eight ounces of POM Juice daily "experienced a significantly extended PSA doubling time. Doubling time is an indicator of prostate cancer progression – extended doubling time may indicate slower disease progression"; testing on "patient" blood serum showed a decrease in "cancer cell proliferation," and "increase in cancer cell death"; (4) in another study, "in vitro laboratory testing at UCLA showed that POMx significantly decreased human prostate cancer cell growth and increased cancer cell death"; and (5) POMx has the same active ingredients in POM Juice. F. 352-353. *See also* F. 311 (regarding CX0314, CX0372, CX0379, CX0380, representing, *inter alia*, that according to a published study on men treated for prostate cancer, those consuming POM Juice "experienced significantly slower" "PSA doubling times," and that PSA "is a biomarker that indicates the presence of prostate cancer. 'PSA doubling time' is a measure of how long it takes for PSA levels to double. A longer doubling time may indicate slower progression of the disease"); F. 371, 380-381, 403-404, 409, 430.

e. Erectile dysfunction

The evidence demonstrates that Respondents disseminated advertisements that impliedly represented that the POM Products are clinically proven to treat, prevent or reduce the risk of erectile dysfunction ("ED"). F. 582. Respondents disseminated print advertisements that stated and represented, for example, that: (1) the superior antioxidants in the POM Products protect against free radicals, which can damage the body; (2) powerful antioxidants enhance the actions of nitric oxide in vascular endothelial cells, showing potential for management of "ED"; and (3) a preliminary study on "erectile function" showed that men who consumed POM Juice reported "a 50% greater likelihood of improved erections," as compared

to a placebo. F. 323-324. Similarly, in April 2009, the "Erectile Function" section of the health benefits webpage on pomwonderful.com reported that a 2007 "pilot" study, published in the *Journal of Impotence Research*, involving 61 male subjects with "mild to moderate erectile dysfunction," showed that those men drinking eight ounces of POM Juice daily for four weeks were "50% more likely to experience improved erections." F. 372. *See also* F. 380-381, 433-437. Presenting a study on "erectile function" showing "improved erections" is reasonably read to imply effectiveness for erectile dysfunction, particularly when juxtaposed to an express reference to management of "ED." F. 323-325. *See also* F. 408 (response to the FAQ "Erectile Dysfunction" "Can pomegranate juice benefit men with erectile dysfunction?" stating, "Initial results linking POM Wonderful 100% Pomegranate Juice and erectile performance are promising. In a soon-to-be-published clinical study on men with erectile dysfunction, the group who consumed 8oz. of POM Juice daily experienced better erectile performance than the group who drank a placebo"). Moreover, as Respondents' expert, Dr. Butters, acknowledged, contemporary speakers of American English could interpret the phrase "erectile function" to relate to the ability of men to achieve and maintain erections. Erectile function and the absence of erectile dysfunction are closely related. F. 537.

f. Respondents' arguments as to advertisement interpretation

As noted above, the determination of whether any of the Challenged Advertisements conveyed the implied claims alleged in the Complaint is a question of fact. *Removatron*, 884 F.2d at 1496; *AHP*, 695 F.2d at 686; *Nat'l Urological Group*, 645 F. Supp. 2d at 1189; *QT*, 448 F. Supp. 2d at 957-58. As to those Challenged Advertisements found herein to have made the challenged claims, this factual question has been resolved against Respondents. This determination is based upon all the evidence, including full consideration and weighing of all the evidence, inferences, and arguments raised by Respondents in opposition to finding that the challenged claims were made. As to those Challenged Advertisements found herein to have made the challenged claims, Respondents' opposing evidence, inferences and arguments, have been rejected as unpersuasive, unsupported, or otherwise outweighed by other evidence, including the overall net impression of the advertisements themselves. Respondents' contentions that require further elaboration are discussed below.

Respondents contend that the challenged claims are not reasonably clear or conspicuous on the face of any of the Challenged Advertisements, and that Complaint Counsel failed to present any reliable extrinsic evidence showing that reasonable consumers would interpret the advertisements to make the alleged claims. Therefore, Respondents argue, Complaint Counsel failed to meet its burden of proving that the challenged claims were made. *See, e.g.*, RB at 71-74. Respondents accurately assert that Complaint Counsel did not offer a copy test on the Challenged Advertisements. Complaint Counsel also did not proffer any expert opinion or analysis of the Challenged Advertisements to demonstrate that reasonable consumers would interpret the Challenged Advertisements as making the alleged claims. F. 513. As to those Challenged Advertisements for which the alleged claims were not reasonably clear or conspicuous on the face of the advertisements alone, *see* F. 587-588; *see also* F. 585, such a copy test or expert analysis provided by Complaint Counsel might have made a material difference. However, the failure of Complaint Counsel to proffer such extrinsic evidence is not fatal to Complaint Counsel's case because, for those Challenged Advertisements found to have made the alleged claims, the claims are, in fact, apparent from the overall, common-sense, net impression, of the words and images of the advertisements themselves. F. 293, 299, 310, 325, 331, 338, 346, 351, 368, 387, 411, 417, 422, 429, 433, 443, 455, 463, 474. Moreover, Complaint Counsel adduced some extrinsic evidence relevant to consumer interpretation, albeit on cross-examination and rebuttal, which has also been considered. F. 579; *see, e.g.*, F. 527, 533-537, 540-541.

Respondents further contend that the Challenged Advertisements must be interpreted in the context of the purchase of food, or a food-derived product, as opposed to the purchase of a drug, and that when viewed from this perspective, the advertisements are not reasonably interpreted, including by a facial analysis alone, as conveying the claim that the POM Products "prevent," "treat," or "reduce the risk" of any disease. *See, e.g.*, RB at 72, 78-82. Respondents argue in the alternative that, to the extent consumers would interpret the Challenged Advertisements as claiming that the POM Products "may help prevent" or "reduce the risk" of heart disease, prostate cancer or erectile dysfunction, it is in the same sense that broccoli, a healthy diet, or exercise "reduce the risk" of disease, and not in the sense of a drug, with a single target of action. *Id.*; *see also* RRB at 20-22. Further, Respondents argue that to the

extent reasonable consumers would interpret the Challenged Advertisements as making a "treatment" claim, it would not be in the sense of a substitute for medical treatment. RB at 72. Respondents fail to explain how such a limited interpretation is legally significant since such claims would still appear to be within the scope of the claims alleged in the Complaint. In any event, Dr. Butters, whose testimony Respondents cite, did not testify to the interpretation urged by Respondents. RB at 73-74, 78-82 (citing Butters, Tr. 2817-18, 2821). In the cited testimony, Dr. Butters opined that what people might infer with respect to a food product might be different than what they might infer with respect to a drug; that an advertisement promoting the consumption of food is far less likely to be interpreted by a reasonable consumer as conveying a treatment claim; and that the word "treatment" means medical treatment. *See* F. 491-492. Dr. Butters simply did not opine that consumers would interpret the Challenged Advertisements in the manner claimed by Respondents. Moreover, as noted above, the nature of the transaction (*i.e.*, the purchase of a food product or food-derived supplement) has been considered in determining the meaning of the Challenged Advertisements. With respect to those of the Challenged Advertisements for which the challenged claims were not reasonably clear or conspicuous on the face of the advertisements themselves, the opinions of Dr. Butters, set forth above, have been taken into account. As to other advertisements, the nature of the POM Products as food, or food-derived, was insufficient to outweigh the overall net impression that such advertisements conveyed the alleged claims. *See, e.g.*, F. 296, 305.[8]

Respondents argue that the Challenged Advertisements are not reasonably interpreted as making "broad" establishment claims, because they simply report study results, in a qualified manner with words such as "preliminary," "promising," "encouraging," or "hopeful," and are not reasonably interpreted as implying that the study results prove that the POM Products treat, prevent, or reduce the risk of disease. *See, e.g.*, RB at 75-82; RRB at 10-15. However, in the context of the Challenged Advertisements found to have made establishment claims, the foregoing language fails to materially alter the overall net impression that such advertisements were claiming clinical proof. *E.g.*, F. 300-301, 312, 333, 342, 349-350, 354; *see also* F. 519 (Dr. Stewart opining that the typical consumer would likely have little understanding of what

[8] The nature of the POM Products as food, or food-derived, is relevant to, and is considered in connection with, the substantiation analysis in Section III.F.2, *infra.*

"initial" or "pilot" means, particularly in the context of being referred to as having been published in a major journal).

Similarly, Respondents assert that advertising that a study on POM Juice showed "prolongation of PSA doubling times" does not convey the claim that POM Juice has been clinically proven to treat, prevent, or reduce the risk of "prostate cancer," and that advertising a study that POM Juice consumption resulted in "significant reduction of . . . arterial plaque" or "improvement in blood flow" does not convey a claim of clinical proof of prevention, treatment, or reduction of the risk of "heart disease." RRB at 10. However, as explained above, those of the Challenged Advertisements found to have made "clinically proven" claims expressly referred to "heart disease," *e.g.*, F. 294, 301, 348, 374, 407, 414, "prostate cancer," *e.g.*, F. 334, 352, 381, 403, and "erectile dysfunction," F. 408, 413, or "erectile function" together with the phrase, "ED," F. 324, 434, and drew a logical connection for the reader, including through associated explanatory text, between the study results and effectiveness for the referenced maladies. *E.g.*, F. 301-303, 323-325, 348-350, 353, 374, 379-380, 414. Thus, in the context of these advertisements, reasonable consumers would readily infer that the study results constituted clinical proof of effectiveness for the referenced maladies.

In addition, contrary to Respondents' argument, the preponderance of the evidence does not support a finding that the use of qualified language, such as "may" or "can" necessarily prevents communication of a more definitive claim. To the extent Dr. Butters opined to this effect, *see* F. 497, that opinion is rejected as unsupported and inconsistent with common-sense. First, there is academic literature in the record indicating that qualifiers such as "can," "could," "might," or "up to" can create the inference of a stronger claim. F. 589. Moreover, whether a consumer will interpret "may" or "can" to mean "will" depends on the context, and the totality of the advertisement. F. 527.

Finally, Respondents contend that interpreting any of the Challenged Advertisements to make the alleged claims ignores the role of humor, parody, or hyperbole present in Respondents' advertising. Notwithstanding Dr. Butters' opinion on this issue, F. 487-489, the preponderance of the evidence demonstrates that humor, parody, or hyperbole within an advertisement does not necessarily "block" communication of a serious message within that

advertisement. Rather, as Dr. Butters acknowledged, parody and humor have the effect of capturing the attention of the advertisement viewer, to help the viewer connect with the message in the printed portion of the advertisement. F. 534. Humor can induce further processing of an advertisement and a search for further information. F. 535. While readers may discount puffery and hyperbole as an exaggeration, the fact that puffery and hyperbole are not to be taken literally does not mean that advertisements using such elements cannot convey a serious claim. F. 532-533. Thus, the fact that a number of the Challenged Advertisements found to have made the alleged claims made partial use of humor or hyperbole is insufficient, in the context of the other elements of those advertisements, to prevent conveying the challenged claims. *See, e.g.*, F. 300-301, 320, 327, 464, 476.[9]

F. Whether the Challenged Claims are False or Misleading

1. Overview of applicable legal standards

Having found that Respondents disseminated advertisements making the claims alleged in the Complaint, the next step is to determine whether the claims are false or misleading. *Kraft*, 970 F.2d at 314; *Pantron I Corp.*, 33 F.3d at 1095; *Direct Marketing Concepts*, 569 F. Supp. 2d at 297. Two theories have been used to prove that an advertisement is deceptive or misleading: (1) the "falsity" theory or (2) the "reasonable basis" theory. *Pantron I*, 33 F.3d at 1096; *Thompson Medical*, 1984 FTC LEXIS 6, at *380-81. Complaint Counsel contends that Respondents' claims are deceptive because they are both "false" and "unsubstantiated." CCB at 36. Notwithstanding Complaint Counsel's contention, as further explained below, the issue of whether Respondents' claims were deceptive turns on the nature and quality of Respondents' substantiation, and, therefore, "the falsity and reasonable basis theories collapse into the same inquiry: did [Respondents] possess adequate substantiation to make such a claim?" *QT, Inc.*, 448 F. Supp. 2d at 966.

[9] Respondents' contention that the evidence fails to show the date that certain advertisements were disseminated is moot, to the extent that, with one exception, such advertisements are not among those found to have made the challenged claims. *See* RFF 2252. As to that exception, CX0314, the evidence shows that this advertisement was disseminated in 2008. F. 307. Respondents' further contention that some advertisements found herein to have made the challenged claims are "outliers" that cannot support an injunctive order is addressed in Section III.H, *infra*, with respect to remedy. Finally, Respondents assert that certain advertisements should be eliminated from consideration because of an alleged admission by Complaint Counsel's rebuttal expert on marketing and market research, Dr. Michael Mazis, (F. 279-283) that such advertisements were not being challenged. Having fully reviewed the testimony and Dr. Mazis' report in this regard, that assertion is rejected as unsupported by the evidence.

The Complaint charges that Respondents have represented that clinical studies, research, and/or trials prove that the POM Products treat, prevent, or reduce the risk of heart disease, prostate cancer, and/or erectile dysfunction, when in fact, studies, research and/or trials do not prove such claims, and, therefore, Respondents' representations are false or misleading. Complaint ¶¶ 12-18. Complaint Counsel refers to these claims as "false establishment claims." CCB at 20-24. The Complaint also charges that Respondents represented that the POM Products treat, prevent, or reduce the risk of heart disease, prostate cancer, and/or erectile dysfunction without a reasonable basis to substantiate those representations. Complaint ¶¶ 19-21. Complaint Counsel refers to these charges as "unsubstantiated efficacy claims." CCB at 25-26.

Establishment claims are those that contain representations regarding the amount and type of evidence the advertiser has for its product claims. *In re Daniel Chapter One*, No. 9329, 2009 FTC LEXIS 259, at *55 (Dec. 24, 2009); *Direct Marketing Concepts*, 569 F. Supp. 2d at 298 (citing FTC Policy Statement on Advertising Substantiation, appended to *Thompson Medical*, 104 F.T.C. at 839, 1984 FTC LEXIS 6, at *434). The establishment claim theory "is based on the straightforward notion that when an advertiser represents in its ads that there is a particular level of support for a claim, the absence of that support makes the claim false." *Sterling Drug*, 1983 FTC LEXIS 66, at *436. Common examples of establishment claims include statements such as "tests prove," "doctors recommend," or "studies show." *Direct Marketing Concepts*, 569 F. Supp. 2d at 298-99 (citing Policy on Advertising Substantiation; *Thompson Medical*, 791 F.2d at 194) (other citations omitted). Complaint Counsel bears the burden of demonstrating that the level of support represented by Respondents was false, *i.e.*, that Respondents did not have the amount and type of substantiation they claimed to have had. *See Sterling Drug*, 1983 FTC LEXIS 66, at *437; *Thompson Medical*, 791 F.2d at 194; *Bristol-Meyers*, 1983 FTC LEXIS 64, at *252.

Non-establishment claims, or "efficacy claims," are those about a product's attributes, performance, or efficacy, without indicating any particular level of support for such claim. *Thompson Medical*, 1984 FTC LEXIS 6, at *368; *Removatron* 884 F.2d at 1492 n.3 ("'Non-establishment' claims are statements to the effect that a product works."). Under the reasonable

basis theory of deception, because claims about a product's attributes, performance, or efficacy carry with them the express or implied representation that the advertiser had a reasonable basis substantiating such claims, failure to have a reasonable basis for the claim is deceptive or misleading. *Pantron I*, 33 F.3d at 1096; *QT, Inc.*, 448 F. Supp. 2d at 959-60; *Direct Marketing Concepts*, 569 F. Supp. 2d at 298; *Thompson Medical*, 1984 FTC LEXIS 6, at *367; *Daniel Chapter One*, 2009 FTC LEXIS 157, at *222 (Initial Decision). Under the reasonable basis theory, the government has the burden of proving by a preponderance of evidence that the Respondents did not have a reasonable basis for asserting that the challenged claims are true. *Pantron I*, 33 F.3d at 1096; *QT, Inc.*, 448 F. Supp. 2d at 959; *Thompson Medical*, 1984 FTC LEXIS 6, at *379. Thus, as to both the alleged "false establishment claims" and the alleged "unsubstantiated efficacy claims," proof of deception requires proof that Respondents' substantiation failed to meet the level of substantiation required.

The district court in *FTC v. QT, Inc.* described the shifting burdens as follows:

> [T]he Court must first determine what level of substantiation Defendants were required to have for their advertising claims, and this determination is a question of fact. Then, the Court must determine whether Defendants possessed that level of substantiation. . . . Defendants have the burden of establishing what substantiation they relied on for their product claims. The FTC has the burden of proving that Defendants' purported substantiation is inadequate, and the FTC need not conduct or present clinical studies showing that the product does not work as claimed.

448 F. Supp. 2d at 959 (citations omitted).

For efficacy claims, the Commission, in *Thompson Medical*, held that determining the appropriate level of substantiation requires weighing the following factors: (1) the product involved; (2) the type of claim; (3) the benefits of a truthful claim; (4) the ease of developing substantiation for the claim; (5) the consequences of a false claim; and (6) the amount of substantiation experts in the field would agree is reasonable. 1984 FTC LEXIS 6, at *387 (citing *In re Pfizer, Inc.* No. 8819, 81 F.T.C. 23, 1972 FTC LEXIS 13, at *91 (July 11, 1972)). Those factors, known as the "*Pfizer* factors," have been applied to determine the appropriate level of substantiation for non-establishment claims in numerous cases since *Pfizer* was decided. *E.g.*, *Direct Marketing Concepts*, 569 F. Supp. 2d at 299 (citing *Removatron*, 884

F.2d at 1492 n.3); *QT, Inc.*, 448 F. Supp. 2d at 959 (citing Policy on Advertising Substantiation).

For establishment claims, the Commission does not require application of the *Pfizer* factors to determine the required level of substantiation, on the theory that the advertiser must be held to whatever level of substantiation is represented in the advertisement. *In re Removatron Intl Corp.*, No. 9200, 111 F.T.C. 206, 1985 FTC LEXIS 21, at *190 (Sept. 30, 1985); *Thompson Medical*, 1984 FTC LEXIS 6, at *387 n.59. If an advertisement represents that a particular claim has been scientifically established, the advertiser must possess a level of proof sufficient to satisfy the relevant scientific community of the claim's truth. *Removatron*, 1985 FTC LEXIS 21, at *191 (citing *Thompson*, 104 F.T.C. at 821-22 n.59; *Bristol-Meyers*, 102 F.T.C. at 321, 331).

Complaint Counsel charges that Respondents knew that their scientific studies were insufficient to support their efficacy and establishment claims. CCB at 3. *See also e.g.*, CCB at 41 (Complaint Counsel contending that Respondents "recognize[d] that they lack[ed] proof that the POM Products prevent or treat" heart disease). However, any opinions Respondents may have had regarding the adequacy of their substantiation do not constitute expert opinion on what "experts in the field would agree is reasonable" or on whether "the level of proof [relied upon is] sufficient to satisfy the relevant scientific community of the claim's truth." Accordingly, such evidence is not material or probative to the issue of whether Respondents possessed an adequate level of substantiation.

With these generally applicable principles in mind, to determine whether the challenged claims are false or misleading, it must first be determined what level of substantiation Respondents were required to have for their advertising claims. *QT, Inc.*, 448 F. Supp. 2d at 959. This determination is a question of fact to be determined based upon the evidence adduced at trial. *QT, Inc.*, 448 F. Supp. 2d at 959; *FTC v. Braswell*, CV 03-3700 DT, 2005 U.S. Dist. LEXIS 42976, at * 35 (C.D. Cal. 2005). Next, it must be determined whether Respondents possessed that level of substantiation. *QT, Inc.*, 448 F. Supp. 2d at 959. Respondents have the burden of establishing what substantiation they relied on for their

product claims. *Id.* Complaint Counsel has the burden of proving that Respondents' purported substantiation is inadequate. *Id.*

2. Appropriate level of substantiation generally

A review of the briefs in this case reveals that there is no dispute that the appropriate level of substantiation is "competent and reliable scientific evidence," both for Respondents' establishment claims and for Respondents' efficacy claims. The parties' dispute centers upon what constitutes "competent and reliable scientific evidence." *See, e.g.*, CCB at 2-3, 30, 40; CCRB at 18; RB at 32-38.

Complaint Counsel asserts that competent and reliable scientific evidence must include "RCTs," which experts define as well-designed, well-conducted, randomized, double-blind, placebo-controlled human clinical trials, (F. 608) in order to provide adequate substantiation for both the alleged establishment claims and efficacy claims in this case. CCB at 32; CCRB at 18. Respondents dispute this notion, asserting that, in examining the totality of the evidence, basic science and "pilot" studies, not just RCTs, can be relied upon as competent and reliable evidence. RB at 32-38. "Basic science" refers to test-tube (*in vitro*) studies, *in vivo* animal studies, and pre-clinical research. F. 593.

As explained below, neither the FTC Act nor applicable case law imposes a requirement of RCTs to substantiate all "health-related efficacy claims," as urged by Complaint Counsel. CCB at 32. Rather, and as Complaint Counsel's cited cases make clear, the determination of the appropriate level of substantiation is a question of fact to be determined based upon the expert testimony adduced at trial. *QT, Inc.*, 448 F. Supp. 2d at 959; *FTC v. Braswell*, 2005 U.S. Dist. LEXIS 42976, at *35.

a. RCTs are not a legal requirement

In its Post-Trial Brief, Complaint Counsel asserts that "[c]ourts have consistently found or upheld that double-blind, randomized, placebo-controlled trials ("RCTs") are required to provide adequate substantiation for the truthfulness of health-related claims." CCB at 32. As a matter of law, "[n]othing in the Federal Trade Commission Act . . . requires placebo-controlled, double-blind studies." *FTC v. QT, Inc.*, 512 F.3d 858, 861 (7th Cir. 2008). Further, contrary to

Complaint Counsel's assertion, the cases upon which Complaint Counsel rely do not compel a conclusion that RCTs are required.

Complaint Counsel cites *FTC v. Direct Marketing Concepts, Inc.*, 569 F. Supp. 2d at 303, for the proposition that double-blind, placebo controlled studies are required to substantiate health-related efficacy claims. Although the district court in *Direct Marketing* stated, "it seems well-accepted that double-blind, placebo-controlled studies are necessary to substantiate health-related efficacy claims," *id.* at 303, the First Circuit Court of Appeals, when reviewing the district court's opinion, expressly noted that while the FTC had argued and produced expert testimony that the claims at issue should be substantiated by double-blind, placebo-controlled studies, "there may be other scientific evidence that could be sufficient, and we may assume for these purposes that a double-blind study is not necessarily required." *FTC v. Direct Marketing Concepts, Inc.*, 624 F.3d 1, 9 (1st Cir. 2010).

Complaint Counsel next cites *National Urological Group*, 645 F. Supp. 2d at 1202-03. However, in that case, which was before the court on the FTC's motion for summary judgment, the court did not hold that claims for erectile dysfunction "required" double-blind placebo-controlled studies, as Complaint Counsel suggests. Instead, the court stated, "what constitutes competent and reliable scientific evidence in this case is a question of fact for expert interpretation." *Id.* at 1190. In *National Urological Group*, the expert testimony was undisputed that the erectile dysfunction claims made in that case required well-designed, placebo-controlled, randomized, double-blind clinical trials for substantiation. Because the "defendants ha[d] not countered the testimonies of the FTC's expert regarding what level of substantiation is required for the claims made," the court concluded that there was no genuine dispute of fact on the requisite level of substantiation. *Id.* at 1202. In the instant case, by contrast, expert testimony on whether RCTs are required was clearly disputed and conflicting.

In *FTC v. Braswell*, 2005 U.S. Dist. LEXIS 42976, also cited by Complaint Counsel, defendants advertised the dietary supplements Lung Support Formula, AntiBetic Pancreas Tonic and Gero Vita GH3, one of which was advertised as a substitute for medical treatments. *Id.* at *4, *20-21 (AntiBetic). The court found that, by offering unrefuted evidence that the standard should be double-blind, placebo-controlled tests, the FTC had offered sufficient

evidence to withstand summary judgment. *Id.* at *35. The court further noted that the ultimate determination of the level of substantiation required would be determined by the court based upon the evidence at trial. *Id.*

Complaint Counsel also relies on *Removatron*, 884 F.2d 1489 (1st Cir. 1989), where the Court of Appeals upheld the Commission's determination that a well-controlled scientific study was necessary to substantiate the respondent's claims that a radio frequency energy hair removal device would permanently remove hair. *Id.* at 1498. The court explained the basis for its holding as follows: "The FTC's expert, Dr. Van Scott, testified that, in this field, at least one well-controlled test would be needed to establish a permanency claim. He also testified that two tests would be better and three superb. The ALJ found that petitioners needed two well-controlled tests in order to establish their claims; the Commission decided one was sufficient. Thus, petitioners needed to present evidence that they possessed at least one well-controlled scientific study that supported their permanency claim." *Id.* Since the only substantiation evidence in that trial was a single experiment which, according to the doctor who conducted it, did not actually demonstrate permanent hair removal, the respondent's substantiation was found to be inadequate. *Id.* *Removatron*, therefore, is consistent with the requirement that the appropriate level of substantiation is determined by the evidence, and does not hold that RCTs are required as a general matter.

Additionally, in another case relied upon by Complaint Counsel, *Thompson Medical* 1984 FTC LEXIS 6, which involved an arthritis medication, Aspercreme, the Commission evaluated the efficacy of an over-the-counter analgesic drug, utilizing the six *Pfizer* factors, to conclude that the proper level of substantiation was two well-controlled clinical tests. 1984 FTC LEXIS 6 at *291, 398. However, there the Commission also noted, "we do not preclude ourselves from also permitting advertisers to use other types of evidence to comply with our substantiation requirement." *Id.* at *399.

Finally, Complaint Counsel relies on *QT, Inc.*, 448 F. Supp. 2d at 961. In determining the appropriate level of substantiation in that case, the court stated at the outset: "The Court must first determine what level of substantiation Defendants were required to possess for [the claim that an 'ionized' bracelet was proven, by scientific tests, to provide immediate pain

relief]. *This is a question of fact*." *Id.* (emphasis added). The expert testimony in that case was that "at least one well-conducted, placebo-controlled, randomized, double-blind or sham-controlled clinical trial would be required by qualified experts in the field of pain due to rheumatic disease to support a claim that a product relieves or treats musculoskeletal pain," and that "a placebo-controlled, randomized, double-blind trial is the gold standard in the scientific community and depending on the claims an advertiser wishes to make, such a gold-standard study should be attempted to support those claims." *Id.* at 961-62. The court concluded that "with medical, health-related claims, a well-conducted, placebo-controlled, randomized, double-blind study, the gold standard, should have been conducted." *Id.* at 962. On appeal, the court expressly rejected the notion that RCTs are required as matter of law, stating: "Placebo-controlled, double-blind testing is not a legal requirement for consumer products." *QT, Inc.*, 512 F.3d at 861. Thus, *QT* does not stand for the proposition that RCTs are necessarily required, but is consistent with the proposition that the appropriate level of substantiation is determined by what the evidence shows that experts in the relevant field would deem adequate.

b. Summary of expert testimony on the appropriate level of substantiation

Detailed findings of fact on the expert testimony adduced at trial on the appropriate level of substantiation are set forth in Section II.F, *supra*. In summary, Complaint Counsel's experts in the fields of antioxidants and epidemiology (Dr. Meir Stampfer), heart disease (Dr. Frank Sacks), prostate cancer (Dr. James Eastham), and erectile dysfunction (Dr. Arnold Melman) each separately opined on the level of substantiation they would expect, as experts in their respective fields, to support claims that the POM Products treat, prevent, or reduce the risk of heart disease, prostate cancer, or erectile dysfunction, and claims that Respondents' clinical research proves such benefits. These experts all testified that well-designed, well-conducted RCTs showing statistically and clinically significant improvements in valid endpoints are necessary to make claims that: (1) the Challenged Products treat, prevent, or reduce the risk of heart disease, prostate cancer, and/or erectile dysfunction; or (2) studies show that the Challenged Products treat, prevent, or reduce the risk of heart disease, prostate cancer, and/or erectile dysfunction. F. 626, 638, 648, 654.

Respondents' experts in the fields of the design of clinical research protocols (Dr. Denis Miller), nutrition (Dr. David Heber), cardiovascular health (Dr. Dean Ornish), urology and prostate health (Dr. Jean deKernion), and urology and sexual medicine (Dr. Arthur Burnett and Dr. Irwin Goldstein) offered rebuttal to Complaint Counsel's experts' testimony. Dr. Miller testified that Respondents do not need RCTs to substantiate POM's claims because the POM Products are absolutely safe, pure fruit products and Respondents have not suggested that the Challenged Products be used as substitutes for conventional medical treatment. F. 661; *see also* F. 662-670. Dr. Heber opined that experts in nutrition evaluate whether competent and reliable science supports health claims for safe, pure fruit products, such as pomegranate juice, based on the totality of evidence, which does not necessarily include RCTs. F. 671-673. Dr. Ornish testified that, in a nutritional context, *in vitro* and animal studies may be more effective in testing the efficacy of a nutrient and that the totality of Respondents' scientific evidence must be considered in evaluating cardiovascular health claims, which need not be substantiated by expensive RCTs. F. 674; *see also* F. 675-679. Dr. deKernion testified that in the case of a fruit juice, which has low or no toxicity, it is not necessary to use an RCT. F. 682. Dr. Burnett opined that a safe pure fruit juice, like pomegranate juice, which is not used as a substitute for proper medical treatment, does not require RCTs to substantiate health claims. F. 683. Dr. Goldstein testified that RCT studies are not required to substantiate claims that pomegranate juice can aid in erectile health. F. 685-686.

c. Overview as to the appropriate level of substantiation

i. Expert testimony does not establish that RCTs are required in this case

The expert testimony in this case demonstrates that competent and reliable scientific evidence is required for claims about nutritional supplements when such products are advertised to treat diseases or medical conditions. *E.g.*, F. 662, 711, 964. *See also Daniel Chapter One*, 2009 FTC LEXIS 157, at *233-35 (Initial Decision) (summarizing expert testimony and citing *Natural Solution*, 2007 U.S. Dist. LEXIS 60783, at *11-12; *National Urological Group*, 645 F. Supp. 2d at 1190; *Direct Marketing Concepts*, 569 F. Supp. 2d at 300, 303). The greater weight of the persuasive expert testimony adduced at trial does not, however, support Complaint Counsel's position that, in order to have the required competent

and reliable scientific evidence, Respondents must have had RCTs. F. 706, 707. Instead, the more persuasive expert testimony shows that RCTs are needed for a nutrient supplement if one makes a claim that the product causes the effect of treating, preventing, or reducing the risk of a disease and one offers the nutrient supplement as a replacement to medical care to treat, prevent, or reduce the risk of diseases. F. 706. The evidence further shows that RCTs are not required to convey information about a food or nutrient supplement where, as here, the safety of the product is known; the product creates no material risk of harm; and the product is not being advocated as an alternative to following medical advice. F. 707.

ii. Expert testimony on the appropriate level of substantiation

Having determined that RCTs are not required in this case, the next step is to determine what level of substantiation Respondents were required to have for their advertising claims. *QT, Inc.*, 448 F. Supp. 2d at 959. As stated above, for efficacy claims, the appropriate level is determined by weighing the six *Pfizer* factors, one of which is "the amount of substantiation experts in the field would agree is reasonable." *Thompson Medical*, 1984 FTC LEXIS 6, at *387. For establishment claims, the appropriate level of substantiation is determined by what would "satisfy the relevant scientific community that the claim[s are] true." *Removatron*, 111 F.T.C. at *246, 1985 FTC LEXIS 21 at *195.

As asserted by Complaint Counsel, by virtue of their very nature, the advertisements containing establishment claims also make the efficacy claims that are challenged as unsubstantiated in the Complaint. CCB at 31. Experts in the relevant scientific communities would require the same level of evidence to support claims that a product treats, prevents, or reduces the risk of a disease or dysfunction, as they would require to support claims that clinical studies, research, or trials prove the same claims. *E.g.*, F. 713. All four of Complaint Counsel's experts in the relevant fields applied the same standards in evaluating Respondents' level of substantiation without regard to whether the claims at issue were "clinically proven" establishment claims or whether the claims at issue were efficacy claims without reference to any studies. *E.g.*, F. 190, 199, 207, 214. As discussed below, the experts, including Complaint Counsel's experts, considered evidence relating to the nature of the product, the nature of the claim, and

the feasibility of conducting RCTs. *See* F. 688-705. Thus, while application of the *Pfizer* factors is not necessarily required, because the experts considered essentially the same factors in determining the "proof sufficient to satisfy the relevant scientific community of the claim's truth" (*Removatron*, 1985 FTC LEXIS 21 at *190), and because, with respect to Respondents' heart disease claims, Respondents did make non-establishment claims, a review of the *Pfizer* factors is appropriate.

Under *Pfizer*, "the amount of substantiation experts in the field would agree is reasonable," is one of six factors that must be evaluated to determine the appropriate level of substantiation for non-establishment claims. *Thompson Medical*, 1984 FTC LEXIS 6, at *387. That evaluation is discussed in the three subsequent sections of the Initial Decision specific to what experts in each of the relevant fields believe to be reasonable substantiation for claims regarding heart disease, prostate cancer, and erectile dysfunction, respectively. The remaining five *Pfizer* factors are applicable in determining the required level of substantiation regardless of the relevant field, and are, therefore, addressed below as a preliminary matter, before the evaluation of the evidence on what experts in the fields of heart disease, prostate cancer, and erectile dysfunction would agree is reasonable substantiation. Those five *Pfizer* factors, analyzed below, are: (1) the products involved; (2) the type of claim; (3) the benefits of a truthful claim; (4) the ease of developing substantiation for the claim; and (5) the consequences of a false claim. *Thompson Medical*, 1984 FTC LEXIS 6, at *387.

(a) The products involved

The POM Products are either food products or dietary supplements wholly derived from the pomegranate fruit. F. 57-58, 61, 67, 70-71. POM Juice is produced by pressing the whole fruit containing both arils (pomegranate berries) and the peel (husk) and internal membrane. F. 57-58. POMx is an extract from the pomegranate, made through a process by which POMx Liquid is first derived from the whole fruit, and then POMx is extracted from the POMx Liquid. F. 67, 70. POM Juice is sold in the refrigerated produce section of grocery stores. F. 65.

Pomegranate juice and its extract have a "high degree" of safety and are safe for human consumption. F. 78. Humans have consumed pomegranates for centuries as a safe and

nutritious food. F. 77. The U.S. Food and Drug Administration ("FDA") identifies pomegranate as being "generally recognized as safe" for human consumption. F. 82, 84; *see* 32 U.S.C. § 231(s). To establish such recognition, it must be shown that there is a consensus of expert opinion regarding the safety of the use of the substance. 21 C.F.R. § 170.30(a); *see* F. 83. Respondents' expert, Dr. Heber, confirmed that pomegranate juice has no adverse side effects, in contrast to drugs. F. 85-88.

Complaint Counsel's expert, Dr. Sacks, testified that the issue of the safety of the POM Products was not within the scope of his assignment in this case, that his expert report contains no opinions on the safety of the POM Products, and that he has "no opinion about whether [the POM Products are] safe or not." F. 93. Complaint Counsel's expert, Dr. Stampfer, admitted that there are no safety concerns with consuming pomegranate juice apart from "the usual harm that comes with fruit juice, sugary beverages . . . but that is not specific to pomegranate juice." F. 94.

Scientific studies also confirm that POM Juice and POMx are safe for human consumption. F. 87, 88. Researchers validated the safety of POMx Pills in a clinical study where no adverse events or changes in blood count, serum chemistry or urinalysis were observed in the human subjects after consuming the extract for four weeks. F. 92. Researchers confirmed in a clinical study that the consumption of pomegranate juice had no drug interaction in the human volunteers. F. 91.

Complaint Counsel's experts agreed that the level of scientific evidence required to support a claim considers the product being promoted. F. 695. The greater weight of the persuasive expert testimony is that RCTs are needed for pharmaceutical drugs to assess safety and efficacy because pharmaceutical drugs are unnatural, developed in laboratories, and have toxicities. F. 666, 675, 682, 686, 696. Pharmaceutical drugs, which are not known to be safe and always have toxicities and side effects, are held to a higher standard than a juice that is derived from a fruit that has been around for thousands of years. F. 666, 675, 682, 686, 697. Complaint Counsel's expert, Dr. Sacks, testified that you do not need RCT trials to test the benefit of food categories that are included in a diet already tested, like the DASH diet, which includes pomegranates. F. 645. Complaint Counsel's expert, Dr. Stampfer, conceded that

RCTs are not required (or better) for nutritional-based research and admitted that he has made public statements or recommendations that food and beverage products lower the risk of certain diseases in the absence of RCTs. F. 631, 632.

The standard applied to new drugs should not be applied to nutrients as long as the product is not claimed to be a substitute for conventional drug therapies or medical care and is shown to be safe. F. 666, 682, 697, 698. Thus, the facts that the POM Products are derived from a fruit and are known to be safe weigh in favor of a standard for substantiation that is less than that required for pharmaceutical drugs.

(b) The type of claim

The type of claim Respondents have been found to have made – that the POM Products treat, prevent, or reduce the risk of heart disease, prostate cancer, or erectile dysfunction and that the POM Products are clinically proven to do so – weighs in favor of a high standard for substantiation. Where defendants make a "medical, health-related claim, . . . such a claim must be based on a heightened level of substantiation." *QT*, 448 F. Supp. 2d at 962. In *QT*, where the expert testimony established that "a well-conducted, placebo-controlled, randomized, double-blind study, the gold standard, should have been conducted," the court held that "Defendants would not be required to have a gold-standard study to substantiate the Q-Ray bracelet if they did not make such a strong, medical claim." *QT*, 448 F. Supp. 2d at 962. In addition, where defendants claim that a product's efficacy has been "test-proven," such a statement must be substantiated by "a reliable test" with "statistically significant results achieved." *QT*, 512 F.3d at 862; *Removatron*, 884 F.2d at 1498 ("reasonable basis" for establishment claims meant well-controlled scientific studies).

While Respondents here have been found to have made claims that the POM Products treat, prevent, or reduce the risk of diseases or dysfunction, it is significant to note that Respondents did not advertise or market the POM Products as an alternative to medical treatment. "The Complaint does not allege, and it is neither Complaint Counsel's contention nor its burden, to demonstrate that Respondents are selling the POM Products as a substitute for conventional medical treatment." CCRB at 40 n.36.

The greater weight of the persuasive expert testimony in this case confirms that the appropriate level of substantiation depends on the claims. If the claim does not suggest that an individual should forgo conventional medical care or treatment based on the consumption of a safe product and does not imply that a causal link between the product and the effect has been established, then evidence short of RCTs can be sufficient. F. 631, 707. Complaint Counsel's expert, Dr. Stampfer, testified that if, for example, nuts are not being offered as a substitute to medical care, and the claim is that there is some evidence to suggest the possibility that nuts may reduce the risk of diabetes, then evidence short of RCTs can support that claim. F. 631. While claims of efficacy can be made only when a causal relationship with human disease is established by competent and reliable scientific evidence (F. 627; *see also* F. 629-631), based on the evidence and the law as applied to this case, competent and reliable scientific evidence does not mean RCTs.

(c) The benefits of a truthful claim and the ease of developing substantiation for the claim

"These two factors -- the benefits of a truthful claim and the ease of developing substantiation for the claim -- are typically considered together." *Daniel Chapter One*, 2009 FTC LEXIS 157, at *232-33 (Initial Decision). "The consideration of these factors seeks to ensure that the level of substantiation required is not likely to deter product development or prevent disclosure of potentially valuable information about product characteristics to consumers." *Id.* at *233 (citing *Removatron*, 1985 FTC LEXIS 21, at *212 n.20; *Thompson Medical*, 104 F.T.C. at 823-24, 1984 FTC LEXIS 6, at *391).

The fact that individuals could benefit from truthful claims about a product's ability to treat, prevent, or reduce the risk of diseases or medical conditions is obvious. Complaint Counsel's expert, Dr. Stampfer, conceded that he "believe[s] that it may be appropriate to use evidence short of an RCT for crafting public health recommendations regarding nutrient guidelines even when causality cannot be established, because everyone eats and the public should be given advice based on the best evidence available." F. 631. Dr. Stampfer further testified that the failure to act, in the absence of conclusive RCT evidence, increases the risk of forgoing benefits to the public that might have been achieved with little risk and little cost and that one should "definitely" make that potential benefit available to the public rather than

withhold it. F. 633. Although advertising is not a "public health recommendation," it does convey a message and provides "potentially valuable information" about products. *Thompson Medical*, 1984 FTC LEXIS 6, at *391.

In a nutritional context, RCTs are prohibitively expensive and often not feasible because of the costs of conducting them. F. 632, 647, 673, 704. Complaint Counsel's expert, Dr. Eastham, testified that disease prevention studies should involve ten to thirty thousand participants which are "incredibly expensive" and in the range of $600 million. F. 704. Foods, unlike pharmaceutical drugs, are not patentable, and manufacturers cannot recoup the costs of conducting RCTs through profits from exclusive intellectual property rights. F. 705.

Complaint Counsel's expert, Dr. Sacks, acknowledged that RCTs may also not be feasible because of logistical and ethical considerations. F. 641, 704. In studying a fruit or food, it is difficult to do double-blind, randomized, placebo-controlled trials because the subjects know what they are consuming. F. 641, 679, 703. Once a participant is assigned to the control group and they know what the intervention is, the participant can consume the food or juice anyway, whereas one would not be able to do so with an experimental drug. F. 703. Moreover, in a nutritional context, a hypothesis about disease causation can rarely, if ever, be directly tested in humans using the RCT design. F. 701.

The greater weight of the persuasive expert testimony in this case leads to the conclusion that where the product is absolutely safe, like the POM Products, and where the claim or advertisement does not suggest that the product be used as a substitute for conventional medical care or treatment, then it is appropriate to favor disclosure. *See* F. 633, 709; *see also Pearson*, 164 F.3d at 657 (under the First Amendment commercial speech doctrine, there is a "preference for disclosure over outright suppression").

(d) The consequences of a false claim

The consequences of a false claim do not compel requiring a high level of substantiation. As analyzed above, there is no evidence to suggest, and Complaint Counsel does not argue, that Respondents urge individuals to consume the POM Products in place of conventional medical treatment. CCRB at 40 n.36. *Compare Daniel Chapter One*, 2009 FTC

LEXIS 157, at *234, *282 (Initial Decision) (finding that where representations in some instances suggested that individuals forego traditional cancer treatments in favor of purchasing and consuming the challenged products and evidence showed that foregoing a proven cancer treatment in favor of an ineffective treatment would be injurious to a patient's health, the consequences of a false claim required a higher level of substantiation). Moreover, the evidence shows that the POM Products are safe. F. 77-78. *See also* F. 94.

In *Pearson v. Shalala*, 164 F.3d 650, 656 n.6 (D.C. Cir. 1999), the court of appeals explained that courts should distinguish between products (*e.g.*, dietary supplements) that do not "in any fashion threaten consumer's health and safety" and "drugs," "wherein the potential harm presumably is much greater," when evaluating restrictions on commercial speech. The court in *Whitaker v. Thompson*, 248 F. Supp. 2d 1 (D.D.C. 2002) further explained:

> It is especially important to recognize that, in the present case, the potential harm to consumers from deception is severely limited . . . At worst any deception resulting from Plaintiffs' health claim will result in consumers spending money on a product that they might not otherwise have purchased.

Id. at 16 (noting also that the economic injury is not insignificant).

Spending money on an ineffective remedy is considered an economic injury for purposes of this *Pfizer* factor. *Daniel Chapter One*, 2009 FTC LEXIS 157, at *234 (Initial Decision) (citing *In re Schering Corp*., No. 9232, 1991 FTC LEXIS 427, at *134 (Sept. 16, 1991)); *Removatron*, 1985 FTC LEXIS 21, at *212 n.20). In this case, for the 52 weeks ending July 20, 2008, the weighted average base price per unit for POM Juice was $2.93 for an 8-ounce bottle or $4.29 for a 16-ounce bottle. F. 97. A serving size of POM Juice is eight ounces and, thus, a one year supply costs at least $780. *See* F. 64, 97. A one year supply of POMx costs approximately $315. *See* F. 97. Although the cost of the POM Products may not be insignificant, when you take into account the fact, at least with respect to POM Juice, that consumers are buying what is considered to be a premium fruit juice (F. 95), the economic injury to consumers is not a material factor in determining the required level of substantiation.

(e) The amount of substantiation experts in the field would agree is reasonable

The last of the six *Pfizer* factors, the amount of substantiation experts in the field would agree is reasonable, must be examined in relation to each field being evaluated. In addition, for Respondents' claims that were establishment claims only, Respondents must "satisfy the relevant scientific community that the claim is true." *Removatron*, 1985 FTC LEXIS 21, at *195. Accordingly, the amount of substantiation experts would agree is reasonable, the amount of evidence that would satisfy the relevant scientific community, and whether Respondents possessed that level of substantiation in regard to each of the three diseases or dysfunction, is evaluated in the following three sections of the Initial Decision.

3. Substantiation for Respondents' heart disease claims

a. Overview

As discussed in Section III.E.2.c, *supra*, the evidence demonstrates that Respondents disseminated advertisements that impliedly represented that the POM Products treat, prevent, or reduce the risk of heart disease and, in many of these same advertisements, are clinically proven to do so, by lowering blood pressure, reducing arterial plaque and/or increasing blood flow to the heart. Complaint Counsel contends that (1) Respondents did not possess and rely upon a reasonable basis to substantiate their efficacy claims that the POM Products treat, prevent, or reduce the risk of heart disease; and (2) clinical studies, research, and/or trials do not prove Respondents' establishment claims that the POM Products treat, prevent, or reduce the risk of heart disease. CCB at 37-44.

i. Summary of expert opinions

In support of its position, Complaint Counsel submitted the expert report and testimony of Dr. Meir Stampfer and Dr. Frank Sacks. Dr. Stampfer is a Professor of Epidemiology and Nutrition, Harvard School of Public Health; Faculty Member, Division of Biological Sciences, Harvard School of Public Health; Professor of Medicine, Harvard Medical School; and Faculty Member, Dana Farber Harvard Cancer Center. F. 182. Dr. Stampfer has been an investigator in several large studies focused on the relationship between nutrition and cardiovascular disease and has published more than 850 articles in medical journals. F. 183,184. Dr. Sacks is a

Professor of Cardiovascular Disease Prevention, Department of Nutrition, Harvard School of Public Health, and Professor of Medicine, Harvard Medical School. F. 191. Dr. Sacks has researched cardiovascular disease ("CVD") and coronary heart disease ("CHD") and their risk factors, including lipid profiles, hypertension, obesity, and diabetes, and the effects of potential risk-modifying diets, foods, food components, and drugs. F. 192. Dr. Sacks has published more than 160 articles in peer-reviewed scientific journals relating to CVD, CHD, and the relationship between nutrition and these diseases. F. 193.

According to Dr. Stampfer, for products such as the POM Products, claims of efficacy can be made only when a causal relationship with human disease has been established and the RCT is the best study design that permits a strong causal inference concerning the relationship between an administered agent and any specific outcome. F. 631, 632. According to Dr. Sacks, to substantiate a claim that a product, including a conventional food or dietary supplement, can treat, prevent, or reduce the risk of heart disease, one must rely on appropriately analyzed results of well-designed, well-conducted RCTs. F. 638. Dr. Sacks further opined that the findings of the RCTs must be statistically significant (*i.e.*, have strong "*p*" values). F. 711. In addition, Dr. Sacks opined that the results of the RCTs must demonstrate significant changes in valid surrogate markers of cardiovascular health, such as blood pressure and LDL cholesterol (two surrogate markers recognized by the FDA) or C-reactive protein, HDL cholesterol, and triglycerides (three surrogate markers recognized by many experts in the field). F. 712, 761-763, 765-766.

In Dr. Sacks' opinion, the same level of evidence is needed to show that clinical studies, research, or trials prove that a product treats, prevents, reduces the risk of heart disease, as is needed to substantiate a heart disease efficacy claim. F. 713.

Dr. Sacks acknowledged that there are common clinical recommendations today that have not been proven by RCTs, that in some instances, such as studies on foods, the blinding of patients is not possible, and that if a study becomes unblinded or does not have a placebo, the study can still have value. F. 641, 647. Moreover, Dr. Sacks testified that you do not need RCTs to test the benefit of food categories that are included in a diet already tested, like the

DASH diet, which includes pomegranates. F. 645. These positions weaken Dr. Sacks' opinion in this case that Respondents must have had two RCTs to support their claims.

In support of their position that they possessed and relied upon a reasonable basis to substantiate their claims, Respondents submitted the expert reports and testimony of Dr. David Heber and Dr. Dean Ornish. Dr. David Heber is a practicing physician, Professor of Medicine and Public Health at UCLA, and the founding Director of the UCLA Center for Human Nutrition, a center for clinical research, education, and public health endeavors. F. 221, 222. Dr. Heber has co-authored over 200 peer-reviewed publications in the field of nutrition and its relation to various diseases and written 25 chapters in other scientific texts. F. 224. Dr. Ornish is a well-known medical doctor and Clinical Professor of Medicine at the University of California at San Francisco. F. 227. Dr. Ornish is also the founder and President of the Preventative Medicine Research Institute ("PMRI"). F. 228. Dr. Ornish has directed clinical research on the relationship between diet and lifestyle and coronary heart disease for over 34 years and has written numerous books and articles for peer-reviewed journals. F. 229, 230.

Both Dr. Heber and Dr. Ornish opined that there is credible scientific evidence showing that pomegranate juice and pomegranate extracts have significant health benefits for human cardiovascular systems, including: (1) decreases in arterial plaque; (2) lowering of blood pressure; and (3) improvement in cardiac blood flow, based on the biological mechanism of prolonging the half-life of nitric oxide in the vasculature. F. 956, 960. Dr. Ornish opined that, taken as a whole, the preponderance of the scientific evidence from basic scientific studies, animal research, and clinical trials in humans reveals that the pomegranate in its various forms (including POM Wonderful 100% Pomegranate Juice, POMx Pills, or POMx Liquid) is likely to be beneficial in maintaining cardiovascular health and is likely to help reduce the risk of cardiovascular disease. F. 959. Dr. Heber also opined that the body of research on pomegranate juice and extract provides support for potential heart benefits for heart disease. F. 954. Dr. Heber explained that although claims that pomegranate juice and extract have not been proven absolutely effective to treat, prevent, or reduce the risk of heart disease, the entire body of scientific evidence should be considered when evaluating nutritional science. F. 957.

Dr. Ornish disagreed that study results must be "statistically significant" with "strong '*p*' values" (*i.e.*, $p \leq 0.05$ or a 5 percent or less chance that the change is due to chance), testifying that: (1) in evaluating scientific research related to a whole food, it is not necessary to reach statistical significance, as opposed to a prescription drug with potential side effects; and (2) the convention that there be a five percent or less finding due to chance is an arbitrary number. F. 958. Respondents' experts further dispute Dr. Sacks' opinion that significant changes must be shown in valid surrogate markers and opine that myocardial perfusion (or blood flow to the heart) and carotid intima-media thickness are more closely related to, and predictive of, cardiovascular disease than blood pressure or LDL cholesterol. F. 764, 765, 771.

ii. Standard for substantiation

Having considered the evidence on all the relevant factors, including the other five *Pfizer* factors analyzed in Section III.F.2, *supra*, the evidence demonstrates that competent and reliable scientific evidence is required to support claims that the POM Products treat, prevent, or reduce the risk of heart disease and that they have been clinically proven to do so. F. 711, 713; *see also* F. 710, 712. Based on the greater weight of the persuasive evidence from the experts at trial, to support claims that the POM Products treat, prevent, or reduce the risk of heart disease, or have been clinically proven to do so, competent and reliable evidence must include clinical studies, although not necessarily RCTs, that show that the POM Products did treat, prevent, or reduce the risk of heart disease. *See id.* As analyzed below, Complaint Counsel has demonstrated that Respondents did not possess adequate competent and reliable scientific evidence to substantiate the implied claims that the POM Products treat, prevent, or reduce the risk of heart disease or that clinical tests show the same. Complaint Counsel has, therefore, met its burden of proving that Respondents' claims are false or misleading. *See QT*, 448 F. Supp. 2d at 959.

b. Scientific evidence relied upon

i. Overview of cardiovascular heart disease

Heart disease, including heart attacks or angina, occurs as the result of decades-long damage to blood vessels. F. 715, 716. The process begins with the oxidation of the protein known as low density lipoprotein ("LDL" or bad cholesterol) which circulates in the blood.

F. 716. Once LDL becomes oxidized, the chemical nature of the protein changes, causing it to reside and accumulate in the blood vessel. F. 717. Macrophages, white blood cells that respond to inflammation by digesting cellular debris, begin to engulf and devour the oxidized cholesterol. F. 719. These macrophages continue to accumulate until they develop into "foam cells." F. 720. These foam cells become full of cholesterol and actually burst, bringing in more macrophages and more inflammation. F. 720. As this process progresses, plaque begins to form as yellow streaks in the coronary arteries. F. 721.

Antioxidants play an important role in mitigating heart disease by, among other things, inhibiting oxidative stress, including reducing LDL oxidation (and its uptake) and inflammation. F. 726, 727. In addition, the presence of nitric oxide in the body also helps offer protection against atherosclerosis by regulating blood flow and contributing to smooth muscle relaxation. F. 723-725, 751. Nitric oxide helps maintain healthy blood vessels, which improves blood flow to almost every organ in the body, including the heart. F. 731. Several studies have indicated that pomegranate juice has antioxidant and anti-atherosclerotic properties due to the presence of multiple polyphenols such as tannins, flavonols, anthocyanins and ellagic acid. F. 725.

ii. *In vitro* and *in vivo* studies

Respondents sponsored several *in vitro* and *in vivo* animal studies to examine the effect of POM Juice and POMx Pills on cardiovascular health. *In vitro* studies are those where blood elements or cells are removed from the body and tested in a controlled laboratory environment, such as a test tube. F. 593. *In vivo* studies are those conducted within the living. Respondents acknowledge that their *in vitro* and *in vivo* studies are "basic science" or "pre-clinical." RRCCFF 1083. Detailed findings on these studies are set forth in Section II.G.3, *supra*, and are summarized below.

Respondents have sponsored many published studies in cellular and animal models evaluating the effects of pomegranate juice and/or its extracts on cardiovascular function. F. 732. Beginning around 2000, and continuing to the present time, Dr. Michael Aviram began studies investigating pomegranate juice's potential benefits to the cardiovascular system. F. 744. Dr. Aviram and his colleagues observed several beneficial effects of pomegranate juice

and its extracts at the cellular and animal stage including, but not limited to: (1) reduction in oxidation of LDL cholesterol; (2) lessening the "uptake" of oxidized LDL by macrophage foam cells; (3) decrease in size of atherosclerotic lesions and foam cells; and (4) diminishing of platelet aggregation. F. 744.

Respondents have also sponsored research in the area of nitric oxide and understanding its role in cardiovascular health *in vitro* and in animals. F. 747. Dr. deNigris, Dr. Napoli, and, Dr. Ignarro conducted a number of studies in which they found that POM Juice and/or POMx Pills demonstrated: increasing and preserving levels of nitric oxide, decreasing expression of genes associated with stress, and progression of atherosclerosis; reducing LDL oxidation, size of atherosclerotic plaques, and formation of foam cells; reversing effects of shear stress, which can damage the endothelial cells or thin layer of cells that line the interior of blood vessels; decreasing cellular production and release of oxygen radicals in the vascular wall; inhibiting activation of oxidation-sensitive genes; and improving biological activity of nitric oxide. F. 751.

Complaint Counsel's expert, Dr. Sacks, acknowledges that some of Respondents' *in vitro* studies have shown pomegranate juice's favorable effects on the mechanisms involved in cardiovascular disease and that *in vitro* studies, like Dr. Aviram's, can be competent and reliable scientific evidence of an agent's effect on a particular mechanism. F. 745, 746. However, Dr. Sacks also opined regarding Respondents' basic research that *in vitro* and animal studies do not provide reliable scientific evidence of what effects a treatment will have inside the human body and, thus, do not provide reliable scientific evidence on whether an agent can treat, prevent or reduce the risk of cardiovascular disease in humans. F. 752. Respondents' expert, Dr. Ornish, testified that *in vitro* and animal studies are important in considering the totality of evidence in determining whether or not pomegranate juice in its various forms is beneficial, but that there are limitations to extrapolating from *in vitro* and animal studies to humans. F. 753.

Respondents' basic science indicates that pomegranate juice may be beneficial to cardiovascular health. F. 754. The basic research relied upon by Respondents is part of the

totality of evidence that must be examined in evaluating the effects of the POM Products. F. 755. However, experts in the field agree that *in vitro* and animal studies need to be replicated in humans to show an effect on preventing or treating a disease. F. 755.

iii. Clinical trials; overview

Complaint Counsel charges that Respondents did not have a reasonable basis and did not have clinical studies, research, or trials to prove that the POM Products prevent, reduce the risk of, or treat heart disease, by: (1) lowering blood pressure; (2) decreasing arterial plaque; and/or (3) improving blood flow to the heart. (Complaint ¶¶ 17-19). Respondents have sponsored approximately 10 published and several unpublished studies on humans, evaluating the effect of pomegranate juice and/or its extracts on cardiovascular health. F. 756. The results of the studies relied upon by Respondents and the conflicting expert opinions on these studies are found in Section II.G.5, *supra*, and discussed below.

iv. Clinical trials; improving blood pressure

In support of claims that the POM Products treat, prevent, or reduce the risk of heart disease by lowering blood pressure, in addition to the basic science discussed above, Respondents rely on the Aviram ACE/BP Study[10] and the Aviram CIMT/BP Study[11] of POM Juice. RRB at 106.

(a) About the studies

The Aviram ACE/BP Study was a study with ten elderly, hypertensive patients who drank 50 ml. of pomegranate concentrate daily, for two weeks. F. 774. The Aviram ACE/BP Study was unblinded and had no control group; instead, each patient's "before" measures were compared to his or her "after" measures. F. 776. The Aviram ACE/BP Study indicated that all ten patients experienced a statistically significant 5% reduction in systolic blood pressure from

[10] The Aviram ACE/BP Study, conducted by Dr. Michael Aviram and his co-workers, was published as "*Pomegranate juice consumption inhibits serum angiotensin converting enzyme activity and reduces systolic blood pressure*," 158 Atherosclerosis 195-98 (2001). F. 774.

[11] The Aviram CIMT/BP Study, conducted by Dr. Aviram and his co-workers, was published as, *"Pomegranate juice consumption for 3 years by patients with carotid artery stenosis reduces common carotid intima-media thickness (CIMT), blood pressure and LDL oxidation"* by Aviram M, Rosenblat M, Gaitini D, Nitecki S, Hoffman A, Dornfeld L, Volkova N, Presser D, Attias J, Liker H, and Hayek T, (Clin Nutr. 2004; 23:423-33). F. 789.

their baseline blood pressure measure. F. 778. The Aviram ACE/BP Study concluded that "pomegranate juice consumption can offer a wide protection against cardiovascular disease." F. 779.

In the Aviram CIMT/BP Study, a group of ten patients with severe carotid artery stenosis consumed 50 ml. of concentrated pomegranate juice daily for one year and five of them continued for up to three years. F. 790. A second group of nine patients who did not consume pomegranate juice acted as a control. F. 790. The Aviram CIMT/BP Study indicated that the pomegranate juice group members' systolic blood pressure was significantly ($p < 0.05$) reduced by 12% after one year of pomegranate juice consumption, compared to their baseline values. F. 794. In the group that did not consume pomegranate juice, blood pressure was unchanged. F. 794.

(b) Expert opinions on the studies

Complaint Counsel's experts criticized the Aviram ACE/BP Study on the following grounds: the sample size of ten patients was too small to provide reliable evidence that the observed effects would be generally applicable to a larger population; the two-week period of the study was too short to provide reliable evidence that the indicated improvement in blood pressure would be enduring; and the Aviram ACE/BP Study did not have a control group, thus, it is not possible to conclude what caused the indicated improvements in the subjects' blood pressure levels. F. 780. Complaint Counsel's experts criticized the Aviram CIMT/BP Study for the lack of a randomized, placebo-controlled group; the fact that the patients in the active and control groups received different treatment; the small sample size; and the lack of any between-group statistical analysis. F. 798.

Respondents' expert, Dr. Ornish, responded that there is a common misconception that a larger study is a better study, but the opposite can be argued; with a smaller number of patients, the treatment has to be more powerful and consistent in order to show a statistically significant effect. F. 783, 803; s*ee also* F. 785. Dr. Aviram testified that it is entirely appropriate for each patient to serve as his or her own control and that if a study is conducted without a placebo, that fact does not weaken its importance. F. 784.

Complaint Counsel's experts additionally opined that one cannot extrapolate the results of the two Aviram studies of POM Juice to the POMx products. *See* F. 948. Respondents counter this criticism by stating that, with respect to POMx Pills and POMx Liquid, Respondents detailed the findings of eight scientific studies that document the beneficial effects of POMx Pills and POMx Liquid on cardiovascular health. RRCCFF 965 (citing CX0053; PX0057; PX0056; PX0008; PX0017; PX0038; PX0139; PX0127; RFF 831-840, 924, 930-957, 1100). Furthermore, Dr. Heber, the only expert who opined on the bioavailability of pomegranate polyphenols, explained that because both the 100% Pomegranate Juice product and the POMx products contain ellagitannins that contribute to the antioxidant activity of the products (and because both are bioavailable (absorbed) in humans), there is no difference in the antioxidant effect between POM Juice and POMx products in laboratory studies. F. 953.

Lastly, Complaint Counsel charges that five subsequent RCTs sponsored by Respondents showed no benefit to blood pressure. These include the Ornish MP Study[12]; the Ornish CIMT Study[13]; the Davidson BART/FMD Study[14]; the Davidson CIMT Study[15]; and

[12] The Ornish MP Study was conducted by Dr. Dean Ornish and colleagues and published as Sumner M, et al., *Effects of Pomegranate Juice Consumption on Myocardial Perfusion (MP) in Patients with Coronary Heart Disease*, 96 Am. J. Cardiology 810 (2005). F. 805. The Ornish MP Study was a randomized, placebo-controlled, double-blind study of 45 patients. F. 808. The Ornish MP Study indicated that there were no statistically significant differences between the two groups in blood pressure. F. 813.

[13] The Ornish CIMT Study was an unpublished, randomized, double-blind, placebo-controlled 73-person study that measured carotid intima-media thickness (CIMT), blood pressure, and other related mechanisms for 12 months. F. 850. The Ornish CIMT Study indicated that there were no significant differences in the treatment group relative to the placebo group, over time, for any of the other heart-related measurements, including systolic and diastolic blood pressure. F. 859.

[14] The Davidson BART/FMD Study, titled, *The Effects of Pomegranate Juice on Flow-Mediated Vasodilation*, is a published study. F. 871. Brachial artery reactivity testing ("BART") is a measurement of how much the brachial artery dilates (enlarges) after a blood pressure cuff is inflated, and then released. F. 901. This is also called flow mediated dilation ("FMD") testing. F. 901. The Davidson BART/FMD Study took measurements of blood pressure, although blood pressure was not a primary or secondary endpoint of the study. F. 905. At the end of the Davidson BART/FMD Study, there were no significant differences between treatment and placebo groups in blood pressure. F. 906.

[15] The Davidson CIMT Study, was published as Davidson MH., *et al.*, *Effects of Consumption of Pomegranate Juice on Carotid Intima-Media Thickness in Men and Women at Moderate Risk for Coronary Heart Disease*, 104 Am. J. Cardiology 936 (2009). F. 871. In the Davidson CIMT Study, exploratory endpoints included changes in blood pressure, and the study indicated: "there were no differences between treatment groups for changes from baseline in traditional cardiovascular risk markers, including . . . blood pressures . . . ." F. 877, 878.

the San Diego Study.[16] Complaint Counsel's expert, Dr. Sacks, opined that the Ornish CIMT Study's and the Davidson BART/FMD Study's findings of no statistically significant difference in blood pressure due to POM Juice consumption undermine the credibility of the results of the Aviram ACE/BP Study and Aviram CIMT/BP Study. F. 862, 909.

Respondents counter this criticism by stating that none of Respondents' subsequent studies examined blood pressure as a primary endpoint and, as a result, one cannot conclude that there was no effect of POM Juice or POMx on blood pressure. RRB at 94; F. 864, 866, 912. In any clinical study, it is routine to record blood pressure, pulse, body temperature, among other measurements, to make sure patients are healthy. F. 842. Although blood pressure is measured in many studies, a specific claim on blood pressure requires a very specific study involving special equipment and personnel. F. 842. Thus, Dr. Heber testified, where blood pressure was not the endpoint, any results for blood pressure cannot be relied upon as negative evidence. F. 841, 912. Complaint Counsel's expert, Dr. Sacks, concedes that in subsequent studies showing no statistically significant changes in blood pressure, the absence of such evidence is not proof that there is no effect. F. 867, 911.

(c) Determination

As discussed above, the expert testimony regarding the Aviram ACE/BP Study and Aviram CIMT/BP Study is conflicting. The greater weight of the persuasive expert testimony on the studies sponsored by Respondents measuring blood pressure demonstrates that the scientific evidence relied upon by Respondents is not adequate to substantiate a claim that the POM Products treat, prevent, or reduce the risk of heart disease through reducing blood pressure, or that clinical studies show the same.

[16] The San Diego Study was published as Heber D. *et al*., *Safety and Antioxidant Activity of a Pomegranate Ellagitannin-Enriched Polyphenol Dietary Supplement in Overweight Individuals with Increased Waist Size*, J. Agric Food Chem., Vol. 55, No. 24 (2007). F. 924. The San Diego Study measured blood pressure, but this was not a primary endpoint. F. 927. The study indicated: "[t]here were no apparent treatment related changes in weight, systolic blood pressure, diastolic blood pressure, pulse rate, respirations, or temperature." F. 928.

v. Clinical trials; reducing arterial plaque

(a) About the Aviram CIMT/BP Study

In support of claims that the POM Products treat, prevent, or reduce the risk of heart disease by reducing arterial plaque, in addition to the basic science discussed above, Respondents rely on the Aviram CIMT/BP Study and the Davidson CIMT Study. RRB at 106.

Carotid intima media thickness ("CIMT") testing measures the combination of the vessel muscle and atherosclerosis (arterial plaque). F. 767. Measures of CIMT are usually relevant to cardiovascular health, and if CIMT measures show consistent improvement, this would be an indicator that a treatment may be beneficial. F. 769. However, such measures alone are not conclusive evidence that an intervention treats existing heart disease. F. 769.

In the Aviram CIMT/BP Study, a group of ten patients with severe carotid artery stenosis ("CAS") consumed 50 ml. of concentrated pomegranate juice daily for one year and five of them continued for up to three years. F. 790. A second group of nine patients who did not consume pomegranate juice acted as a control. F. 790. The results of the Aviram CIMT/BP Study showed that, in the control group that did not consume pomegranate juice, the patients' CIMT increased by 9% during one year, whereas, pomegranate juice consumption resulted in a significant CIMT reduction, by up to 30%, after one year. F. 791. The Aviram CIMT/BP Study concluded that the "results of the present study . . . suggest that [pomegranate juice] consumption by patients with CAS decreases carotid IMT and systolic blood pressure and these effects could be related to the potent antioxidant characteristics of [pomegranate juice] polyphenols." F. 797.

(b) Expert opinions on the Aviram CIMT/BP Study

Complaint Counsel's expert, Dr. Sacks, testified that a qualified scientist would not be able to conclude with any credibility that the improvements in the treatment group indicated by the Aviram CIMT/BP Study were caused by the group's consumption of pomegranate juice and not some other factor because of: the lack of a randomized, placebo-controlled group; the fact

that the patients in the active and control groups received different treatment; the small sample size; and the lack of any between-group statistical analysis. F. 798.

Dr. Ornish testified that the findings in the Aviram CIMT/BP Study suggest that oxidative stress may have been reduced by pomegranate juice consumption in these patients. F. 793. Respondents assert that the fact that the Aviram CIMT/BP Study is considered "unblinded and uncontrolled" by Complaint Counsel does not invalidate the results. RRB at 95. However, Respondents' expert, Dr. Ornish, agreed that the Aviram CIMT/BP Study was limited in scope and opined: "Thus, while not at all conclusive, the study suggests a benefit." F. 802. He further testified that the Aviram CIMT/BP Study was "very provocative and interesting and laid the groundwork for even more conclusive studies." F. 802.

(c) About the Davidson CIMT Study

The Davidson CIMT Study was an 18-month, 289-person randomized, double-blinded, placebo-controlled clinical trial conducted at two clinical research sites in accordance with good clinical practice guidelines and under a protocol approved by an institutional review board. F. 872. Participants in the Davidson CIMT Study drank eight ounces of pomegranate juice or placebo juice daily. F. 876. Adherence to product consumption was assessed at each visit by reviewing daily consumption diaries maintained by the subjects. F. 876. The protocol for the Davidson CIMT Study called for ultrasound testing of the carotid artery at baseline, at 12 months, and at 18 months. F. 877.

Among other findings, the Davidson CIMT Study indicated the following:

- Anterior and posterior wall CIMT values and progression rates did not differ significantly between treatment groups at any time point.

- The composite measurement of CIMT showed a significantly smaller value at 12 months in the pomegranate juice group compared to the control group . . . However, this difference was no longer significant at the end of the treatment period [18 months].

- Results of the present study showed no significant influence of 18 months of pomegranate juice consumption on CIMT progression in the overall study sample. However, results from *post hoc* exploratory analyses, which should be interpreted with caution, suggest that the rate

of CIMT progression may have been slowed in subgroups characterized by more rapid CIMT progression, including those with increased levels of TG-rich lipoproteins, low levels of HDL cholesterol, and greater oxidative stress.

- Whether possible benefits of pomegranate juice consumption on CIMT progression in some subgroups relate to antioxidant activity is uncertain. A lack of significant improvements in most markers of oxidative stress argues against an important role for antioxidant activity. However, specific reactive oxygen/nitrogen species may be scavenged by pomegranate unique polyphenolic hydrolysable tannins. Indeed, a subgroup for whom there was an apparent benefit was the top tertile for baseline PD – AAPH, suggesting that antioxidant effects may have played a role in the protection against CIMT progression by pomegranate juice consumption.

F. 878.

(d) Expert opinions on the Davidson CIMT Study

Complaint Counsel charges that Respondents "cherry-picked observations from the Davidson CIMT Study" by, *inter alia*, (1) relying on the results at 12 months, rather than the results at 18 months; and (2) focusing on results of an exploratory sub-group analysis performed *post hoc*. CCB at 38. Respondents rejoin that: (1) the fact that differences in the composite measurement of CIMT were not statistically significant at 18 months does not change the fact that these differences were statistically significant at 12 months; and (2) findings related to subgroups cannot be ignored merely because they were formed in a *post hoc* analysis. RRB at 94-95.

Complaint Counsel's expert, Dr. Sacks, testified that the Davidson CIMT Study is the largest of the heart studies conducted on pomegranate juice; was carefully designed, in that the protocol identified the endpoints to be measured, the procedures to be followed, inclusion and exclusion criteria, and the statistical analysis to be conducted; and that there was no evidence of critical problems in the conduct or analysis of the study (except its over-emphasis on the subgroup results). F. 884. Based on the findings of the Davidson CIMT Study (summarized above), particularly that, at the end of the study, there were no significant differences in CIMT progression rates between the subjects in the pomegranate juice and control groups, Dr. Sacks concluded that the Davidson CIMT Study is "competent and reliable evidence that

consumption of pomegranate juice did not improve CIMT in subjects with one or more cardiovascular risk factors." F. 884. Dr. Stampfer agreed and opined that that the main result from the Davidson CIMT Study provides substantial evidence *against* the hypothesis that pomegranate juice can reduce the progression of CIMT. F. 892.

Respondents' experts opine that the Davidson CIMT Study constitutes competent and reliable scientific evidence that the consumption of POM Juice is beneficial to cardiovascular health by, among other things, reducing arterial plaque. F. 885. Dr. Ornish stated that the bottom line of the Davidson CIMT Study is that pomegranate juice *did* show a statistically significant improvement in CIMT after 12 months in the measure that was most clinically relevant; the fact that these differences in CIMT measurements were not statistically significant at 18 months does not change the fact that these differences were statistically significant after 12 months. F. 888.

Dr. Ornish explained that a potential reason for lack of a change in the CIMT progression rate at 18 months was that participants in the Davidson CIMT Study may have stopped drinking the juice after 12 months. F. 890. Dr. Ornish observed that it is not unusual for patients to be less than honest in describing their compliance, as patients often describe that it is embarrassing and even humiliating to report that they have not done what they were supposed to do. F. 890. However, Dr. Davidson, who evaluated compliance with the product consumption guidelines during the Davidson CIMT Study, testified that his review of compliance diaries showed high levels of compliance with the product consumption guidelines. F. 891.

Respondents' experts also opine that the Davidson CIMT Study provides supporting evidence that there were statistically significant lower CIMT progression rates for pomegranate versus control in the subgroup of persons with higher cardiovascular disease risk factors. F. 888. The Davidson CIMT Study described the subgroup analyses as "*post hoc* exploratory analyses, which should be interpreted with caution[.]" F. 878. Respondents' experts opined that in scientific research, *post hoc* analysis is routine. F. 896.

Complaint Counsel's expert, Dr. Sacks, opined that a *post hoc* analysis is one that is conceived after the researchers have seen the data and is, thus, generally a less valid approach than one planned for in the protocol, because it is more subject to bias. F. 895. Dr. Sacks further opined: because the subgroup data is hypothesis generating only, and has not been corrected for multiple comparisons, a qualified scientist could not rely on the *post hoc* analysis of the subgroup populations as reliable scientific evidence to support claims that POM Juice or POMx prevent, reduce the risk of, or treat heart disease in the subgroup populations identified. F. 899.

(e) The Ornish CIMT Study

Complaint Counsel further charges that Respondents, in making claims that the POM Products can treat or prevent heart disease by reducing arterial plaque, discount the outcome of the Ornish CIMT Study. CCB at 38. The Ornish CIMT Study was an unpublished, randomized, double-blind, placebo-controlled 73-person study, conducted by Dr. Ornish, one of Respondents' experts in this case. F. 850. The primary endpoint of the Ornish CIMT Study was to investigate the effects of pomegranate juice on CIMT in patients with at least one cardiovascular risk factor. F. 850. The treatment group drank eight ounces of pomegranate juice concentrate daily, and the control group drank eight ounces of placebo beverage daily, for one year. F. 850. According to the Ornish CIMT Study unpublished final report, there were no significant changes in the treatment group relative to the placebo for CIMT thickness or elastic properties. F. 858.

Dr. Sacks described the results of the Ornish CIMT Study as "convincingly null, showing that pomegranate juice treatment did not improve CIMT" and opined that the Ornish CIMT Study confirmed that the purportedly positive results of Dr. Aviram's unrandomized, uncontrolled 19-patient CIMT/BP Study lacked credibility. F. 861, 862. However, Dr. Sacks admitted that the lack of statistical significance for a positive result in the Ornish CIMT Study is not proof of a negative. F. 867.

Dr. Ornish testified that the Ornish CIMT Study was an indeterminate study that cannot be relied upon; "it neither proves or disproves." F. 864. Dr. Ornish

explained that the protocol for the Ornish CIMT Study called for 200 patients, but ultimately, only 73 patients were recruited, 56 of whom completed one-year testing. F. 851. Dr. Ornish further stated: Even in this smaller group, we found improvements in right CIMT that approached statistical significance and that if these changes had been seen in a sample of 200 patients, then it would have been statistically significant. F. 857, 863. Dr. Heber observed that the Ornish CIMT Study "had inadequate power at that number of subjects," so no conclusions could be drawn from the study. F. 865.

(f) Determination

As discussed above, the expert testimony regarding the studies measuring CIMT to support Respondents' claims is conflicting. The greater weight of the persuasive expert testimony on the studies sponsored by Respondents measuring CIMT demonstrates that the scientific evidence relied upon by Respondents is not adequate to substantiate a claim that the POM Products treat, prevent, or reduce the risk of heart disease through reducing arterial plaque, or that clinical studies show the same.

vi. Clinical trials; improving blood flow

In support of claims that the POM Products treat, prevent, or reduce the risk of heart disease by improving blood flow (myocardial perfusion), in addition to the basic science discussed above, Respondents rely on the Ornish MP Study. RRB at 106.

(a) About the Ornish MP Study

In the Ornish MP Study, Dr. Ornish and his colleagues investigated whether the daily consumption of pomegranate juice for three months would affect myocardial perfusion ("MP") in 45 patients who had coronary heart disease and myocardial ischemia (narrowing of the arteries) in a randomized, placebo-controlled, double-blind study, which was subsequently published. F. 805, 808. The Ornish MP Study indicated that after three months there was a significant ($p = 0.05$) improvement of 17% in the summed differences score ("SDS")[17] in the

[17] The Ornish MP Study provides data on three imaging measures at baseline and three months for myocardial perfusion: the summed rest score, or "SRS" (imaging results before the pharmacologic or exercise challenge), the summed stress score, or "SSS" (imaging results after the pharmacologic or exercise challenge), and the summed difference score, "SDS" (calculated by subtracting the SRS from the SSS). F. 810.

POM Juice group, as compared to an average worsening of 18% in the control group. F. 811. Thus, after three months, the comparative benefit in blood flow of the pomegranate juice group to the placebo group in the Ornish MP Study was about 35 percent. F. 811. The Ornish MP Study concluded: "Although the sample in this study was relatively small, the strength of the design and the clinically significant and statistically significant improvements in myocardial perfusion observed in the experimental group over a rather short period suggest that daily consumption of pomegranate juice may have important clinical benefits in this population." F. 815.

(b) Expert opinions on the Ornish MP Study

Complaint Counsel criticizes the Ornish MP Study, *inter alia*, on the following grounds: (1) change in myocardial perfusion is not a recognized surrogate marker of therapeutic effects on coronary heart disease; (2) the Ornish MP Study indicates significant changes in only one of three measures of blood flow – in summed difference score (SDS), but not summed rest score (SRS) or summed stress score (SSS); (3) the study was designed to last 12 months, but was cut short at 3 months; (4) the study showed no improvement in other measures, such as blood pressure, cholesterol, inflammatory biomarkers, and oxidative stress; and (5) there were problems in the design and conduct of the study. Respondents' replies to each of these challenges to the adequacy of the Ornish MP Study to substantiate claims regarding improving blood flow are addressed, in order, below.

First, the Ornish MP Study measured improvements in myocardial perfusion. F. 808. Complaint Counsel's experts opined that myocardial perfusion is a research tool, but is not recognized as a surrogate marker for heart disease and is not used as the primary outcome in studies of treatment efficacy for coronary heart disease. F. 825. Dr. Sacks further opined that even where blood flow is shown to have been improved, it will not necessarily result in improved cardiovascular health, such as reductions in heart attack and stroke. F. 825. However, Dr. Sacks conceded that proper blood flow from the coronary artery and to the heart is fundamental to lowering the risk of cardiovascular disease. F. 826.

Dr. Ornish, for Respondents, opined that blood flow is essential to life, an important measure of heart disease, and the "bottom line" in coronary heart disease (along with how well the heart is pumping blood) and, thus, when researchers measure myocardial perfusion, researchers are measuring what actually matters most. F. 827. As Dr. Ornish explained, blood carries oxygen and nutrients that feed the heart. F. 828. If the blood flow to the heart (perfusion) is reduced, then the heart is no longer receiving enough blood flow to maintain itself. F. 828. Coronary heart disease, which is the most common form of heart disease, occurs when the heart does not get enough blood to fuel itself and blood carries oxygen, which is the fuel for the heart. F. 828.

In addition, Respondents' experts opined that myocardial perfusion is more closely connected as a surrogate marker for cardiovascular disease than LDL cholesterol, which has been accepted by the FDA as a surrogate marker. F. 829. Dr. Ornish explained that when a person has a biomarker such as high LDL cholesterol, which increases his or her risk, that is far away from the actual event of a heart attack, which may be affected by many other factors, such as inflammation and oxidation. F. 829. There are a number of people who have low cholesterol levels, but get heart disease. F. 829. About 50 percent of the people who die from a heart attack actually have cholesterol in the normal range. F. 829. There are people who have high cholesterol levels who do not have heart disease, and the same is true for blood pressure. F. 829.

Second, the Ornish MP Study report indicates significant changes in only one of three measures of blood flow. F. 833. Complaint Counsel's experts testified that the .05 "*p*" value of the SDS improvement is not very persuasive where, as in the Ornish MP Study, there were three possible outcome measures (SSS, SRS, and SDS), and only one just met significance. F. 833.

Responding to these criticisms, Dr. Ornish explained that he did not ignore the SRS and SSS measures, but that those were not the objective of the Ornish MP Study because they measure infarcted or dead heart tissue. F. 832, 834. SDS is derived by subtracting SRS from SSS and the finding of statistically significant changes in SDS confirmed what the researchers

were hoping to find -- an improvement in blood flow to the heart when compared to rest and stress. F. 832, 834.

Complaint Counsel's experts also opined that there was a large discrepancy between the pomegranate juice and the control groups in the baseline values of SRS and SSS, the two components of the SDS. F. 835. The control group's baseline values were worse than those of the pomegranate group, and, thus, it could be predicted that the control group, having worse coronary perfusion than the pomegranate group at baseline, would have a more accelerated form of the disease and show worsening on follow-up, according to Dr. Sacks. F. 836.

Dr. Ornish explained that there was a difference in SSS at baseline, but no statistically significant differences in SRS or SDS. F. 837. Dr. Ornish further testified that the Ornish MP Study employed an "analysis of variance," which took into account any baseline differences. F. 837.

Third, the Ornish MP study was originally designed to last 12 months, with measurements at baseline, 3 months, and 12 months. F. 843. Complaint Counsel charges that the study was cut short when the three-month data came in favorably and Dr. Ornish faced cost overruns. CCB at 39. Dr. Sacks opined that the shortened study period and failure to report the planned duration are inconsistent with widely-accepted standards for conduct of clinical trials and undermine any confidence in the findings. F. 843.

Dr. Ornish testified that the Ornish MP Study was terminated after three months only because the Resnicks did not provide the funding that they had previously committed to this study, not because the *p*-value was statistically significant at three months. F. 844. Dr. Ornish further opined that while he did not have 12 months of follow-up data, this does not reduce the confidence in the three-month findings of the Ornish MP Study. F. 844.

Fourth, Complaint Counsel's expert criticized the Ornish MP Study on the additional basis that blood pressure, cholesterol, inflammatory biomarkers, and oxidative stress were not improved. F. 838. Dr. Ornish himself concluded that "blood pressure . . . did not improve" in the Ornish MP Study. F. 839. However, Dr. Ornish explained, the fact that other factors such as blood pressure and cholesterol did not improve does not in any way provide evidence that

pomegranate juice was not beneficial, as its effects may have been mediated via other pathways. F. 840.

Fifth, Complaint Counsel's experts point out various other problems in the design and conduct of the study, including providing data on only 39 of the 41 patients and unblinding of 6 patients mid-way through the Ornish MP Study. F. 820, 824. In trial testimony and in his expert report, Dr. Ornish acknowledged that "some problems" occurred during the Ornish MP Study that were not "optimal," but opined that the difference in SDS remained statistically significant and, therefore, the conclusions of the study remain valid. F. 819, 821.

Complaint Counsel's expert, Dr. Sacks, concluded, "the interpretation of [the Ornish MP] study that is most consistent with the principles of clinical study design and conduct is that the treatment had no effect on any measure of cardiac health" and that experts in the field of cardiovascular disease would not consider the Ornish MP Study to support the proposition that pomegranate juice provides a heart disease benefit. F. 845.

Respondents' expert, Dr. Ornish, the author of the study, concluded that the Ornish MP Study constitutes credible and reliable science showing that pomegranate juice lessens the risk of cardiovascular problems; that in people who have already had heart disease, it improves blood flow and reverses the progression of heart disease; and if you can begin to reverse a disease, it would only make sense that pomegranate juice would work even better to help prevent heart disease in the first place. F. 847.

(c) Determination

As discussed above, the expert testimony regarding the Ornish MP Study is conflicting. The greater weight of the persuasive expert testimony on the Ornish MP Study demonstrates that the scientific evidence relied upon by Respondents is not adequate to substantiate a claim that the POM Products treat, prevent, or reduce the risk of heart disease through improving blood flow, or that clinical studies show the same.

c. Conclusion

Having fully considered and weighed all the evidence and the conflicting expert testimony on Respondents' basic science and clinical trials, the greater weight of the persuasive expert testimony demonstrates that there is insufficient competent and reliable scientific evidence to substantiate a claim that the POM Products treat, prevent, or reduce the risk of heart disease, by lowering blood pressure, reducing arterial plaque and/or increasing blood flow to the heart, or are clinically proven to do so. F. 962. Accordingly, Complaint Counsel has met its burden of proving that Respondents' substantiation was inadequate to make the implied heart disease claims found to have been made in this case, and that, therefore, such claims were false or misleading.

4. Substantiation for Respondents' prostate cancer claims

a. Overview

As discussed in Section III.E.2.d, *supra*, the evidence demonstrates that Respondents disseminated advertisements that impliedly represented that the POM Products are clinically proven to treat, prevent, or reduce the risk of prostate cancer, by prolonging prostate-specific antigen ("PSA") doubling time. Complaint Counsel contends that (1) Respondents did not possess and rely upon a reasonable basis to substantiate their efficacy claims that the POM Products treat, prevent, or reduce the risk of prostate cancer; and (2) clinical studies, research, and/or trials do not prove Respondents' establishment claims that the POM Products treat, prevent, or reduce the risk of prostate cancer. CCB at 44-50. With respect to claims made about prostate cancer, although Respondents have been found to have made establishment claims only, by virtue of their very nature, the advertisements containing establishment claims also make the efficacy claims that are challenged as unsubstantiated in the Complaint. CCB at 31.

i. Summary of expert opinions

In support of its position, Complaint Counsel submitted the expert report and testimony of Dr. James Eastham and Dr. Stampfer. Dr. Eastham is Chief of Urology, Department of Surgery, and Director of Clinical Research, Urology Department at Memorial Sloan Kettering

Cancer Center. F. 200. He is a board-certified urological surgeon who has treated more than 2,000 patients with prostate cancer and has extensive experience, including as an investigator, in the design and conduct of clinical trials studying prostate cancer. F. 200, 201. Dr. Eastham is an expert in the fields of urology, including the prevention and treatment of prostate cancer, as well as clinical testing related to the prevention and treatment of prostate cancer. F. 204. Dr. Stampfer has participated in research investigating risk factors (including food intake and dietary factors) associated with prostate cancer. F. 183. An expert in nutrition, including its relation to the prevention and treatment of prostate cancer, and clinical testing related to the prevention of prostate cancer, Dr. Stampfer also reviewed Respondents' prostate cancer research and provided his independent opinion. F. 190.

Dr. Eastham and Dr. Stampfer state that to support claims that the POM Products prevent prostate cancer, or that they have been clinically proven to do so, experts in the field of prostate cancer would require at least one well-designed, randomized, double-blind, placebo-controlled clinical trial involving an appropriate sample population and endpoint. F. 626, 648. Dr. Eastham opined that the appropriate sample population for a cancer prevention trial "would involve more than 10,000 healthy men, ages 50 to 65, having no sign of prostate cancer." F. 1092. Dr. Eastham also testified that "[a] prostate cancer prevention study must be conducted over a long enough period of time to see an effect over time." F. 1093. Dr. Eastham states that "[t]he primary endpoint in a prostate cancer prevention trial for measuring whether a product has been effective is the prevalence or incidence of prostate cancer between the treatment and placebo groups at the conclusion of the study." F. 1089.

Dr. Eastham and Dr. Stampfer also state that to support claims that the POM Products treat prostate cancer, or that they have been clinically proven to do so, experts in the field of prostate cancer would require a randomized, placebo-controlled, double-blind clinical trial with an appropriate sample population and endpoint. F. 626, 648. Dr. Eastham and Dr. Stampfer further opine that PSA doubling time is not recognized by experts in the field as a surrogate endpoint in prostate cancer clinical trials. F. 1100.

Complaint Counsel's experts concluded that evidence relied upon by Respondents does not constitute adequate substantiation for claims that the POM Products treat, prevent, or

reduce the risk of prostate cancer or have been clinically proven to do so. F. 1019, 1086-1094, 1096-1099.

In support of their position that they possessed and relied upon a reasonable basis to substantiate their claims, Respondents submitted the expert reports and testimony of Dr. David Heber and Dr. Jean deKernion. Dr. Heber is a practicing physician, Professor of Medicine and Public Health at UCLA, and the Director of the UCLA Center for Human Nutrition. F. 221, 222. Dr. Jean deKernion is the Chairman of the Department of Urology and Senior Associate Dean for Clinical Affairs at the UCLA School of Medicine and served as the Dean of Urology at the UCLA School of Medicine for twenty-six years. F. 251. Dr. deKernion is also a practicing urologist certified by both the American Board of Surgery and the America Board of Urology. F. 250.

Dr. Heber reviewed Respondents' science in the area of prostate cancer and testified at trial that there is competent and reliable science showing that POM Juice and POMx Pills lengthen the PSA doubling time for men who have had prostate cancer and, thus, it is likely for those men to have a deferred recurrence or death from that disease; and that POM Juice and POMx Pills are likely to lower the risk of prostate problems for men who have not yet been diagnosed with prostate cancer. F. 1120. Dr. Heber's expert report, however, was more limited than his trial testimony, opining: the statistically significant prolongation of PSA doubling time, coupled with corresponding laboratory effects on prostate cancer *in vitro* cell proliferation and apoptosis [programmed cell death], as well as oxidative stress and inflammation, provides strong scientific rationale for the statement that pomegranate juice promotes prostate "health." F. 1121.

Dr. deKernion testified that the POM Products are beneficial to prostate health. F. 1124. Dr. deKernion opined that although there is not 100% proof that the POM Products reduce the risk of prostate cancer, the same mechanism shown in the *in vitro* and animal studies and in the Pantuck and Carducci human studies (discussed below) showed, with a "high degree of probability," that POM Juice and POMx would inhibit the clinical development of prostate cancer in men who have not been diagnosed with that disease. F. 1124. Dr. deKernion

testified also that there is a high probability that the POM Products provide a special benefit to men with detectable PSA after radical prostatectomy. F. 1125.

ii. Standard for substantiation

Having fully considered and weighed the evidence adduced at trial, the evidence demonstrates that competent and reliable scientific evidence is required to support claims that the POM Products treat, prevent, or reduce the risk of prostate cancer, or that they have been clinically proven to do so. *See* F. 963-966. Based on the greater weight of the persuasive evidence from the experts at trial, to support claims that the POM Products treat, prevent, or reduce the risk of prostate cancer, or that they are clinically proven to do so, competent and reliable evidence must include clinical studies, although not necessarily RCTs, that show that the POM Products did treat, prevent, or reduce the risk of prostate cancer. *See id*. As analyzed below, Complaint Counsel has demonstrated that Respondents did not possess adequate competent and reliable scientific evidence to substantiate the implied claims that the POM Products treat, prevent, or reduce the risk of prostate cancer or that clinical tests show the same. Complaint Counsel has, therefore, met its burden of proving that Respondents' claims are false or misleading. *See QT,* 448 F. Supp. 2d at 959.

b. Scientific evidence relied upon

i. *In vitro* and *in vivo* studies

The mechanism by which pomegranates promote prostate health is through potent antioxidant and antiatherosclerotic properties[18] attributed to pomegranates' high content of polyphenols, including ellagic acid and tannins. F. 725. Ellagic acid and tannins have been shown to exhibit *in vitro* and *in vivo* anticarcinogenic properties, such as induction of cell cycle arrest and apoptosis, as well as the inhibition of tumor formation and growth in animals. F. 990. *In vivo* research has demonstrated that pomegranate polyphenols reduce inflammation in prostate tumors. F. 995. *In vitro* and *in vivo* research has also demonstrated that in tumors treated with pomegranate extract, the nuclear factor-*kappa*B decreased (see below), thereby causing decrease of tumor growth. F. 1007.

[18] Atherosclerosis is a buildup of plaque in arteries. F. 988.

Working from these foundations, Respondents sponsored several *in vitro* and animal studies to examine the effect of POM Juice and POMx Pills on prostate health. F. 1010. Detailed findings of fact on these studies are set forth in Section II.H.3, *supra*. In summary, in this pre-clinical research, which studied human prostate cancer cells in the lab and inside of mouse models, POM Juice was found to inhibit cancer cell growth, promote prostate cell death, and inhibit the inflammatory process, which is correlated with the growth of cancer. *See id*.

For example, in a study titled, "*Pomegranate Ellagitannin-Derived Metabolites Inhibit Prostate Cancer Growth and Localize to the Mouse Prostate Gland*," Dr. David Heber and colleagues evaluated the effects of pomegranate extract on prostate cancer growth in severe combined immunodeficient mice injected with human prostate cancer cells. F. 1014. The study showed that pomegranate extract significantly inhibited prostate cancer in the mice, as compared to the control. F. 1014. Researchers also found that ellagic acid and synthesized urolithins from the pomegranate extract were shown to inhibit the growth of human prostate cancer cells *in vitro*. F. 1014. The researchers concluded that the chemopreventive potential of pomegranate ellagitannins and localization of their bioactive metabolites in mouse prostate tissue *suggest* that the pomegranate *may play a role* in prostate cancer treatment and chemoprevention. F. 1014 (emphasis added). The researchers also stated that "[t]his warrants future human tissue bioavailability studies and further clinical studies in men with CaP [prostate cancer]." F. 1014.

Another study by Dr. Rettig and Dr. Heber, et al., titled, "*Pomegranate extract inhibits androgen-independent prostate cancer growth through a nuclear factor-kappaB-dependent mechanism*," evaluated POMx Pills and POM Juice and found that their consumption was linked to reduction in cancer growth and decreased plasma PSA levels. F. 1016. The study found that one of the most well-established signaling pathways mediating inflammatory responses relevant to cancer is the nuclear factor-*kappa*B ("NF-*k*B") pathway, which serves as a predictor for recurrence of prostate cancer after radical prostatectomy, and that POMx inhibited NF-*k*B and cancer cell viability in a dose response fashion *in vitro* and in a human LAPC4 prostate cancer xenograft mouse model. F. 1016. Based on the results, the researchers concluded "that pomegranate juice *could have potential* as a dietary agent to prevent the

emergence of androgen-independence," thus, potentially prolonging life expectancy of prostate cancer patients, and suggested "that this may be a high priority area for future clinical investigation." F. 1016 (emphasis added).

As testified to by Dr. deKernion, Respondents' *in vitro* and animal studies showed that pomegranate juice inhibited the growth of prostate cancer cells and actually killed cancer cells from humans that had been inserted into mice. F. 1020. However, as Dr. deKernion also testified, and Complaint Counsel's experts concurred, one cannot always extrapolate from *in vitro* and animal results to what the results would be in humans. F. 1022. Experts in the field agree that even where the animal and *in vitro* evidence is strong and shows that an agent's mechanism of action works, this evidence alone does not prove that an agent works in humans and, thus, does not show that the POM products treat, prevent, or reduce the risk of prostate cancer. F. 1024.

ii. Clinical trials

Respondents have sponsored one human clinical study, which is completed and published, and one human clinical study that is not yet published. F. 1025. The published study, titled, *Phase II Study of Pomegranate Juice for Men with Rising Prostate-Specific Antigen Following Surgery or Radiation for Prostate Cancer* by Pantuck, et. al, was published in the journal Clinical Cancer Research in 2006. ("Pantuck Study"). F. 1030. The ongoing human clinical study, by Dr. Michael A. Carducci, is completed, and an abstract summarizing the results has been published, but a final, peer-reviewed study report had not been published at the start of trial in this matter. The abstract is titled, *A Phase II Study of Pomegranate Extract for Men with Rising Prostate-Specific Antigen Following Primary Therapy*, J Clin Oncol 29: 2011 (suppl 7; abstr 11) ("Carducci Study"). Detailed findings of fact on the Pantuck Study and the Carducci Study are set forth in Section II.H.4, *supra*, and summarized here.

(a) The Pantuck Study

The Pantuck Study was conducted by Dr. Allan Pantuck, an Associate Professor of Urology at UCLA Medical School who maintains a clinical practice at UCLA. F. 1026. Dr. Pantuck's study was the first clinical trial of pomegranate juice in patients with prostate cancer.

F. 1036. According to the published study report, the Pantuck Study was "an open-label, single-arm [one treatment group] clinical trial," meaning it was not an RCT and did not have a placebo group. F. 1037. The Pantuck Study included 46 patients who had been diagnosed with prostate cancer. F. 1039. All 46 patients in the Pantuck Study drank eight ounces of pomegranate juice daily and had their blood drawn every three months to have their PSA determined. F. 1043. The presence of detectable PSA after radical prostatectomy or other radical treatment usually indicates cancer is present. F. 1041. PSA doubling time ("PSADT") is a mathematical expression of the rapidity with which the prostate specific antigen is rising, and an expression of the rapidity of growth and number of prostate tumor cells. F. 1042.

Patients in the Pantuck Study who consumed POM Juice experienced a statistically significant increase in PSADT, when compared to their own baseline pre-treatment PSADT. F. 1044. In the Pantuck Study, the average pre-treatment PSADT before intervention was approximately 15 months, and after 33 months, the average post-treatment PSADT was approximately 54 months. F. 1054. Thus, mean PSADT significantly increased from a mean of 15 months at baseline to 54 months post-treatment. F. 1045. The Pantuck Study concluded that the statistically significant prolongation of PSA doubling time, coupled with corresponding laboratory effects on prostate cancer *in vitro* cell proliferation and apoptosis, as well as oxidative stress, warrant further testing in a placebo-controlled study. F. 1047.

In 2008, Dr. Pantuck presented a follow-up report and released the abstract titled, Pantuck, AJ, et al., "*Long term follow up of pomegranate juice for men with prostate cancer and rising PSA shows durable improvement in PSA doubling times*," American Society of Clinical Oncology ("Pantuck Phase II Follow-Up Results"), which summarized follow-up results for the Pantuck Study. F. 1048. According to the published abstract, fifteen active patients (31%) remained on the study. F. 1049. All of the men who had dropped out of the Pantuck Study did so because their PSA had increased. F. 1049. The Pantuck Phase II Follow-Up Results stated that those who continued on pomegranate juice maintained a lengthening of their PSA doubling time compared to men who did not continue on pomegranate juice. F. 1050. The Pantuck Phase II Follow-Up Results found that long-term follow up of pomegranate juice consumption in men with prostate cancer and rising PSA following primary therapy demonstrates a durable increase in PSA doubling time and concluded that a multi-

center, randomized phase III study is ongoing to further evaluate the benefits of pomegranate in a placebo-controlled manner. F. 1052.

When the Pantuck Study report was released in 2006, Dr. Pantuck was quoted in an American Association for Cancer Research press release, as stating: "[w]e don't believe we are curing anyone from prostate cancer." F. 1054. He pointed out that "although a third of patients experienced a decrease in PSA during the study, nobody's PSA went to zero." F. 1054. Dr. Pantuck further explained: "The PSA doubling time, however, was longer. For many men, this may extend the years after surgery or radiation that they remain recurrence free and their life expectancy is extended." F. 1054.

(b) The Carducci Study

The Carducci Study was conducted by Dr. Michael Carducci, a Professor of Oncology and Urology at the Johns Hopkins University School of Medicine, in Baltimore, Maryland. F. 1065. Dr. Carducci has conducted 40 to 50 clinical trials relating to prostate cancer and has published approximately 80 articles related to prostate cancer. F. 1067.

In 2006, Dr. Carducci began working with Respondents to design the Carducci Study. F. 1068. Dr. Carducci submitted a proposed protocol for the Carducci Study to Respondents for a larger randomized three-arm (three groups) study, with two treatment arms and one placebo arm. F. 1068. Respondents conducted a cost and feasibility analysis and decided that the study proposed by Dr. Carducci was too costly, and, thus, the placebo arm was dropped from the study. F. 1069. The Carducci Study began in January 2008. F. 1070. In 2011, Dr. Carducci presented the abstract of his clinical research study titled, "*A Phase II Study of Pomegranate Extract for Men with Rising Prostate-specific Antigen Following Primary Therapy*" at the disease specific meeting of the American Society of Clinical Oncology ("Carducci abstract"). F. 1072.

The Carducci Study was a multi-center, double blind Phase II randomized trial that studied the effect of two different doses of POMx Pills (one or three capsules) on PSADT in men who had received initial therapy for prostate cancer. F. 1070. One hundred and four (104) men were enrolled and treated for up to six months (92%), 12 months (70%), and 18 months

(36%). F. 1075. PSA levels were obtained every three months. F. 1074.

The Carducci abstract stated: median PSADT lengthened from 11.9 months at baseline to 18.5 months after treatment, a within group measurement, which showed that POMx treatment significantly increased the PSA doubling time by over six months in both treatment arms. F. 1076. There was no significant treatment difference in PSADT between the group who took one capsule and the group who took three capsules of POMx. F. 1075. The Carducci abstract also stated that 13 patients (13%) had declining PSA levels during the study. F. 1077. The Carducci abstract concluded that POMx demonstrates "promising antitumor effects in prostate cancer." F. 1078.

(c) Expert Opinions of the Pantuck and Carducci Studies

Complaint Counsel's experts, Dr. Eastham and Dr. Stampfer, opined that the Pantuck Study and Carducci Study do not constitute adequate substantiation for Respondents' claims that the POM Products treat, prevent or reduce the risk of prostate cancer, for a number of reasons, including: (1) the studies lacked a placebo-control group; (2) PSA doubling time is not a valid endpoint; (3) the studies do not assess whether the POM Products prevent prostate cancer; and (4) the results of the Pantuck Study on POM Juice cannot be used to support claims made about POMx Pills. Respondents' replies to each of these challenges to the adequacy of Respondents' substantiation are addressed, in order, below.

First, the Pantuck Study and Carducci Study did not have a placebo-control group. F. 1037, 1069, 1070. Complaint Counsel's experts opined that without a control group, it is not possible to conclude that the POM Products alone had an effect on the patients' PSA. F. 1087, 1088, 1096. Respondents' expert, Dr. deKernion testified that in both the Pantuck Study and the Carducci Study, the control was the previous PSA doubling time prior to treatment. F. 1115. The researchers measured the doubling time before patients took POM Juice or POMx and then measured doubling time afterwards, comparing one to the other. F. 1115. Dr. deKernion further testified that a control arm is often used to control for the placebo effect and that the use of a placebo group is more important when you have a subjective reporting (such as level of pain), as opposed to an objective reporting (such as PSADT). F. 1116, 1117.

However, Dr. deKernion also acknowledged that without a placebo, one cannot be certain that the effect on PSA doubling time seen in the Carducci Study is attributable to POMx. F. 1118. Furthermore, Dr. Pantuck testified that the lack of a "blinded control" group was the "greatest limitation" of his study, and Dr. Carducci testified that without a placebo, he cannot be sure that the effect on PSADT observed in the Carducci Study is attributable to POMx.[19] F. 1060, 1083.

Second, the Pantuck Study and the Carducci Study used mean PSA doubling time as the primary endpoint. F. 1040, 1070. The expert testimony on the validity of PSA doubling time as a primary endpoint is conflicting. Complaint Counsel's experts, Dr. Stampfer and Dr. Eastham, both criticized this method, opining that it is unknown if PSADT predicts overall survival in prostate cancer patients throughout its range, PSADT is not a surrogate for overall survival, and PSADT is not a relevant surrogate marker for prostate cancer prevention. F. 1089, 1097. However, Dr. Stampfer also testified that PSA doubling time is a "predictor of disease and mortality" and that, if the extension of PSA doubling time is true, it would substantially prolong lives. F. 1104. Dr. Eastham, too, offered a contradictory opinion to his opinion at trial in an article wherein he concluded, "PSADT is an important prognostic marker in men with biochemical failure after local therapy for prostate cancer, and it predicts the probable response to salvage radiotherapy, progression to metastatic disease and prostate cancer specific death." F. 1102.

Respondents' expert, Dr. Heber, testified that PSA doubling time is a "very important clinically utilized marker of clinical status." F. 1112. *See also* F. 1113 (Dr. Heber testifying that there is a lot of support from the urological community to get the FDA to accept PSA doubling time as a surrogate endpoint). Dr. deKernion testified that given the understanding of PSA doubling time in predicting risk of clinical recurrence and to some extent survival, it is logical to use changes in PSADT as indicative of an intervention's effectiveness regarding prostate tumor behavior. F. 1110. Dr. deKernion also acknowledged, however, that PSA

[19] In addition, the Carducci Study showed no difference between a one pill dose and a three pill dose. Complaint Counsel's expert, Dr. Stampfer, testified that the lack of a dose response, despite a three-fold difference in dosage, does not support a causal relationship between POMx and change in PSADT. F. 1075.

doubling time is not accepted by experts in the field of prostate cancer as a surrogate endpoint for clinical benefit in chemotherapy trials. F. 1111.

As testified to by Dr. Pantuck, "[i]t remains controversial whether modulation of PSA levels represents an equally valid clinical end point." F. 1059. On the one hand, Dr. Pantuck testified that "PSA has not been validated prospectively as a surrogate endpoint for a meaningful prostate cancer outcome." F. 1059. On the other hand, Dr. Pantuck stated that "although PSA changes are thought to be prognostically important, it is based on level 2 evidence, and nobody has ever shown conclusively that changes in PSA kinetics arising from therapeutic intervention is meaningful." F. 1059. Dr. Carducci's testimony on this point also underscores this conflict. While Dr. Carducci testified that the use of PSA doubling time as a primary endpoint to determine if POMx has an effect on the disease state was a scientifically valid way to conduct the Carducci Study, he also acknowledged that PSA doubling time as a marker or surrogate has not been proven and that the endpoint of PSA doubling time is not a standard for regulatory approval of drugs at the FDA level. F. 1079, 1080.

There are no studies proving that changing the rate of PSA doubling time changes the natural history of prostate cancer by delaying the development of metastases or death from the disease. F. 1131. Experts in the field of prostate cancer agree that PSADT is not an accepted surrogate endpoint for survival or prostate cancer-specific mortality in prostate cancer treatment clinical trials. F. 1134. Although this Initial Decision does not require Respondents to meet FDA standards for clinical trials to substantiate claims about a food or food-derived product that is safe and not being sold as an alternative to medical treatment, because the use of PSA doubling time as a valid endpoint is controversial, this factors into evaluating the adequacy of Respondents' substantiation.

Third, Complaint Counsel's experts point out that the clinical studies examining the effect of the POM Products on prostate cancer have been conducted on men who either have prostate cancer, or have been treated for prostate cancer and have experienced a biochemical recurrence. F. 1039, 1070. Because the Pantuck Study and Carducci Study were designed as treatment studies, Dr. Eastham and Dr. Stampfer opine that there is no competent and reliable

scientific evidence supporting a claim that the POM Products prevent prostate cancer. F. 1091, 1099.

Respondents' expert, Dr. deKernion, explained that in order to show an effect of POM Products on prostate cancer, the best way to do that research is on patients whose prostate had been removed, because the presence of PSA elevation is almost always an indication of remaining cancer. F. 1122. Dr. deKernion further opined that although there is not proof that POM Products reduce the risk of prostate cancer, the same mechanism shown in the *in vitro* and animal studies and in the Pantuck and Carducci human studies showed, with a "high degree of probability," that POM Juice and POMx would inhibit the clinical development of prostate cancer in men who have not been diagnosed with that disease and that POM Juice and POMx could possibly play a role in preventing them from getting prostate cancer. F. 1124; *see also* F. 1123.

Dr. Pantuck acknowledged that the Pantuck Study did not prove that pomegranate juice prevents or reduces the risk of prostate cancer because all the patients in the study already had prostate cancer and, thus, his study did not address anything related to causation. F. 1055. Dr. Carducci similarly testified that the Carducci Study was never designed to prove, and did not prove, that POMx prevents or reduces the risk of prostate cancer. F. 1084.

Fourth, Complaint Counsel's experts state that the Pantuck Study on POM Juice cannot provide reliable evidence to support claims about POMx Pills' benefit for prostate cancer. F. 1094. According to Dr. Eastham: POM Juice is not identical to POMx Pills and POMx Liquid; POM Juice has more than one active ingredient; processing may result in eliminating a needed ingredient; and even if the active ingredient is known and the alternate compound contains the same amount of active ingredient, the alternate compound may contain some other as yet unknown compound that might counter-act the benefit of the active agent. F. 1094. However, Dr. Eastham is not an expert in bioavailability and did not review the equivalency studies or articles on POM Juice, POMx Pills or POMx Liquid. F. 1095.

Dr. Heber, the only expert who opined on the bioavailability of pomegranate polyphenols, explained that because both the 100% Juice and POMx contain ellagitannins that

contribute to the antioxidant activity of the products (and because both are bioavailable (absorbed) in humans), there is no difference in the antioxidant effect between POM Juice and POMx products in laboratory studies. F. 953, 1119. Dr. Heber testified that in laboratory studies he conducted, he found no difference in the antioxidant effect between POM Juice and POMx products and that animal studies indicate that the effects of pomegranate juice and POMx Pills on prostate cancer are equivalent. F. 1119. Moreover, the Carducci Study obtained a result similar to the Pantuck Study regarding the effect of POMx on PSADT. *Compare* F. 1076 *with* F. 1045.

c. Conclusion

As discussed above, the expert testimony regarding the studies relied upon by Respondents is conflicting. The greater weight of the persuasive expert testimony demonstrates the following: The basic research, the Pantuck Study, and the Carducci Study, relied on by Respondents, support the conclusion that pomegranate juice has a beneficial effect on prostate health. F. 1142. Competent and reliable scientific evidence supports the conclusion that the consumption of pomegranate juice and pomegranate extract supports prostate health, including by prolonging PSA doubling time in men with rising PSA after primary treatment for prostate cancer. F. 1142. However, the greater weight of the persuasive expert testimony shows that the evidence relied upon by Respondents is not adequate to substantiate claims that the POM Products treat, prevent, or reduce the risk of prostate cancer or that they are clinically proven to do so. F. 1143. Indeed, the authors of the Pantuck Study and the Carducci Study each testified that their study did not conclude that POM Juice treats, prevents, or reduces the risk of prostate cancer. F. 1055, 1056, 1084, 1085. And, as Respondents' expert conceded, no clinical studies, research and/or trials show definitively that the POM Products treat, prevent, or reduce the risk of prostate cancer. F. 1135-1138.

Having fully considered and weighed all the evidence and the conflicting expert testimony on Respondents' basic research and clinical trials, the greater weight of the persuasive expert testimony demonstrates that there is insufficient competent and reliable scientific evidence to substantiate a claim that the POM Products treat, prevent, or reduce the risk of prostate cancer or that clinical studies, research, and/or trials prove that the POM

Products treat, prevent, or reduce the risk of prostate cancer. F. 1143. Accordingly, Complaint Counsel has met its burden of proving that Respondents' substantiation was inadequate to make the implied prostate cancer claims found to have been made in this case, and that, therefore, such claims were false or misleading.

5. Substantiation for Respondents' erectile dysfunction claims

a. Overview

As discussed in Section III.E.2.e, *supra*, the evidence demonstrates that Respondents disseminated advertisements that impliedly represented that drinking eight ounces of POM Juice daily, or taking one POMx Pill daily, is clinically proven to treat, prevent or reduce the risk of erectile dysfunction. Complaint Counsel contends that (1) Respondents did not possess and rely upon a reasonable basis to substantiate their efficacy claims that the POM Products treat, prevent, or reduce the risk of erectile dysfunction; and (2) clinical studies, research, and/or trials do not prove Respondents' establishment claims that the POM Products treat, prevent, or reduce the risk of erectile dysfunction. CCB at 50-54. With respect to claims made about erectile dysfunction, although Respondents have been found to have made establishment claims only, by virtue of their very nature, the advertisements containing establishment claims also make the efficacy claims that are challenged as unsubstantiated in the Complaint. CCB at 31.

i. Summary of expert opinions

In support of its position, Complaint Counsel submitted the expert report and testimony of Dr. Arnold Melman, M.D., a Professor and Chairman of the Department of Urology at the Albert Einstein College/Montefiore Medical Center in New York. F. 208. Dr. Melman has extensive experience in designing and reviewing protocols for clinical trials. F. 209. Dr. Melman is an expert in the evaluation of whether a product treats, prevents, or reduces the risk of erectile dysfunction, and in the design and conduct of clinical trials involving erectile dysfunction. F. 211. Dr. Melman opined that to constitute a reasonable basis for the claims that the POM Products treat, prevent, or reduce the risk of erectile dysfunction, or have been clinically proven to do so, at least one well-designed, human RCT involving several investigatory sites is required. F. 654. Dr. Melman also opined that a well-designed, human

RCT must use a validated tool for measuring treatment outcomes and that the clinical trial must have a total sample population large enough to produce clinically significant results and a statistical significance of $p < 0.05$. F. 655.

Dr. Melman's opinions are attenuated for several reasons. Although Dr. Melman testified that the Global Assessment Questionnaire ("GAQ") is not a validated measure for assessing erectile function, Dr. Melman had not heard of the term "GAQ" prior to forming his opinions in this case. F. 1196, 1233, 1234. Also, although Dr. Melman testified that Respondents are required to conduct RCTs before making erectile dysfunction claims about the POM Products, Dr. Melman has made claims about a gene transfer therapy for erectile dysfunction called "hMaxi-K," which he patented and hoped to market, based on an animal study and one study of 11 men. F. 659, 660, 1237. In addition, Dr. Melman testified that a study to support a treatment for erectile dysfunction must show that a man can complete intercourse to orgasm. F. 659.

In support of their position that they possessed and relied upon a reasonable basis to substantiate their claims, Respondents submitted the expert reports and testimony of Dr. Arthur Burnett and Dr. Irwin Goldstein. Dr. Burnett is an expert in the area of erectile health, a Professor of Urology at the Johns Hopkins University School of Medicine/Johns Hopkins Hospital, and is well-known for his groundbreaking work on nitric oxide. F. 234, 238, 239. Dr. Burnett has treated between 10,000 and 15,000 patients for erectile dysfunction. F. 237. Dr. Burnett opined that Respondents' basic scientific and clinical evidence supports the conclusion that pomegranate juice's high antioxidant content improves erectile health and function by increasing the level and preservation of nitric oxide. F. 242. Dr. Burnett also concluded that a safe pure fruit juice, like pomegranate juice, which is not used as a substitute for proper medical treatment, does not require RCTs to substantiate erectile health claims. F. 683, 684.

Dr. Irwin Goldstein is an expert in sexual medicine who opined on the impact of pomegranate juice, antioxidants, and nitric oxide on erectile function and dysfunction. F. 243, 247. Dr. Goldstein is a board certified urologist and sexual medicine physician who has been involved in sexual medicine clinical practice, clinical research, and basic research since 1980.

F. 243, 244. Dr. Goldstein testified that competent and reliable scientific evidence fully supports the conclusion that pomegranate juice produces a benefit to proper and effective erectile function. F. 249. Dr. Goldstein opined that RCT studies are not required to substantiate claims that pomegranate juice can aid in erectile health and that *in vitro* and animal studies demonstrated a likelihood that pomegranate juice improves erectile health. F. 686. Dr. Goldstein also opined that the consumption of pomegranate juice is a logical option for men who are not responsive to conventional drugs or who are unwilling to consider invasive or mechanical therapies for treatment of their erectile dysfunction. F. 1307, 1308.

ii. Standard for substantiation

Having fully considered and weighed the evidence adduced at trial, the evidence demonstrates that competent and reliable scientific evidence is required to support claims that the POM Products treat, prevent, or reduce the risk of erectile dysfunction or that they have been clinically proven to do so. *See* F. 1144-1148. Based on the greater weight of the persuasive evidence from the experts at trial, to support claims that the POM Products treat, prevent, or reduce the risk of erectile dysfunction, competent and reliable evidence must include clinical studies, although not necessarily RCTs, that show that the POM Products did treat, prevent, or reduce the risk of erectile dysfunction. *See id*. As analyzed below, Complaint Counsel has demonstrated that Respondents did not possess adequate competent and reliable scientific evidence to substantiate the implied claims that the POM Products treat, prevent, or reduce the risk of erectile dysfunction or that clinical tests show the same. Complaint Counsel has, therefore, met its burden of proving that Respondents' claims are false or misleading. *See QT*, 448 F. Supp. 2d at 959.

b. Scientific evidence relied upon

The mechanism by which pomegranates promote erectile health and function is through potent antioxidant components and the impact on nitric oxide, which is of "paramount importance" to good erectile health and function and is the key molecule that governs penile erections. *See* F. 1165-1184. Detailed findings of fact on Respondents' six *in vitro* and *in vivo* studies and one human clinical study are set forth in Section II.I.3, *supra*. Respondents' studies demonstrate the potential benefits of pomegranate juice on erectile health and function.

F. 1310, 1312. These studies do not, however, show that the POM Products treat, prevent, or reduce the risk of erectile dysfunction or show that clinical tests demonstrate that the POM Products treat, prevent, or reduce the risk of erectile dysfunction. F. 1313, 1314.

i. *In vitro* and *in vivo* studies

Dr. Louis Ignarro is highly respected and won a Nobel prize for his discoveries concerning nitric oxide ("NO"). F. 1292, 1297. He conducted an *in vitro* study to evaluate pomegranate juice's capacity to protect NO against oxidative destruction. F. 1292. Based on his findings, Dr. Ignarro concluded that pomegranate juice possesses potent antioxidant activity that results in marked protection of NO against oxidative destruction, thereby resulting in augmentation of the biological actions of NO. F. 1293, 1294. Other studies show similar results. *See* Section II.I.3, *supra*. For example, using an animal model, Dr. Kazem Azadzoi and colleagues found that, due to high antioxidant capacity, long-term pomegranate juice intake increased intracavernosal blood flow in the penis, improved erectile responses, improved smooth muscle relaxation, and decreased erectile tissue fibrosis. F. 1275-1279. In addition to these *in vitro* and *in vivo* studies, multiple other significant scientific studies exist that not only demonstrate the antioxidative powers of pomegranates in enhancing and preserving NO, but also support the general proposition that antioxidants positively influence erectile health. *See* Section II.I.3, *supra*.

Complaint Counsel's expert, Dr. Melman, opined that basic research studies about antioxidants' effects on NO levels may relate to the biochemical process for erectile function, but that basic research studies do not directly involve erectile function in humans and cannot alone prove that POM Juice treats, prevents, or reduces the risk of erectile dysfunction in humans. F. 1301. Respondents' experts reviewed the basic science relied upon Respondents and concluded: basic science alone supports the potential benefit at the human level to improve the physiology of erectile tissue preserving erect tissue health and, thus, suggests a probable benefit of pomegranate juice on erectile health. F. 1298-1300.

ii. Clinical trial

Respondents also sponsored a clinical study, performed by Dr. H. Padma-Nathan, and published in the *International Journal of Impotence Research* in 2007 ("Forest/Padma-Nathan Study). F. 1206. The Forest/Padma-Nathan Study was an RCT of pomegranate juice versus placebo in men with erectile dysfunction. F. 1210. The Forest/Padma-Nathan Study engaged 53 completed subjects with mild-to-moderate erectile dysfunction who underwent two four-week treatment periods separated by a two-week "washout."[20] F. 1211.

Using a global assessment questionnaire ("GAQ"), Dr. Padma-Nathan found that participants rated pomegranate juice 50% more effective than a placebo at improving erections. F. 1212, 1224. The GAQ results achieved a probability value ("*p*-value") of 0.058, meaning that the positive results of the study were 94.2% likely to be the result of something other than "chance." F. 1225. Although the *p*-value was a few thousandths of a percentage point short of achieving statistical significance of 95%, the study has clinical significance in showing a benefit from pomegranate juice on erectile tissue physiology and health. F. 1248, 1250.

Dr. Melman, Complaint Counsel's expert, criticized the Forest/Padma Nathan Study on grounds that the GAQ is not a validated measure and does not provide clinically significant information; the study was not conducted over a sufficient duration to show a sustained clinically significant effect on erectile function; and the study results did not achieve statistical significance. F. 1233, 1235-1236. Respondents' experts reviewed the clinical evidence that Respondents relied upon and concluded that even though statistical significance was not reached, the Forest/Padma-Nathan Study "provides very valuable information" regarding erectile health and function and is "clinically significant" because "it supports the conclusion that the positive results in the basic science are borne out in human function." F. 1238, 1239, 1245. *See also* F. 1240-1245.

[20] The Forest/Padma-Nathan Study used a crossover design, and the 53 participants who completed the study received a different beverage during the two 28-day treatment periods. Participants in cohort one consumed POM Juice in period one and then switched to the placebo beverage in period two. Participants in cohort two consumed the placebo beverage in period one and POM Juice in period two. F. 1211.

c. Conclusion

The greater weight of the persuasive expert testimony demonstrates the following: The basic research relied upon by Respondents and the Forest/Padma-Nathan Study support the conclusion that pomegranate juice has a beneficial effect on erectile tissue physiology, health, and function. F. 1310, 1312. The evidence relied upon by Respondents also supports the conclusion that pomegranate juice is a *potential* treatment for erectile dysfunction. F. 1147, 1243, 1252. The evidence relied upon by Respondents is not, however, adequate to substantiate a claim that clinical studies show that the POM Products treat, prevent, or reduce the risk of erectile dysfunction or that clinical studies show the same. F. 1253, 1313, 1314. Indeed, the authors of the Forest/Padma-Nathan Study each testified that the study did not conclude that POM Juice treats, prevents, or reduces the risk of erectile dysfunction. F. 1230.

Respondents' defense on this issue is that they did not make any claims that the POM Products treat, prevent, or reduce the risk of erectile dysfunction. As such, Respondents' experts did not provide expert opinion on whether Respondents' science was adequate to support a claim that the POM Products treat, prevent, or reduce the risk of erectile dysfunction. Rather, the expert report of Dr. Goldstein states: "The available body of scientific literature – including *in vitro, in vivo*, and preliminary clinical trials – strongly suggests that consuming pomegranate juice promotes erectile health." F. 249. The expert report of Dr. Burnstein concludes that the basic scientific and clinical evidence is sufficient to support the use of pomegranate juice as a potential benefit for vascular blood flow and the vascular health of the penis. F. 242, 1184. Thus, Respondents have failed to provide expert opinion on the central issue of whether Respondents' science was adequate to support an implied claim that the POM Products treat, prevent, or reduce the risk of erectile dysfunction, or that they are clinically proven to do so. *See Daniel Chapter One*, 2009 FTC LEXIS 157, at *243 (Initial Decision).

Based on the more persuasive expert testimony at trial, competent and reliable scientific evidence demonstrates that pomegranate juice in its various forms provides a positive benefit to erectile health and erectile function. F. 1312. However, as testified to by Respondents' expert, the use of pomegranate juice to promote erectile *health* is a separate and distinct concept from

the use of this neutraceutical as a safe and effective treatment for the medical condition of erectile *dysfunction* such as with a PDE5 inhibitor. F. 249, 1311 (emphasis in original).

Having fully considered and weighed all the evidence and the conflicting expert testimony on Respondents' basic science and clinical trial, the greater weight of the persuasive expert testimony demonstrates that there is insufficient competent and reliable scientific evidence to substantiate claims that the POM Products treat, prevent, or reduce the risk of erectile dysfunction or that they are clinically proven to do so. F. 1313, 1314. Accordingly, Complaint Counsel has met its burden of proving that Respondents' substantiation was inadequate to make the implied erectile dysfunction claims found to have been made in this case, and that, therefore, such claims were false or misleading.

6. Summary

To summarize, in finding that Respondents' substantiation was not adequate, the facts that the POM Products are derived from a fruit, are safe, and are not advocated as an alternative to medicine were all considered. In addition, the cost and feasibility of conducting RCTs and the benefits of truthful claims were also considered. Ultimately, however, the determination as to what "amount of substantiation experts in the field would agree is reasonable" and "the level of proof sufficient to satisfy the relevant scientific community of the claim's truth" must, in accordance with applicable law, turn on the nature of the claims made by Respondents.

In this case, as found in Section III.E.2., *supra*, Respondents disseminated advertisements that impliedly represented that the POM Products treat, prevent, or reduce the risk of heart disease, prostate cancer, and/or erectile dysfunction, and/or that "clinical studies, research, and/or trials prove" that the POM Products treat, prevent, or reduce the risk of the same. As to these advertisements, whether or not Respondents' substantiation was adequate to support general and highly qualified health claims is not the material issue. Having crossed the line from making general and highly qualified health claims to making implied disease claims, "the level of proof sufficient to satisfy the relevant scientific community of the claim's truth" and "the amount of substantiation experts in the field would agree is reasonable" were necessarily heightened. *QT*, 448 F. Supp. 2d at 962 (where defendants make a "medical, health-related claim," . . . such a claim must be based on a heightened level of substantiation").

With respect to both the establishment and efficacy claims that Respondents have been found to have made, Respondents' substantiation failed to meet the level of substantiation required. Because Complaint Counsel met its burden of proving that Respondents' substantiation was inadequate, the advertisements compiled in the Appendix to this Initial Decision are false and misleading.

G. Whether Respondents' Claims are Material

1. Overview

Having found that Respondents disseminated advertisements conveying the claims alleged in the Complaint and that those claims were false or misleading, the next step is to determine whether those claims are material to prospective consumers. *Kraft*, 970 F.2d at 314. "The basic question" on the issue of materiality "is whether the act or practice is likely to affect the consumer's conduct or decision with regard to a product or service. If so, the practice is material, and consumer injury is likely, because consumers are likely to have chosen differently but for the deception." *Deception Statement*, 1984 FTC LEXIS 71, at *171; *see also* Joint Stipulations of Law and Facts, Stipulations of Law ¶ 4 (stipulating that "[a] 'material' misrepresentation or practice is one which is likely to affect a consumer's choice of or conduct regarding a product"). In other words, information is material if it is "important to consumers." *Deception Statement*, 1984 FTC LEXIS 71, at *188.

Materiality is a test of the likely effect of the claim on the conduct of a consumer. *Novartis Corp.*, 127 F.T.C. at 691. "Materiality turns upon whether those consumers who have drawn the claim from the advertisement and been misled by it are also likely to have their conduct affected by the misrepresentation." *Id.* To be material, "a claim does not have to be the *only* factor or the *most* important factor likely to affect a consumer's purchase decision, it simply has to be *an* important factor." *Id.* at 683 (emphasis in original).

Complaint Counsel contends that the challenged claims are presumed to be material because, among other reasons, the claims are "health-related efficacy claims." CCB at 26-27. *See Daniel Chapter One*, 2009 FTC LEXIS 157, at *245 (Initial Decision). Moreover, Complaint Counsel asserts, there is evidence, including Respondents' own marketing surveys,

demonstrating that the challenged claims are material. CCB at 28-29. Respondents contend that regardless of whether a presumption of materiality applies in this case, Respondents have rebutted the presumption, with survey evidence and expert opinion that the claims are not material to consumers' purchase decisions, and that Complaint Counsel has failed to adduce evidence that the challenged claims are, in fact, material. Therefore, Respondents argue, Complaint Counsel has failed to meet its burden of proof on materiality. RB at 82-92.

The presumption of materiality simply reflects the "general judgment that substantive claims in advertisements (in other words, claims other than "puffery" or window-dressing) would not have been made except to affect a consumer's choice of or conduct regarding a product. Thus, the very existence of the claim ordinarily is sufficient evidence for the Commission to conclude it is material. "However, respondent is always free to counter this evidence either with arguments pertaining to the content of the ad itself or with extrinsic evidence." *Thompson Medical*, 1984 FTC LEXIS 6, at *374 n.45.

In *Novartis*, the Commission explained the operation of the presumption of materiality as follows:

> Certain categories of information are presumptively material, including, but not limited to, express claims, claims significantly involving health or safety, and claims pertaining to the central characteristic of the product. *Deception Statement*, 103 F.T.C. at 182. Similarly, the Commission will infer materiality where the record shows that respondent intended to make an implied claim.
>
> *Id.* . . .
>
> "To establish a 'presumption' is to say that a finding of the predicate fact, here, any of the factors listed above, produces a required conclusion in the absence of explanation," here, materiality. *St. Mary's Honor Ctr. v. Hicks*, 509 U.S. 502, 506 (1993) (internal quotation marks omitted). In order to rebut the presumption, respondent must come forward with sufficient evidence to support a finding that the claim at issue is not material. Respondent can present evidence that tends to disprove the predicate fact from which the presumption springs (*e.g.*, that the claim did *not* involve a health issue) or evidence directly contradicting the initial presumption of materiality. This is not a high hurdle. Unless the rebuttal evidence is so strong that the fact finder could not reasonably find materiality, the fact finder next proceeds to weigh all of the evidence presented by the parties on the issue. *See id.* at 516 (noting that after the presumption drops out, "the inquiry . . . turns from the few generalized factors

> that establish [the presumption] to the specific proofs and rebuttals … the parties have introduced"). While the presumption itself is negated by sufficient rebuttal evidence, as previously noted, the predicate facts that gave rise to the presumption are not. These facts remain evidence from which materiality can be inferred. *See Boise Cascade*, 113 F.T.C. at 975 (1990). However, this evidence is simply part of the entire body of evidence considered. *See also* 21 *Charles Alan Wright and Kenneth W. Graham, Jr., Federal Practice and Procedure: Evidence* §§ 5122 *et seq.* (1977 and 1998 Supp.) (discussing the history and application of presumptions).

Novartis, 127 F.T.C. at 686-87.

Applying the principles of *Novartis* to the evidence in this case, it is unnecessary to rely on any presumption because, as further discussed below, the preponderance of the evidence shows that the challenged claims are material. Even if a presumption arises, and even if Respondents' evidence sufficiently rebuts the presumption, a "weigh[ing] of all of the evidence presented by the parties on the issue" shows that the challenged claims would be important to consumers, and likely to affect consumers' conduct or decisions. *Novartis*, 127 F.T.C. at 686. Accordingly, because the evidence is sufficient to prove materiality in the instant case, irrespective of any legal presumption, logic dictates that this Initial Decision need not, and it does not, analyze the effect of a presumption of materiality in this case.

2. Evidence of materiality

The evidence shows, and Respondents have failed to effectively rebut, the "predicate fact" that the advertising claims at issue involve health-related matters; specifically, efficacy for disease or dysfunction, and clinical proof of such efficacy. F. 580-583; *see Novartis*, 127 F.T.C. at 686-87. Common sense and experience readily support the conclusion that Respondents' claims in this regard would be important to consumers considering a purchase and likely affected consumers' decisions. Such a conclusion requires "no great leap." *Novartis*, 127 F.T.C. at 687.

Moreover, the evidence shows that advertising the results of studies related to heart disease, prostate cancer, and erectile dysfunction resulted in sales and that Respondents were aware of this fact. F. 1317, 1321, 1323-1324, 1326. *See Kraft*, 114 F.T.C. 40, 1991 FTC LEXIS 38, at *46 (finding that materiality was shown by evidence that the challenged

advertisement copy led to increased sales). For example, in evaluating how copy-dense or "medically oriented" to make a planned POMx Pill advertisement, Diane Kuyoomjian, Senior Vice President of Marketing for POM from 2008 to 2009, reminded Mrs. Resnick in a January 2009 e-mail: "[y]ou'll recall that a previous ad test with less copy did not generate as many orders. That would suggest we keep the research info in the new ad, which would make it information dense as well." F. 1323. In addition, Ms. Leow, a creative director for Roll, stated that scientific information in advertising and marketing material helps sell the products, because the scientific information provided the consumer with a "reason to believe." F. 1326. *See also* F. 1321. (September 2006 press article, stating "every time a new study [was] released touting" a health benefit of pomegranate juice, there was a "spike in sales. The study . . . linking the consumption of pomegranate juice to a reduction in prostate cancer was especially helpful."). Further, Mr. Resnick testified that POM communicates to consumers the "[company's] belief that pomegranate juice is beneficial in treating some causes of impotence, for the purpose of promoting sales of its product," F. 1316, and he further acknowledged that the kinds of benefits revealed by POM's research results are the primary reason people buy pomegranate juice. F. 1317; *see also* F. 1319 (draft creative brief describing concept behind advertising dollars spent on research as, "We don't just say our product is great, we have clinical studies that prove its efficacy"). Mr. Resnick also acknowledged that consumers buy pomegranate juice "because they believe and in fact it does postpone the onset of prostate cancer, which postpones the onset of death." F. 1317-1318.

In addition, in the ordinary course of business, POM conducted consumer research to understand the characteristics, attitudes and usage habits of POM customers and to identify barriers and opportunities for increasing consumption, particularly in relation to other brands of pomegranate juice. F. 1330. These studies also support a conclusion that the challenged claims are material to consumers. *See Kraft*, 1991 FTC LEXIS 38, at *40 (relying on consumer survey evidence to finding of materiality). The 2009 OTX Attitudes and Usage Study ("OTX A&U Study") (F. 1331) found that, of the survey respondents that identified "health" as a reason for drinking pomegranate juice, 47% of the POM Juice drinkers chose the further response, "helps protect against prostate cancer." F. 1332-1335. Similarly, in August 2007, Respondents commissioned a Zoomerang online survey of the general public, "[t]o better

understand pomegranate and non-pomegranate juice consumers," with respect to, among other things, "[i]mportance of certain health benefits." F. 1342. Six health benefits were listed and these survey respondents were asked to rank which was the most important to them personally. F. 1342. For heavy pomegranate juice drinkers, the number one response, for both males and females was "cardiovascular," and the number two choice for men was "prostate." F. 1342. For members of the general public responding to the Zoomerang question regarding ranking of health benefits, 60% ranked cardiovascular health as the first or second most important benefit, 40% of males ranked prostate health as the first or second most important benefit, and approximately 18% of males did so for erectile dysfunction. F. 1343. While Respondents' marketing expert, Dr. David Reibstein, criticized the methodology of using closed-ended questions, such as were used in the OTX A&U Study, because they can "cue" the survey respondent to certain answers and inflate results, F. 1340, closed-ended questions tend to be used when studying purchase motivations and have the advantage of allowing the researcher to obtain specificity in the responses. F. 1341. The materiality survey relied on in *Kraft* also made use of similar closed-ended questions. 1991 FTC LEXIS 38, at *40 (relying on survey asking respondents to rate the importance of a claim that cheese was "a source of calcium").

Additional evidence of the materiality of Respondents' advertising claims is demonstrated by Respondents' "creative briefs," which served to direct the content of their advertising. F. 145-151. For example, a creative brief for the POM Wonderful website, from approximately June 2008, shows that the purpose of the "Health Benefits" section of the POM Wonderful website was to communicate the "heart health," "prostate health," and "E.D." "health benefits," including by explaining how such benefits are provided. F. 1325. Further, in order to engage website viewers, the "Health Benefits" section was to provide "expert" information on heart and prostate matters, as well as a database of studies and results, searchable by subject matter, including heart and prostate. F. 1325; *see also* F. 1327-1328 (creative briefs describing main creative focus for advertising assignments as "prostate cancer"). Respondents' arguments that creative briefs cannot be relied upon because they reflect the opinions of low level employees, is unsupported by the evidence, *see e.g.*, F. 154, 181, and is unpersuasive.

Finally, in over a decade, POM sponsored over 100 studies at 44 different institutions, and over $35 million has been invested in POM's research program. F. 128, 131. POM uses the results of studies it has sponsored for marketing purposes, as part of POM's "unique selling proposition." F. 113. Considering these circumstances, particularly that POM was aware that among those purchasing the POM Products were "people that have heart disease or prostate cancer in their family, or have a fear of having it themselves," F. 1320, it defies credulity to suggest that Respondents would advertise study results related to these conditions if such advertising did not affect consumer behavior. In fact, Respondents' marketing expert, Dr. Reibstein, stated that it was indeed possible, and he would expect that, to consumers who were concerned about heart disease, prostate cancer, or erectile dysfunction, a claim that drinking a bottle of POM Juice a day was effective for these conditions would be important to their purchasing decisions. F. 1329.

3. Respondents' evidence of immateriality

Respondents rely on the results of the Reibstein Survey, which showed, among other things, that a very small number of survey respondents (12 out of 750), when asked to identify their reasons for purchasing, repurchasing, or recommending pomegranate juice, including POM Juice, identified a specific disease, and of those who did, fewer still mentioned "heart disease" or "cancer." F. 1344, 1351-1365. Based on these study results, Dr. Reibstein expressed the opinion that there is a very small percentage of people that bought, would buy again, or would recommend POM Juice to a friend because they believe that it cures or prevents a specific disease. F. 1372. The Reibstein Survey obtained these results by asking a series of open-ended questions, such as: "Why did you purchase POM Wonderful 100% Pomegranate Juice?" and asking survey respondents to provide "*specific details*." F. 1354. In this regard, the Reibstein Survey was flawed because it only assessed consumer motivations generally; it did not actually assess whether any of the challenged claims in the Complaint would be important to the survey respondent's decision to purchase the products. F. 1373. Moreover, the survey did not ask any follow-up questions, including of the 35.2% of POM Juice purchasers who stated that they bought or would repurchase POM Juice because it was "healthy." F. 1354, 1361, 1375. The failure to probe further as to what these survey respondents meant by "healthy" and whether there were specific reasons or benefits that

underlay their "healthy" responses, constitutes methodological flaws that render the Reibstein Survey insufficiently probative to outweigh the substantial, probative evidence, summarized above, showing that disease claims are likely to be important to, and to influence, consumer decision making. *See Kraft*, 1991 FTC LEXIS 38, at *47 (rejecting materiality survey as insufficiently probative because limited response options offered to survey participants failed to adequately elicit all of the ways in which consumer conduct with respect to the product might be affected by the implied claims at issue). A more probative survey on materiality would have provided survey respondents with a statement about what the claim was, and inquired how important they think that claim would be to their potential purchase decision, F. 1374, as did the survey in *Kraft*, 1991 FTC LEXIS 38, at *40. Also affecting the relative weight of the Reibstein Survey is the fact that it was commissioned and designed for use in litigation, F. 1344, while the OTX A&U Study and the Zoomerang online survey were conducted in the ordinary course of business. F. 1330, 1331, 1342.

4. Conclusion

The evidence of materiality in the record outweighs Respondents' evidence of immateriality and, therefore, Complaint Counsel has met its burden of proof on the third element of its deceptive advertising claim. Accordingly, because Complaint Counsel has met its burden as to all three elements of a deceptive advertising claim, liability has been established. The Initial Decision next addresses the appropriate remedy.

H. Remedy

1. General legal principles

Having concluded that Respondents violated the FTC Act, that Act authorizes an order requiring respondents to cease and desist from such acts or practices. 15 U.S.C. § 45(b); *FTC v. Nat'l Lead Co.*, 352 U.S. 419, 428 (1957). "As the Court has said many times before, the Commission may exercise only the powers granted it by the Act. The relevant sections empower the Commission to prevent the use of unfair methods of competition and authorize it, after finding an unfair method present, to enter an order requiring the offender 'to cease and desist' from using such unfair method." *Nat'l Lead Co.*, 352 U.S. at 428 (1957) (internal citation omitted).

The purpose of a cease and desist order is to prevent the violations from being repeated, including by "creating stringent monetary incentives (in the form of civil penalties) for its observance." *In re Litton Indus., Inc.*, No. 9123, 97 F.T.C. 1, 1981 FTC LEXIS 94, at *147 (Jan. 5, 1981); *accord Thompson Medical*, 1984 FTC LEXIS 6, at *405-06 (describing order as appropriate "to prohibit and prevent [the respondent] from engaging in deceptive acts or practices"). Thus, "'[t]he Commission is not limited to prohibiting the illegal practice in the precise form in which it is found to have existed in the past.'" *FTC v. Colgate-Palmolive Co.*, 380 U.S. 374, 395 (1965) (quoting *FTC v. Ruberoid Co.*, 343 U.S. 470, 473 (1952)). The FTC is permitted "to frame its order broadly enough to prevent respondents from engaging in similarly illegal practices in future advertisements." *Colgate-Palmolive Co.*, 380 U.S. at 395. "Having been caught violating the Act, respondents 'must expect some fencing in.'" *Id.* (quoting *Nat'l Lead*, 352 U.S. at 431). The cease and desist order must be sufficiently clear so that it is comprehensible to the violator, and must be reasonably related to the violations found to exist. *Colgate-Palmolive*, 380 U.S. at 392, 395.

Applying the foregoing principles, and after consideration of all the arguments of the parties and the entire record of the case, the attached order, to be entered herewith (hereafter, "Order"), will serve to prohibit and prevent Respondents from engaging in deceptive advertising practices in the future, is reasonably related to the unlawful acts or practices found to exist, and is sufficiently clear and precise. The scope and terms of the Order are substantially the same as was entered by the Commission, and upheld on appeal to the United States Court of Appeals, to redress unsubstantiated disease claims in *Daniel Chapter One*, No. 9329, 2010 FTC LEXIS 11 (Jan. 25, 2010), *review denied, Daniel Chapter One v. FTC*, No. 10-1064, 2010 U.S. App. LEXIS 25496 (D.C. Cir. Dec. 10, 2010), *cert. denied*, 131 S. Ct. 2917 (2011).

2. Respondents' preliminary arguments

Respondents argue on various grounds that no cease and desist order should issue in this case, despite violations having been found. These arguments are addressed below

a. Outliers

Respondents assert that no cease and desist order may issue in this case based on eight of the Challenged Advertisements, which Respondents assert should be considered "outliers." Respondents define these "outliers" as advertisements run in the 2003-2006 timeframe, and not thereafter, in which the images and the language regarding the health benefits of POM Juice were "more aggressive than was typical of Respondents." RB at 67-68. According to Respondents, no relief can be based upon these "outliers" because such advertisements have stopped and Complaint Counsel has failed to demonstrate that such conduct will be repeated. RB at 68-69, citing *FTC v. Evans Products Co.*, 775 F.2d 1084, 1087 (9th Cir. 1985) (stating that past wrongs are not enough for the grant of an injunction, and that an injunction will issue only if the wrongs are ongoing or likely to recur).

Respondents' argument is unconvincing. Of the eight asserted "outliers," only four are among the Challenged Advertisements found to have made the implied claims alleged in the Complaint: (1) CX0036 ("Cheat Death" print advertisement); (2) CX0016 ("Drink and be healthy" print advertisement); (3) CX0314 (magazine wrap advertisements); and (4) CX0034 ("Amaze your cardiologist" print advertisement). *See* F. 580-583. In addition, even if the exact same advertisements have not been repeated, this does not mean that Respondents' violations will not be repeated, particularly in light of the fact that numerous advertisements disseminated after 2006 were found to have made implied disease claims, without adequate substantiation. F. 307-308, 321, 328, 344, 365, 432, 580-583, 962, 1143, 1313-1314. That the form of the advertisements communicating these implied claims may have changed is not persuasive evidence that Respondents' past wrongs are not likely to reoccur. Furthermore, even if the "outliers" were not considered violations for purposes of injunctive relief, there would be sufficient violations based upon other advertisements to justify injunctive relief in this case. *Bristol-Meyers*, 1983 FTC LEXIS 64, at *250-51 (finding adequate number of deceptive advertisements to support the order, even though the number was fewer than the number found by the ALJ); *In re Fedders Corp.*, No. 8932, 85 F.T.C. 38, 71-72 (Jan. 14, 1975) (holding that one or two advertisements can be sufficient number of violations to support order).

Accordingly, Respondents' "outlier" defense is rejected.

b. Liability of Roll

Complaint Counsel argues that both POM and Roll are liable for the violations in this case and should both be subject to a cease and desist order, based upon two alternative theories: the "common enterprise" theory, based on the interrelated nature of the two corporate Respondents; and the "active participant" theory, based on Roll's direct activities with regard to POM's advertising, including through Roll's internal advertising agency, allegedly with knowledge of the deceptive nature of the POM advertisements. CCB at 54-56. Respondents contend that no cease and desist order should issue against Roll. RRB at 169-171.

It is well established that "[w]here one or more corporate entities operate in a common enterprise, each may be held liable for the deceptive acts and practices of the others." *FTC v. Bay Area Bus. Council, Inc.*, No. 02-C-5762, 2004 U.S. Dist. LEXIS 6192, at *33-34 (N.D. Ill. Apr. 8, 2004) (finding a common enterprise where the corporate defendants were owned by the same person, were operated by the same people, often shared offices, did business under each other's names, accessed the same customer databases, shared and transferred proceeds as needed, and were considered a collaborative effort by the owner), *aff'd*, 423 F.3d 627 (7th Cir 2005); *Telebrands Corp.*, 140 F.T.C. at 451 (Initial Decision) ("Corporate respondents acting in concert to further a common enterprise are each liable for the acts and practices of the others in furtherance of the enterprise."). To determine whether a common enterprise exists, courts will consider a variety of factors including: "common control; the sharing of office space and officers; whether business is transacted through a maze of interrelated companies; the commingling of corporate funds and failure to maintain separation of companies; unified advertising; and evidence that reveals that no real distinction exists between the corporate defendants." *Nat'l Urological Group*, 645 F. Supp. 2d at 1182. Courts look for vertical or horizontal commonality. *FTC v. Network Servs. Depot, Inc.*, 617 F.3d 1127, 1142-43 (9th Cir. 2010) (noting evidence showing that the companies pooled resources, staff, and funds; shared common owners and managers; and participated to some extent in a common venture).

Applying the foregoing principles, the evidence demonstrates that POM and Roll are a "common enterprise." F. 12, 19-21, 27-28, 1380, 1382, 1384, 1386-1390. Among other things,

Respondents Stewart and Lynda Resnick are the sole owners of Roll and its affiliated companies, including POM Wonderful. F. 12. Mr. Resnick is Chairman and President, and Mrs. Resnick is a director and Vice Chairman of Roll. F. 19. Mr. Resnick is also Chairman and Chief Executive Officer of POM. F. 20-21. POM is headquartered in the same building as Roll, in many cases with employees of both companies occupying the same floor. F. 1380. Roll provides risk management, human resources, consulting, and travel services to POM without any reimbursement, and advertising and marketing services have been provided by Roll to POM without necessarily receiving reimbursement. F. 1385. In addition, for accounting purposes, Roll and its affiliated companies, including POM, were represented as being under common control or ownership and have been included together on consolidated financial and tax statements. F. 1387. Moreover, the Resnicks have had ultimate say over all business functions of both Roll and POM, including setting policy and supervising the senior executives of both companies, disregarding corporate formalities. F. 1386.

Respondents fail to make any discernable argument that POM and Roll are not a common enterprise, focusing their argument instead on whether Roll was an "active participant" in POM's advertising and/or had actual or constructive knowledge of any deception. RRB at 169-171. Considering the facts clearly supporting liability of Roll based on the common enterprise theory, Roll is jointly liable with POM and will be held to the provisions of the attached Order. It is, therefore, unnecessary to determine whether or not Roll is also liable under the "active participant" theory. Thus, this Initial Decision need not, and does not, include any conclusions or analysis regarding that issue.

3. Liability of Individual Respondents

a. Applicable legal principles

"To obtain injunctive relief against an individual for a business entity's acts or practices, the FTC first must prove the entity violated § 5. *See Federal Trade Comm'n v. Think Achievement Corp.*, 144 F. Supp. 2d 993, 1009-11 (N.D. Ind. 2000), *aff'd*, 312 F.3d 259 (7th Cir. 2002). The FTC must further show the individual participated directly in the business entity's deceptive acts or practices, or had the authority to control them. *See Federal Trade Comm'n v. Publishing Clearing House, Inc.*, 104 F.3d 1168, 1170 (9th Cir. 1997)." *FTC v.*

Freecom Communs., Inc., 401 F.3d 1192, 1202-03 (10th Cir. 2005); *FTC v. Amy Travel Serv., Inc.*, 875 F.2d 564, 573 (7th Cir. 1989). An individual's authority to control the corporation's deceptive acts may be "evidenced by active involvement in business affairs and the making of corporate policy, including assuming the duties of a corporate officer." *Amy Travel Serv.*, 875 F.2d at 573.

b. Stewart and Lynda Resnick

While Respondents assert generally that no liability should attach to any of the individual respondents, Respondents specifically address their argument only to the liability of Respondent Matthew Tupper, which is discussed below. Applying the well-established principles of individual liability, summarized above, the evidence amply supports the conclusion that both Respondents Lynda Resnick and Stewart Resnick actively participated in the acts and practices found to have violated the FTC Act and/or had the authority over them. The Resnicks are the sole owners of POM and Roll. F. 12. Mr. Resnick is the Chairman of both corporate entities, and the Chief Executive Officer of POM with overall responsibility and control over the business, including setting the budgets for marketing, advertising and medical research. F. 19-20, 22-23, 1393. He considers himself ultimately responsible for whether advertising should or should not go out, although he delegated day-to-day responsibility to Mr. Tupper. F. 25. In addition, Mr. Resnick has been involved at a high level with POM's advertising and marketing campaigns, including on occasion seeing headlines before advertisements were disseminated, when Mrs. Resnick has chosen to involve him, and has been intimately involved in POM's scientific research program. F. 23, 26, 1392-1395. The facts support Mr. Resnick being subject to a cease and desist order in this case.

Mrs. Resnick is a director and Vice Chairman of Roll. F. 27-28. According to Mrs. Resnick, when it comes to marketing and creative issues, everyone has a "dotted line" to her. F. 35. Although Mrs. Resnick was not an officer of POM, Mrs. Resnick participated in POM's business on almost a daily basis in the company's early years, and on a weekly or biweekly basis thereafter and through 2010. F. 30. As of 2011, Mrs. Resnick was still the chief marketing person at POM. F. 31. Mrs. Resnick has had a principal role in approving advertising content since POM's inception. F. 143, 160-161, 166-168, 1399. For example,

Mrs. Resnick requested that copies of all advertising campaigns be submitted to her for final approval including headlines used in POM's advertisements. F. 1399. Mrs. Resnick held regular creative meetings with the senior in-house representatives of POM and Roll, including representatives of POM's marketing department, Roll's public relations department and Roll's advertising agency, Fire Station, to review and approve advertising concepts. F. 33, 141-143. If there were disputes or issues to resolve regarding advertising decisions, the final authority was either Mr. or Mrs. Resnick; however, as the overseer of all branding and marketing, Mrs. Resnick had the "final word" on advertising content and concepts. F. 1397, 1400. *See also* F. 33-34. Moreover, Mrs. Resnick was involved in several of the specific advertisements found herein to have violated the FTC Act. Mrs. Resnick was "very involved" in developing the POMx brochure, identified as CX1426, Exhibit I "Antioxidant Superpill" package insert, when it was first produced; Mrs. Resnick was involved in the approval of the print advertisement identified as CX0029 ("10 OUT OF 10 PEOPLE DON'T WANT TO DIE"); Mrs. Resnick approved the headline for the POMx print advertisement headlined "The Only Antioxidant Supplement Rated X"; and Mrs. Resnick approved the print advertisement identified as CX0031 ("Floss your arteries" print advertisement). F. 1401-1404. The evidence is more than sufficient for Mrs. Resnick to be subject to a cease and desist order.

As the Commission stated in *Telebrands Corp.*, "it is not only appropriate but sometimes preferable to make the principal of a corporation subject to fencing-in so that the individual cannot circumvent the order by establishing a new company with a different name." 140 F.T.C. 278, 344 n.62. Accordingly, based on the Resnicks' participation in and control over the acts and practices in this case, it is appropriate for them to be subject to a cease and desist order individually, along with the corporate Respondents. Indeed, as to Mr. and Mrs. Resnick, Respondents fail to articulate any factual or legal basis for a contrary result.

c. Matthew Tupper

i. "Control" as a mandatory prerequisite to finding individual liability of corporate officer

Mr. Tupper has been an officer of POM since 2003, first with the title of Chief Operating Officer and then with the title of President. F. 37-38. Mr. Tupper acknowledges that

he was involved in POM's operations, science research, and marketing. However, according to Mr. Tupper, none of these aspects of POM's business were under his ultimate control, but rather were under the ultimate control of Mr. and/or Mrs. Resnick. RTB at 2, 6-8. Mr. Tupper acknowledges, as he must, that the applicable test for individual liability is met by evidence of *either* participation in the deceptive practices at issue *or* authority to control them. RTB at 3-5. *See, e.g.*, *Freecom Communs.*, 401 F.3d at 1203; *Amy Travel Serv.*, 875 F.2d at 573. Mr. Tupper contends, however, that despite being stated in the alternative, "in practice," authority to control is the key factor for liability, not participation. RTB at 3. To the contrary, "[e]ither participation or control suffices." *QT*, 512 F.3d at 864. In *Direct Marketing Concepts*, a case upon which Mr. Tupper relies, the court reaffirmed the "either/or" nature of the individual liability test by rejecting the argument by the defendant co-owner of the corporation "that he did not edit the content of advertising." Relying on *Freecom Communications*, the court held it sufficient that the co-owner controlled the corporations, and, therefore, "could have nipped the offending infomercials in the bud . . . ." 624 F.3d at 13. Similarly, in *Freecom Communications*, upon which Mr. Tupper also relies, the court held that the lower court's "finding that [the individual defendant] never personally [made the misrepresentations at issue] is beside the point because the law did not require the FTC to make such a showing. To justify the imposition of injunctive relief against the individual, the FTC is required to show the individual participated directly in the business entity's deceptive acts or practices, or had the authority to control such acts or practices." 401 F.3d at 1204.[21]

Mr. Tupper further maintains that, despite the well-established rule that evidence of either participation or control can support imposing individual liability, he is "unaware of any case" in which individual liability of a corporate officer was based on participation alone, and cites cases in which the corporate officer was found liable based on evidence of *both*

[21] Mr. Tupper also relies on an initial decision in an FTC case from 1974, *In re Auslander Decorator Furniture, Inc.*, 83 F.T.C. 1542, 1974 WL 175916 (April 23, 1974), in which the hearing examiner declined to find individual liability on the part of two nominal officers because "the record [was] devoid of evidence of actual control or responsibility by [the two individuals] . . . over the affairs of ADF, and . . . their participation in the unlawful acts and practices of ADF was that of employees working under the direction and supervision of" the owner of the company. That case pre-dates by many years the long line of federal appellate court cases, from *Amy Travel* to *QT*, cited above, which make clear that participation is one of two grounds that justify individual liability. *Auslander* is contrary to such cases. Under these circumstances, *Auslander* cannot reasonably be deemed controlling authority. In any event, unlike *Auslander*, both participation and control have been demonstrated in this case, as more fully discussed below, and for that reason as well, *Auslander* is not dispositive.

participation by the corporate officer *and* authority to control the corporation. RTB at 4-5. *E.g., In re Universal Electronics Corp.*, No. 8815, 78 F.T.C 265, 1971 FTC LEXIS 55, at *65-66 (Jan. 28, 1971) (Initial Decision) (finding that evidence demonstrated that officer formulated, directed, and controlled the acts and practices of the corporate respondent; and that he was responsible for, familiar with, and personally participated in, the specific acts and practices at issue); *FTC v. Neovi, Inc.*, 598 F. Supp. 2d 1104, 1117 (S.D. Cal 2008) (stating that "the Court agrees with the FTC that [the individual defendants] had the authority to control the corporate Defendants' unfair practices, [and] that they participated in those activities . . . ."); *FTC v. Transnet Wireless Corp.*, 506 F. Supp. 2d 1247, 1271-1272 (S.D. Fla. 2007) (concluding, based on evidence, that individual defendants had "authority to control the corporation" and directly participated in the practices at issue); *Amy Travel Serv.*, 875 F.2d at 574 (affirming individual liability of principal officers and shareholders where it was found they controlled the corporations and where it was also "clear that [the individual defendants] were the ones behind the vacation passport scheme," including writing telemarketing scripts); *FTC v. Publ'g Clearing House, Inc.,* 104 F.3d 1168, 1171 (9th Cir. 1997) (noting that individual defendant's activities as corporate officer "included obtaining and signing PCH's business license and signing the fund-raising agreement between PCH and [a fraudulent charity whose] application to conduct charitable solicitation identified [her] as the person in 'direct charge of conducting the solicitation'"). *See generally* cases cited at RTB 4-5. Mr. Tupper's cited cases do not support interpreting the rule that "[e]ither participation or control suffices," *QT, Inc.*, 512 F.3d at 864, to mean that only "authority to control" will suffice. Furthermore, consistent with the above-cited cases, individual liability is warranted in this case because, as further discussed below, Mr. Tupper both participated in the deceptive advertising practices at issue and had the authority to control POM's practices in this regard. *See also FTC v. Consumer Alliance, Inc.*, No. 02C2429, 2003 U.S. Dist. LEXIS 17423, at *20-22 (N.D. Ill. Sept. 29, 2003) (finding individual liability where the defendants reviewed, approved, and drafted telemarketing scripts used to deceive consumers and had authority to supervise and discipline employees).

ii. Mr. Tupper's participation in and control over the practices at issue in this case

On the issue of participation, the evidence shows that Mr. Tupper's responsibilities within POM included implementing POM's direction with regard to health benefit advertising and the use of science in connection with the advertising. F. 51. With respect to this advertising, Mr. Tupper was the "connecting piece" between the marketing vision and the communication of the science. F. 51-52, 1409, 1411. Mr. Tupper participated in meetings in which Fire Station and POM personnel presented and reviewed advertising concepts and advertising. F. 156, 1419. Mr. Tupper has reviewed and given direction to POM's marketing staff on parts or elements of creative briefs. F. 1417. Mr. Tupper reviewed advertising copy (including headlines), made changes to copy, and, depending on the project, had final say over POM advertising content and which advertisements should or should not run. F. 160, 162, 1420. Mr. Tupper led meetings to review advertising copy from a scientific perspective prior to dissemination of the advertising. F. 1410, 1416. Sometimes, Mr. Tupper would provide the specific words to use when presenting medical research facts, and in other instances, POM Marketing or Fire Station employees would "take a stab at writing [this information] and send it to [Mr. Tupper] to approve." F. 1421. Mr. Tupper participated in drafting the *Time* magazine cover wraps found herein to have made the claims alleged in the Complaint. F. 306-310, 581, 1431. Mr. Tupper also reviewed press releases prior to issuance. F. 1430. In addition, as POM's President, Mr. Tupper attended most of the marketing meetings with Mrs. Resnick, which included discussions of POM's scientific research. F. 142, 144, 1412. In fact, Mr. Tupper had a significant degree of involvement in the research aspects of POM's business, and his responsibilities included discussing which research areas are appropriate for funding, participating in the internal decision-making as to what research to fund, and overseeing for POM the clinical trials on POM's products that were conducted by research institutions. F. 53, 1424-1429; *see also* F. 119 (finding and contacting scientific experts to conduct research). POM's former Senior Vice President of Marketing, Ms. Kuyoomjian, relied on her conversations with Mr. Tupper to understand content in POM's advertising regarding the relationship between POM advertisements and the scientific support for these advertisements. She also relied on Mr. Tupper to be the "arbiter" of whether people felt POM's advertising was accurate. F. 1414, 1418, 1421. Accordingly, Mr. Tupper's level of participation is more than

adequate to support individual liability for POM's deceptive advertisements. *See Amy Travel Serv.*, 875 F.2d at 573 (affirming finding proof of participation based on individual defendants' writing telemarketing script used in deception); *Publ'g Clearing House*, 104 F.3d at 1171 (affirming lower court's finding of proof of participation based on individual defendant's signing a contract used in a fraudulent scheme); *Consumer Alliance*, 2003 U.S. Dist. LEXIS 17423, at *20-22 (finding individual liability where the defendant reviewed, approved, and drafted telemarketing scripts used to deceive); *In re Griffin Sys., Inc.*, No. 9249, 117 F.T.C. 515, 1994 FTC LEXIS 76, at *25 (April 29, 1994) (finding participation based upon individual respondents' preparing solicitation materials that contained misrepresentations, including making changes in the content of those materials).[22]

The evidence also demonstrates that Mr. Tupper had authority to control the practices of POM. Mr. Tupper was an officer of POM and, in his capacity as an officer, Mr. Tupper, together with others, formulated, directed, or controlled the policies, acts, or practices of POM. F. 37-38, 42. Mrs. Resnick considered Mr. Tupper her partner at POM since 2003 and relied on him to oversee POM's marketing when she reduced her day-to-day involvement beginning in 2007. F. 39, 1407. Mr. Resnick delegated the authority to decide which advertisements should run to Mr. Tupper. F. 1406. Mr. Tupper was responsible for managing the day-to-day affairs of POM, including management of the day-to-day operations of the POM marketing team. F. 25, 44. Mr. Tupper oversaw and administered POM's budget for all departments, and had authority to sign checks and contracts on behalf of the company. F. 45. Mr. Tupper had numerous POM employees reporting to him directly, including the vice presidents for marketing, corporate communications, clinical development, and operations. F. 47-50. Mr. Tupper had the authority to hire and fire POM employees, including the head of POM's marketing department, on his own, or, depending on the situation, in consultation with either

[22] Mr. Tupper also argues that he was less involved in POM's advertising during the period 2003 to 2006, and for this reason, he cannot be deemed to have "participated" in any deceptive advertisements from this period. RTB at 10. However, the evidence shows that Mr. Tupper was, in fact, engaged in the medical research aspect of POM's business from the time he first joined POM full time in 2003, although beginning in late 2006 or 2007, he became more engaged, as the "connecting piece" between research and marketing. F. 37, 1411. In any event, as explained above in connection with Respondents' "outlier" argument, even if advertisements from 2003 to 2006 are not considered, the violations would be sufficient to justify a cease and desist order against Mr. Tupper. *See Bristol-Meyers*, 1983 FTC LEXIS 64, at *250-51; *Fedders Corp.*, 85 F.T.C. at 71-72. Thus, whether or not Mr. Tupper was less involved in these earlier advertisements is not determinative as to whether a cease and desist order may issue against him.

Mr. or Mrs. Resnick. F. 46. Thus, the evidence is sufficient to show authority to control. *Benrus Watch Co. v. FTC*, 352 F.2d 313, 325 (8th Cir. 1965) (affirming individual liability against officers who "formulated, directed, and controlled" the policies and practices of the corporate respondents); *accord In re Universal Electronics Corporation*, 1971 FTC LEXIS 55, at *65-66 (Initial Decision); *FTC v. World Media Brokers*, 415 F.3d 758, 764-65 (7th Cir. 2005) (finding that individual defendants' assumption of duties of corporate officers, such as corporate signing authority, "establishe[d] a level of corporate involvement sufficient to demonstrate" authority to control); *FTC v. Bay Area Bus. Council, Inc.*, 423 F.3d 627, 636-38 (same); *Consumer Alliance*, 2003 U.S. Dist. LEXIS 17423, at *20-21 (finding liability where individual had authority to control based upon hiring, supervision, and disciplinary authority over employees). *Compare QT, Inc.*, 448 F. Supp. 2d at 973-74 (finding FTC failed to meet burden under test for individual liability where corporate secretary "did not participate directly in the deceptive acts and practices carried out by the corporate Defendants" or "possess 'a level of corporate involvement sufficient to demonstrate the requisite authority to control the corporate defendants.'" (citation omitted)).

Mr. Tupper's contention that he did not have "sole" or "ultimate" control of POM, RTB at 2, 7, even if true, is not determinative. A similar argument was made and rejected in *Griffin Systems, Inc.*, 1994 FTC LEXIS 76. In that case, the evidence showed that the corporate officer, Mr. Giordano, like Mr. Tupper in this case, administered the day-to-day affairs of the office, and, like Mr. Tupper, had duties including, among other things, hiring and supervising employees, and advising employees about the challenged solicitation materials. 1994 FTC LEXIS 76, at *4; *see* F. 25, 44, 46-50, 1414, 1418, 1421. The Commission found these facts sufficient to support individual liability, despite evidence showing that the officer shared his authority with the other individual respondents in that case. *Id.* at *23. The Commission explained:

> In support of their argument that it is inappropriate to hold Mr. Giordano individually liable for the actions of Griffin, the respondents emphasize that Mr. Giordano was not in sole control of Griffin. We are not aware of any authority indicating that sole control of a company is necessary to establish individual liability. Indeed, there have been a number of cases in which more than one individual has been held to formulate, direct, and control the practices of a single corporation.

Id. at *24. In the instant case, the evidence, summarized above, amply demonstrates that Mr. Tupper had sufficient authority, particularly with regard to the content of advertisements, to control the practices at issue. Moreover, Mr. Tupper does not cite to any evidence that he ever expressed concerns about, or objections to, the POM advertisements at issue to Mr. or Mrs. Resnick or that any such concerns or objections were overruled by either of them. As in *Griffin Systems*, the evidence is clear that Mr. Tupper "was part of the inner circle that formulated, controlled, and directed" POM and "therefore it is appropriate to place him under order." *Id.*

iii. Breadth of cease and desist order

Mr. Tupper contends that it is unnecessary and unreasonable to bind him to a cease and desist order in addition to the other Respondents. He asserts that extending the proscriptions in the order to any food, drug, or dietary supplement would "potentially attach to any company he is associated with for the next twenty years" and, thereby, "effectively ensure that no company, with interests in foods, drugs or supplements would ever employ" Mr. Tupper. RTB at 9-10. This argument is unpersuasive. The Order binds Mr. Tupper personally, and his successors or assigns. Order, Definitions para. 2. The cease and desist Order does not, by its terms, bind Mr. Tupper's future employers.[23]

In addition, Mr. Tupper contends that the proposed order is unreasonable and overbroad as applied to him, based upon his asserted limited control over and participation in the challenged practices, when considering the seriousness of the conduct, the deliberateness of the conduct and its transferability to other products. RTB at 10-12; *see Telebrands*, 457 F.3d at 358. As noted above, Mr. Tupper's participation in and control over the deceptive practices at issue in this case is more than sufficient to justify a cease and desist order against him. The *Telebrands* factors are analyzed below in Section III.H.4.a.

[23] Of course, Mr. Tupper's future employers would be bound, as would any business, to compliance with the FTC Act. As noted above, the "competent and reliable evidence" substantiation standard for disease or efficacy claims only obliges advertisers "to do that which the case law under Sections 5 and 12 of the FTC Act has defined as necessary to avoid deception." *Daniel Chapter One*, 2009 FTC LEXIS 259, at *70.

4. Provisions of the Order

Having determined that a cease and desist order is required against POM, Roll, Mr. and Mrs. Resnick, and Mr. Tupper, this section of the Initial Decision addresses the specific provisions of the Order. The provisions of the Order are substantially the same as Complaint Counsel's proposed order, which is the Notice Order that was attached to the Complaint issued in this case (hereafter, "proposed order"), except that the Order does not include Complaint Counsel's proposed part I, as further explained in Section III.H.4.b.

a. Multi-product coverage (Order, Definitions para. 5)

The FTC's authority includes power to issue orders "encompassing all products or all products in a broad category, based on violations involving only a single product or group of products." *ITT Continental Baking Co. v. FTC*, 532 F.2d 207, 223 (2d Cir. 1976).

> Coverage of all products in a broad category is a means of "fencing-in" one who has violated the statute. Fencing-in provisions serve to "close all roads to the prohibited goal, so that (the FTC's) order may not be by-passed with impunity." *FTC v. Ruberoid Co.*, 343 U.S. 470, 473, 72 S. Ct. 800, 803, 96 L. Ed. 1081 (1952) (footnote omitted). Fencing-in provisions must bear a "reasonable relation to the unlawful practices found to exist." *FTC v. Colgate-Palmolive Co.*, 380 U.S. at 394-95, 85 S. Ct. at 1047-1048 (footnote omitted).

Litton Indus., Inc. v. FTC, 676 F.2d 364, 370 (9th Cir. 1982).

In determining whether a fencing-in order bears a "reasonable relationship" to a violation of the FTC Act, courts and the Commission consider: (1) the degree of transferability of the violation to other products; (2) the deliberateness and seriousness of the violation; and (3) any history of prior violations. *Telebrands*, 457 F.3d at 358; *Kraft*, 970 F.2d at 326. "The reasonable relationship analysis operates on a sliding scale -- any one factor's importance varies depending on the extent to which the others are found. In other words, the more serious a violation, the less important transferability and prior history become. . . . All three factors need not be present for a reasonable relationship to exist." *Telebrands Corp.*, 457 F.3d at 358-59 (citation omitted). "[T]he more egregious the facts with respect to a particular element, the less important it is that another negative factor be present. In the final analysis, [courts] look to

the circumstances as a whole and not to the presence or absence of any single factor." *Sears, Roebuck & Co. v. FTC*, 676 F.2d 385, 392 (9th Cir. 1982); *see also Kraft*, 970 F.2d at 327.

Applying the foregoing principles to the facts of this case, and as discussed below, the Order's provisions will apply to the POM Products as well as to any other food, drug or dietary supplement products sold by POM and the other Roll entities. *See* Order, Definitions para. 5.

(i) Transferability

As the Commission stated in *Litton Industries,*

> The rationale for entry of a multi-product order based upon violations in the advertising of only one or a few products is that many kinds of deceptive advertising are readily transferrable to a variety of products, and it would serve the public poorly to halt the use of a deceptive tactic in the advertising of one product if the respondent remained free to repeat the deceptive practice in another guise, with no threat of sanction save for another order to cease and desist. *FTC v. Colgate-Palmolive Co.*, 380 U.S. at 394-95 (1965).

Litton Indus., Inc., 1981 FTC LEXIS 94, at *147. Indeed, the "prevention of 'transfers' of unfair trade practices is a fundamental goal of the Commission's remedial work." *Sears, Roebuck*, 676 F.2d at 394. Where a violation has been demonstrated, "the Commission need not wait until a 'transfer' occurs" to other products. *Id.* at 395.

A violation is considered transferable when other products could be sold utilizing similar techniques. *Colgate-Palmolive*, 380 U.S. at 394-95; *Sears, Roebuck*, 676 F.2d at 392. For example, "misrepresenting that doctors prefer a product, or that tests prove the product's superiority, is a form of deception that could readily be employed for any non-prescription drug product." *American Home Prods. v. FTC*, 695 F.2d 681, 708 (3rd Cir. 1982). In the instant case, this transferability factor weighs strongly in favor of a multi-product order. As in *Daniel Chapter One*, Respondents' advertising techniques "could readily be employed" for any food, drug or dietary supplement. *Daniel Chapter One*, 2009 FTC LEXIS 157, at *284 (Initial Decision).

Respondents argue that the POM Products are only a small portion of the products Respondents sell. RRB at 204-205. Such assertion, even if true, is not material to whether the

advertising claims made for the POM Products are nevertheless transferable to the other categories of products that are covered by the Order and that are sold by POM and/or the affiliated Roll entities, such as other pomegranate-based products (sold by POM); citrus fruits (sold by Paramount Citrus), nuts (sold by Paramount Farms); bottled water (sold by FIJI Water); and wine (sold by Justin Vineyards). F. 56, 1378. *Standard Oil v. FTC*, 577 F.2d 653 (9th Cir. 1978), upon which Respondents rely, is readily distinguishable because in that case, as the court stated, "[t]he over-breadth of the order results from its coverage of "any . . . product in commerce" which is advertised by Standard . . . ." *Id. at* 661. In the instant case, the Order is limited to Respondents' advertising of food, drugs and dietary supplements. Order, Definitions para. 5.

Respondents further contend that their other products that do not involve pomegranates, such as citrus fruits, water, nuts and wine, are so "dramatically different" from the POM Products that Respondents would not use POM research to understand any components of such products. RRB at 205-206. Even if true, this contention is beside the point because the advertising technique, *i.e.*, sponsoring research of a product's health benefits and using the results to make disease claims, is readily transferable to advertising any food, drug or dietary supplement. In this regard, Respondents admit that they have sponsored "research exploring the health benefits of Wonderful Pistachios and Fiji Water" but assert that they have a "history" of "not advertising those benefits until the science is sufficiently developed." RRB at 207. This case demonstrates, however, that Respondents' judgment as to what constitutes advertising "health benefits" as opposed to what constitutes advertising a scientifically proven effect for disease, has not always been exercised appropriately.

Finally, Respondents assert that the deceptive claims found to have been made in this case are "peripheral" to their advertising strategy, and that their central advertising and marketing strategy has evolved away from health advertising and more toward "history" and "sexuality." RRB at 208. However, Respondents' asserted change of strategy does not make their past advertising themes and techniques any less transferable. As previously noted, such themes and the techniques used to communicate them are fully transferable – whether Respondents may opt to engage in other strategies in the future is not determinative.

Thus, the ease of transferability strongly supports the provisions in the Order making the Order applicable to any food, drug, or dietary supplement products.

(ii) Seriousness and deliberateness

The seriousness of the Respondents' conduct is evidenced by the fact that the deceptive advertising claims found to have been made in this case pertained to serious diseases and dysfunction of the body, including cancer. *See Daniel Chapter One*, 2009 FTC LEXIS 157, at *282 (Initial Decision); *see also Stouffer,* 1994 FTC LEXIS 196, at *39 (holding that deceptive low sodium health claim was serious because of overall health ramifications). The seriousness of Respondents' conduct is further demonstrated by the inability of consumers to evaluate whether Respondents' implied disease claims are true or actually supported by cited studies. *Id.*; *Thompson Medical*, 1984 FTC LEXIS 6, at *417. Thus, Respondents' claims concerning product effectiveness and clinical proof are "ones to which consumers were particularly susceptible." *Id.*; *see also Litton Indus. Inc.*, 1981 FTC LEXIS 94, at *150 (holding that use of survey results to support claim of product superiority has considerable potential to deceive, and, therefore, misuse of surveys in this regard is a serious violation). Respondents' assertion that consumers can access the identified studies themselves, RRB at 181, even if true, is not persuasive evidence that consumers can accurately assess the significance of the studies, much less in relation to Respondents' advertising claims.

The deliberateness of Respondents' conduct is also shown by the consistency of Respondents' advertising themes over the years, which supports a conclusion that the advertisements found herein to have violated the FTC Act did not constitute accident or an "isolated instance." *Thompson Medical*, 1984 FTC LEXIS 6 at *417. Respondents' contention that representations in certain advertisements were the result of mistake, RRB at 182; *see* RB at 67-68, even if assumed to be true, is insufficient to support a conclusion that Respondents' violations on the whole were accidental or inadvertent. Moreover, while it is arguable that the language used to make their advertising claims became less "aggressive" over the years, as Respondents contend, RB at 67-68; RRB at 182, there is little doubt that a central, and persistent, theme of Respondents' advertising was the POM Products' purported ability to affect diseases and dysfunction, and the scientific studies purportedly showing such effects.

See, e.g., Appendix to Initial Decision; F. 145-151. In addition, the advertising appeared in a wide variety of national and local media, for multiple years. F. 169-170, 291, 297, 307-308, 321, 328, 344, 365, 416, 421, 428, 432, 440, 449, 456, 469, 580-583. *See Sears, Roebuck*, 676 F.2d at 394 (in upholding multi-product order, noting that advertising campaign cost $8 million, ran for four years, and appeared in magazines, newspapers and on television throughout the country); *Daniel Chapter One*, 2009 FTC LEXIS 157, at *281 (Initial Decision) (noting that respondents made numerous deceptive representations over the Internet, in their publications, and through the DCO radio program, over the course of several years).

Respondents contend that POM's internal procedures for evaluating its advertisements and science should also be considered. Specifically, Respondents point to testimony that since 2007, POM has implemented a more formalized vetting process for advertisements relating to the health benefits of its products, which requires multiple stages of review that ultimately culminate in approval by the legal department before any advertisement is run. (Tupper, Tr. 2977-78). The evidence shows, however, that a number of the advertisements found to have violated the FTC Act were disseminated after 2007, when Respondents' review process was purportedly implemented. F. 307-308, 321, 365, 580-583, 962, 1143, 1313-1314. Therefore, it cannot be concluded, as Respondents urge, that their internal processes will ensure that only accurate information will be presented to the public in the future.[24]

[24] Complaint Counsel argues that deliberateness is also demonstrated by what Complaint Counsel asserts is evidence that "[d]espite concerns expressed by the New York State Attorney General's Office, the Council for Better Business Bureaus' National Advertising Division ("NAD"), NBC television, Dr. Pantuck, several IRBs [Institutional Review Boards], the FTC, and the FDA that POM's advertising claims misled consumers, POM continued to make the same or similar claims." CCB 59-60. Complaint Counsel further contends that "Respondents' own internal assessments recognized that their research was not sufficient to substantiate POM's claims," citing evidence regarding Respondents' evaluation of their research in relation to FDA approval standards. CCB at 60. *See, e.g.*, F. 1133 (internal document stating, "it is unclear whether PSADT is acceptable as a registrational endpoint for a drug designed to prolong the time to disease progression after initial therapy for prostate cancer"). Respondents strongly dispute the evidence upon which Complaint Counsel relies to make these charges, and/or the inferences Complaint Counsel draws from the cited evidence. RRB at 183-201. However, this Initial Decision need not, and does not, decide whether or not these additional potential grounds for finding deliberateness have been demonstrated because the evidence already demonstrating seriousness and deliberateness, and particularly transferability, more than adequately supports the multi-product Order entered in this case. Moreover, whether or not Respondents knew their studies were inadequate to obtain FDA drug approval for the POM Products, as Complaint Counsel contends, is not material since, as this Initial Decision has determined, Respondents were not required to substantiate their claims with the type of clinical trials that might be deemed necessary for drugs. *E.g.*, F. 693, 694-710, 963, 1147-1148; Analysis Section III.F.2-5, *supra*.

(iii) Prior violations

There is no evidence of prior violations of the FTC Act by Respondents. However, as noted above, all of the three relevant elements need not be present to warrant a multi-product order. *Telebrands Corp.*, 457 F.3d at 358-59. Courts look to the circumstances as a whole "and not to the presence or absence of any single factor." *Sears, Roebuck*, 676 F.2d at 392. In *Telebrands*, the Court of Appeals upheld the Commission's conclusion that the strength of the evidence as to the first two factors sufficiently established that there was a reasonable relationship between the remedy and the violation, and it was not necessary to also consider any prior consent orders. *Telebrands Corp.*, 457 F.3d at 362. Thus, while here there is no history of violations in this case, that factor is less important, taking into account the strength of the other relevant factors, particularly the ease of transferability to other products.

b. Part I of the Order

Part I of the Order prohibits Respondents from making representations that any Covered Product, as defined in the Order, "is effective in the diagnosis, cure, mitigation, treatment, or prevention of any disease, including, but not limited to, any representation that the product will treat, prevent, or reduce the risk of" heart disease, prostate cancer, or erectile dysfunction, "unless, at the time it is made, the representation is non-misleading and, Respondents possessed and relied upon competent and reliable scientific evidence that is sufficient in quality and quantity based on standards generally accepted in the relevant scientific fields, when considered in light of the entire body of relevant and reliable scientific evidence, to substantiate that the representation is true." Order, Part I. "Competent and reliable scientific evidence" is defined in the Order to mean "tests, analyses, research, or studies, that have been conducted and evaluated in an objective manner by persons qualified to do so, using procedures generally accepted in the profession to yield accurate and reliable results." Definitions, para. 4. Commission orders requiring respondents to have competent and reliable scientific evidence, as defined in this Order, that is based on the expertise of professionals in the relevant area and that has been conducted and evaluated by persons qualified to do so, are typical and have been consistently upheld by the appellate courts. *E.g.*, *Daniel Chapter One*, 2010 FTC LEXIS 11, *review denied*, 2010 U.S. App. LEXIS 25496 (D.C. Cir. 2010); *Telebrands Corp.*, 140 F.T.C. at 347, *aff'd*, 457 F.3d 354 (4th Cir. 2006); *In re Kraft*, 1991 FTC LEXIS 38, at *59-60, *aff'd*, 970

F.2d 311 (7th Cir. 1992). Such a requirement in this case serves the purpose of preventing future violations, is reasonably related to the violations found to exist, is sufficiently clear and precise, and is amply supported by legal precedent and the facts of this case.

c. Part I of the proposed order (FDA pre-approval substantiation requirement)

(i) Overview

Part I of the Order entered herewith differs from Part I of Complaint Counsel's proposed order. Part I of the proposed order would prohibit Respondents from making any representation that any POM Product "is effective in the diagnosis, cure, mitigation, treatment, or prevention of any disease, including, but not limited to, any representation that the product will treat, prevent, or reduce the risk of" heart disease, prostate cancer, or erectile dysfunction, unless, at the time it is made, the representation is non-misleading and:

> A. the product is subject to a final over-the-counter ("OTC") drug monograph promulgated by the Food and Drug Administration ("FDA") for such use, and conforms to the conditions of such use;
>
> B. the product remains covered by a tentative final OTC drug monograph for such use and adopts the conditions of such use;
>
> C. the product is the subject of a new drug application for such use approved by FDA, and conforms to the conditions of such use; or
>
> D. the representation is specifically permitted in labeling for such product by regulations promulgated by the FDA pursuant to the Nutrition Labeling and Education Act of 1990 ["NLEA"].

As Complaint Counsel explains, part I of the proposed order:

> provides that the necessary substantiation for future claims that any POM Product is effective in the diagnosis, cure, mitigation, treatment, or prevention of any disease – including heart disease, prostate cancer, or erectile dysfunction – is FDA approval, which may be provided in the form of a tentative final or final over-the-counter ("OTC") drug monograph, a new drug application, or labeling approval under regulations promulgated pursuant to the Nutrition Labeling and Education Act of 1990 ("NLEA"). For example, a claim that POM Juice reduces the risk of heart disease would need to be supported by an FDA

regulation authorizing such a claim in labeling.

CCB at 62-63. Complaint Counsel refers to these provisions as the "requirement of FDA pre-approval." CCB at 64-65. (hereafter, "FDA pre-approval requirement").

Complaint Counsel further explains that, under the proposed order, if Respondents "make a *qualified* claim, one that characterizes the limited scientific evidence supporting a relationship between a POM product and reductions in disease risk in a careful manner that eliminates any misimpression that a POM product actually reduces risk," then the substantiation they must possess is "competent and reliable scientific evidence," as provided under part III of Complaint Counsel's proposed order. CCRB at 50-51 (emphasis in original). However, "[i]f Respondents make [an] *unqualified* disease claim" in the future that any POM Product "*is effective* in the diagnosis, cure, mitigation, treatment, or prevention of any disease," then the "substantiation [Respondents] must possess for their claims would be FDA pre-approval." CCRB at 50 (emphasis in original). Thus, pursuant to part I of the proposed order, the FTC would determine (and ultimately have to prove at a contempt proceeding in court) whether Respondents made an "unqualified" disease claim, as opposed to a "qualified" "limited" and "careful" claim, and unless the FDA has already determined, applying FDA regulations, that Respondents' substantiation was adequate for that claim, then Respondents would be in violation of the FTC order. March 6, 2012 Tr. 67 (closing arguments).

As more fully discussed below, Complaint Counsel argues that its proposed FDA pre-approval framework is a form of fencing-in that is reasonably related to the violations in this case, is clear and concise, and provides a necessary "bright-line" rule for future claims. *Id.* at 66-67; CCB at 62-65. Respondents oppose the FDA pre-approval requirement on a variety of grounds, including that the requirement is unlawful because it exceeds the authority granted the FTC under the FTC Act and would violate Respondents' First Amendment freedom to engage in commercial speech. RB at 98-99; RRB at 210-218. Complaint Counsel has failed to demonstrate that the proposed FDA pre-approval requirement is necessary or appropriate for this case, as further explained below.

No previous decision by the Commission or any court has required FDA pre-approval as the required level of substantiation, including for purposes of a cease and desist order. Most

recently, in *Daniel Chapter One*, in which the respondents were found to have made unsubstantiated disease claims in violation of Sections 5 and 12 of the FTC Act, the Commission entered an order prohibiting them from making such claims in the future "unless the representation is true, non-misleading, and, at the time it is made, Respondents possess and rely upon competent and reliable scientific evidence that substantiates the representation." 2010 FTC LEXIS 11, at *3. This is also the standard adopted in the Order entered herewith. *See* Order Parts I and III. "Competent and reliable scientific evidence" was defined in the order entered in *Daniel Chapter One*, as in the instant Order, as "tests, analyses, research, studies, or other evidence based on the expertise of professionals in the relevant area, that has been conducted and evaluated in an objective manner by persons qualified to do so, using procedures generally accepted in the profession to yield accurate and reliable results." 2010 FTC LEXIS 11, at *1.[25] *See* Order, Definitions para. 5. *Daniel Chapter One* is clear authority for entering an order in this case requiring competent and reliable scientific evidence to substantiate disease claims. Indeed, the competent and reliable scientific evidence standard was deemed sufficient to redress the conduct in *Daniel Chapter One*, which was arguably more egregious than that presented by the instant case. The implied claims in *Daniel Chapter One*, unlike the instant case, were found to have been "so strongly implied as to be virtually express." 2009 FTC LEXIS 157, at *53, 55 (Initial Decision). In addition, unlike the instant case, the respondents in *Daniel Chapter One* conducted *no* testing on the effects of the challenged products, much less clinical testing, and the scientific substantiation relied upon by those respondents consisted of nothing more than compilations of citations to literature, mostly non-peer-reviewed papers, on the use of herbal medicines for a number of different diseases. *Id.* at *237-39; *compare* F. 732, 756, 1010, 1185. Moreover, in *Daniel Chapter One*, unlike the instant case, the respondents urged their customers to forgo medical treatment and instead use their products to treat cancer as an alternative to pursuing established medical treatments. *Id.* at *282-83.

Complaint Counsel's arguments in support of deviating from the order entered and

[25] Complaint Counsel's proposed order would apply the competent and reliable evidence standard, as set forth above, to representations "about the health benefits, performance, or efficacy of any Covered Product" under part III. Thus, Complaint Counsel acknowledges that this standard is sufficient for those claims, but nevertheless contends that FDA pre-approval should be the required substantiation for disease claims.

upheld in *Daniel Chapter One* are addressed below.[26]

(ii) Complaint Counsel's "reasonably related" justification for FDA pre-approval requirement

Complaint Counsel contends that requiring FDA pre-approval for disease claims is "reasonably related" to the violations in this case because (1) the FDA's standard for labeling approval for a food-disease relationship claim under NLEA ("significant scientific agreement" by experts that the claim is supported) is "cited" in the FTC *Enforcement Policy Statement on Food Advertising*; and (2) the FDA standard for drug approval under the Food, Drug and Cosmetic Act ("adequate and well-controlled" clinical investigations by experts demonstrating effectiveness), is "similar" to the "competent and reliable scientific evidence" standard applied in *Daniel Chapter One*, and referred to in the FTC publication, *Dietary Supplements: An Advertising Guide for Industry*. However, the foregoing FTC publications do not constitute regulatory law, which is made either by adjudication, 15 U.S.C. §45(b); 5 U.S.C. § 556, or by promulgated regulation, 15 U.S.C. §57b-3; 5 U.S.C. §553.[27] *See Ford Motor Co. v. FTC*, 673 F.2d 1008, 1009 (9th Cir. 1981) (noting that an administrative agency such as the FTC may announce principles through adjudication or rulemaking (citing *NLRB v. Bell Aerospace Co.*,

[26] Relying, *inter alia*, on *Jacob Siegel Co. v. FTC*, 327 U.S. 608 (1946), Complaint Counsel appears to argue that the Commission is empowered to include virtually any provision in a cease and desist order, so long as it is "reasonably related" to the violations in the case and is sufficiently clear and precise. CCB at 57-58. It is, of course, well established that Congress, through the FTC Act, has granted the Commission "wide discretion in its choice of a remedy deemed adequate to cope with . . . unlawful practices" and that "the courts will not interfere except where the remedy selected has no reasonable relation to the unlawful practices found to exist." *Jacob Siegel Co.*, 327 U.S. at 611-613. However, this should not be seen as a directive that any and all "reasonably related" remedies are to be ordered. The "reasonable relation" test is an outside limit on the permissible exercise of the FTC's discretion, rather than a standard for determining what remedy will serve the purpose of prohibiting and preventing the recurrence of deceptive trade practices. *See In re Litton Indus., Inc.*, 1981 FTC LEXIS 94, at *147 ("The purpose of a cease and desist order is to prevent the violations from being repeated, including by creating stringent monetary incentives (in the form of civil penalties) for its observance.").

[27] Complaint Counsel also notes that the Commission has entered into consent orders with other respondents requiring similar FDA pre-approval requirements. CCB at 64. Consent orders do not constitute legal precedent. "The circumstances surrounding . . . negotiated [consent decrees] are so different that they cannot be persuasively cited in a litigation context." *United States v. E. I. du Pont de Nemours & Co.*, 366 U.S. 316, 331 n.12 (1961). Rather, as confirmed by the express terms of the consent orders cited by Complaint Counsel, a consent order "is for settlement purposes only and does not constitute an admission by the respondent that the law has been violated." *In re Dannon Co.*, 151 F.T.C. 62, 91 (2011); *In re Nestle Healthcare Nutrition, Inc.*, 151 F.T.C. 1, 10 (2011); *see also In re Iovate Health Sciences U.S.A., Inc.*, No. 10-CV-587 (W.D.N.Y. July 29, 2010) (stating that Commission and Defendants "stipulate and agree to entry of this Order" but "do not admit or deny any of the allegations . . . .") (available at http://www.ftc.gov/os/caselist/0723187/100729iovatestip.pdf).

416 U.S. 267, 294 (1974)). The standard for substantiation for disease claims that has been reflected in adjudication is the "competent and reliable scientific evidence" standard, based on the opinions of experts in the relevant fields, as applied in this case and as affirmed most recently in *Daniel Chapter One.*

Moreover, as explained in Section III.F.2 of this Initial Decision, applicable case law clearly establishes that the required level of substantiation is a question of fact, based upon evidence on numerous factors, including the nature of the product, the safety of the product, the overall context in which the transaction occurs, and what experts in the relevant field would consider sufficient to support the claim at issue. *E.g., QT, Inc.*, 448 F. Supp. 2d at 959; *FTC v. Braswell*, 2005 U.S. Dist. LEXIS 42976, at *35; *Thompson Medical*, 1984 FTC LEXIS 6, at *387. In the instant case, after conducting the trial, and thoroughly reviewing the evidence and the voluminous transcript and record, it has been determined that the required level of substantiation for Respondents' implied disease claims is "competent and reliable scientific evidence," as defined by experts in the respective fields, and that such evidence does not require RCTs, such as those that would be required under FDA standards, because such claims were made for a safe food product that was not being urged as a substitute for medical treatment or advice. *See* F. 693, 694-710, 963, 1147-1148. This Initial Decision has not determined that FDA standards are the required level of substantiation for the implied disease claims found to have been made in this case, nor have Respondents been held liable herein for failing to meet FDA standards. Rather, it has been determined that, applying the competent and reliable scientific evidence standard, as defined by the experts in the respective fields, Respondents' substantiation was inadequate to support the implied disease claims found to have been made in this case and, therefore, Respondents violated the FTC Act. To the extent that part I of the proposed order seeks to impose a different and/or higher level of substantiation for future implied disease claims, which it effectively would do, part I of the proposed order is not reasonably related to the violations found to exist. *See Daniel Chapter One*, 2009 FTC LEXIS 259, at *70 (stating that order's requirement that "Respondents possess and rely upon competent and reliable scientific evidence that substantiates" their claims "only obliged [them] to do that which the case law under Sections 5 and 12 of the FTC Act has defined as necessary

to avoid deception").[28]

Similarly, Complaint Counsel asserts that it is proper to defer to FDA standards and evaluation of scientific evidence because such deference "is consistent with prior Commission practice." CCB at 63-64. Complaint Counsel cites *Thompson Medical*, in which the Commission noted that it was "additionally persuaded" that two well-controlled clinical tests was the correct level of substantiation for drug efficacy claims because "this is the standard currently being required . . . by the FDA" and advertisers of drug products will benefit from "greater regulatory certainty." *Thompson Medical*, 104 F.T.C. at 826, 1984 FTC LEXIS 6, at *398. In the instant case, however, as noted above, the evidence failed to show that RCTs were required to substantiate Respondents' implied claims because, among other reasons, the POM Products are food, or food-derived products, and were not being urged as an alternative to medical care or advice. F. 693, 694-710, 963, 1147-1148. Thus, *Thompson Medical* does not support imposing the proposed FDA pre-approval requirement in the Order in this case.[29]

(iii) Complaint Counsel's "bright-line rule" justification for FDA pre-approval requirement

Complaint Counsel further argues that the FDA pre-approval requirement is justified because it is "clear and precise," as required under *Colgate-Palmolive*. According to Complaint Counsel, FDA pre-approval is a "bright-line rule" that will "significantly increase . . . enforceability," "eliminate any confusion or ambiguities over the appropriate standard that Respondents must have to make disease claims" and prevent litigation. CCB at 64-65, 67. However, neither FDA pre-approval, nor FDA standards for obtaining such approval,

[28] In support of its argument that FDA drug approval standards are "similar" to FTC requirements, Complaint Counsel cites to the portion of the *Daniel Chapter One* Initial Decision that found as a fact, based on the weight of the expert testimony presented in that case, that "competent and reliable scientific evidence" to support the respondents' cancer effectiveness claims required "well-designed, controlled, clinical trials . . . ." 2009 FTC LEXIS 157, at *109-11. Consistent with that evidence, the order in *Daniel Chapter One*, like the Order in this case, defined competent and reliable scientific evidence as "tests, analyses, research, [or] studies, . . . conducted and evaluated in an objective manner by persons qualified to do so, using procedures generally accepted in the profession to yield accurate and reliable results." Thus, *Daniel Chapter One* is not authority for requiring Respondents in this case to substantiate claims in accordance with FDA approval standards.

[29] However, were Respondents to advertise a "drug" in the future, *Thompson Medical* clearly shows how application of the competent and reliable scientific evidence standard, as defined in the Order, could well result in a required level of substantiation that is consistent with FDA standards for drug approval.

constitutes the required level of substantiation under the FTC Act or applicable case law. Nor have FDA standards been found to constitute the required level of substantiation based on the evidence in the instant case. Thus, the "bright-line" proposed by Complaint Counsel would be imprudently drawn in this case. Moreover, "the complexity of the scientific issues, the unquestioned expertise of the FDA to evaluate scientific evidence relating to disease claims, and the Commission's interest in harmonizing with the FDA," CCB at 67, do not constitute sufficient reasons to create a new level of substantiation, through a cease and desist order against Respondents, *a fortiori*, considering the level of substantiation found to be required in this case. Indeed, the Second Circuit Court of Appeals has indicated that a "bright-line" of FDA approval for FTC cease and desist orders is "unnecessary, if not undesirable." *Bristol-Meyers Co. v. FTC*, 738 F.2d 554, 560 (2d Cir. 1984). In that case, the court rejected Bristol-Meyers' request to modify the FTC's cease and desist order to permit it to rely on demonstrating FDA approval of claims for its over-the-counter analgesics, stating: "FDA determinations are usually complex and subject to varying interpretations. To allow [respondents] to rely on its evaluation of these determinations could conceivably lead to more deceptive advertisements and to more disputes with the FTC." *Id.* The reasoning in *Bristol-Meyers* is equally applicable in the instant case, where Complaint Counsel seeks to replace the governing "competent and reliable scientific evidence" standard with FDA approval standards.[30]

In addition, Complaint Counsel misconstrues the purpose of the requirement that FTC orders be "clear and precise." The Court in *Colgate-Palmolive* explained that "an order's prohibitions 'should be clear and precise in order *that they may be understood by those against whom they are directed* . . . .'" 380 U.S. at 392 (emphasis added) (citation omitted). This language does not indicate that the "clarity and precision" requirement is designed for the benefit of the FTC in litigating potential future enforcement actions. Moreover, some level of uncertainty is contemplated by the FTC Act, as noted by the Supreme Court in *Colgate-Palmolive*: "If, however, a situation arises in which respondents are sincerely unable to determine whether a proposed course of action would violate the present order, they can, by

[30] It must also be noted that there is no evidence in the record of any coordination with, or acceptance by, the FDA with respect to requiring the FDA to pre-approve advertising claims challenged under the FTC Act.

complying with the Commission's rules, oblige the Commission to give them definitive advice as to whether their proposed action, if pursued, would constitute compliance with the order." 380 U.S. at 394; *Kraft*, 970 F.2d at 326 (citing the ability to seek an advisory opinion under 16 C.F.R. § 2.41(d) as a method of reducing advertiser uncertainty).[31] Moreover, whatever bright-line rule might be applied to substantiation will not necessarily reduce the risk of future litigation over whether Respondents made disease claims in the first place. As this case demonstrates, there is ample room for disagreement over whether or not advertisements make "unqualified" disease claims, as opposed to "qualified" "health benefit" claims, and the task of interpreting advertisements clearly does not lend itself to a bright-line rule.

In any event, Complaint Counsel cites no authority supporting a conclusion that the competent and reliable evidence standard, as provided in the Order upheld in *Daniel Chapter One*, is insufficiently clear or precise. In *Colgate-Palmolive*, the Supreme Court upheld the FTC order's requirement of a "test, experiment or demonstration" to substantiate future claims, and rejected the lower court's finding that such provision was invalid as too difficult to interpret. 380 U.S. at 393-94. The Court stated: "We believe that respondents will have no difficulty applying the Commission's order to the vast majority of their contemplated future commercials." *Id.* at 394. *See also Bristol-Meyers Co.*, 738 F.2d at 560 (rejecting argument that order's requirement of "reasonable basis" substantiation "to consist of 'competent and reliable scientific evidence'" was unduly vague). Indeed, Complaint Counsel's proposed order expressly relies on the competent and reliable evidence standard, albeit for claims other than disease claims, pursuant to proposed part III, and this standard has been incorporated into the Order for all claims governed by the Order. For all the foregoing reasons, there is no basis for concluding that the competent and reliable evidence standard is insufficiently clear or precise for purposes of enforcement.

Complaint Counsel further argues that a "bright-line" rule is necessary because, according to Complaint Counsel, Respondents have shown a willingness to "flout the law,"

[31] Rule 2.41 states in pertinent part: "(d) Any respondent subject to a Commission order may request advice from the Commission as to whether a proposed course of action, if pursued by it, will constitute compliance with such order. The request for advice should be submitted in writing to the Secretary of the Commission and should include full and complete information regarding the proposed course of action. On the basis of the facts submitted, as well as other information available to the Commission, the Commission will inform the respondent whether or not the proposed course of action, if pursued, would constitute compliance with its order." 16 C.F.R. § 2.41(d).

including, among other allegations, that Respondents failed to make any specific changes to their advertising in response to an FTC warning letter sent to Respondents in January 2008 and an FDA warning letter sent in January 2010. CCB at 65-66. The evidence upon which Complaint Counsel relies, even if true, indicates a disagreement between the Respondents and regulatory authorities regarding whether Respondents' advertising made disease claims and if so, whether those claims were adequately substantiated. *See id.* The disagreement with the FTC culminated in this litigation, in which neither side's position, as to the claims made or the adequacy of the substantiation, has been totally vindicated. Under these circumstances, Respondents' choice not to "heed warnings" and instead to litigate is not fairly interpreted as a willingness to "flout the law" but could be interpreted as an allowable choice made within the system as it exists.

(iv) Summary

Considering the entire record in this case, implementing Complaint Counsel's proposed FDA pre-approval requirement would constitute unnecessary overreaching. The competent and reliable evidence standard is established precedent, is reasonably related to the violations found to exist, and is sufficiently clear and precise to guide Respondents' future advertising practices. Precedent does not support implementing an FDA pre-approval requirement as a "bright-line" rule in this case. If Respondents choose to go "perilously close to an area of proscribed conduct," then they will "take the risk that [they] may cross the line." *Colgate-Palmolive*, 380 U.S. at 393.[32]

[32] Because Complaint Counsel has failed to adequately justify departing from established precedent to provide for the proposed FDA pre-approval requirement, that requirement is not included in the Order. Thus, this Initial Decision need not, and does not, address whether or not the proposed FDA pre-approval requirement should also be rejected because it exceeds the Commission's authority under the FTC Act and/or violates Respondents' First Amendment rights. It should be noted, however, that Respondents' generalized assertion that none of its commercial speech should be "barred" is without merit. RRB at 177. Requiring adequate substantiation for advertising claims does not "bar" commercial speech, but serves to prevent dissemination of misleading claims. *E.g.*, *Bristol-Meyers*, 738 F.2d at 562 ("Even in the absence of a finding of actual deception, agencies may properly regulate speech that is merely potentially deceptive."); *Sears, Roebuck*, 676 F.2d at 399 ("[T]he Commission may require prior reasonable substantiation of product performance claims after finding violations of the Act, without offending the [F]irst [A]mendment."); *Jay Norris, Inc. v. FTC*, 598 F.2d 1244, 1252 (2d Cir. 1979) ("[B]ecause the FTC here imposes the requirement of prior substantiation as a reasonable remedy for past violations of the Act, there is no unconstitutional prior restraint of petitioners' protected speech."). *See also Zauderer v. Office of Disciplinary Council*, 471 U.S. 626, 638 (1985) (holding that "[t]he States and the Federal Government are free to prevent the dissemination of commercial speech that is false, deceptive, or misleading"); *In re R. M. J.*, 455 U.S. 191, 207 (1982) (stating that "the States retain the authority to regulate advertising that is inherently misleading or that has proved to be misleading in practice").

d. Part II of the Order

Part II of the Order, consistent with the proposed order, prohibits Respondents from misrepresenting "the existence, contents, validity, results, conclusions, or interpretations of any test, study, or research." One of the violations alleged and proved in this case is that Respondents impliedly represented they had clinical proof of the effectiveness of the POM Products, when such clinical proof was not, in fact, adequate to substantiate this implied claim. Requiring Respondents to ensure that any advertised research results are fully accurate and non-misleading is reasonably related to this violation. In their Post-Hearing Briefs, Respondents do not articulate any argument for concluding that the provision is not reasonably related to the violations found in this case.

e. Part III of the Order

Part III of the Order, consistent with the proposed order, prohibits Respondents from making any representation about the "health benefits, performance, or efficacy of any Covered Product" unless the claim is not misleading, and supported by "competent and reliable scientific evidence that is sufficient in quality and quantity based on standards generally accepted in the relevant scientific fields, when considered in light of the entire body of relevant and reliable scientific evidence, to substantiate that the representation is true." This provision is reasonable and appropriate, and obliges Respondents only "to do that which the case law under Sections 5 and 12 of the FTC Act has defined as necessary to avoid deception." *Daniel Chapter One*, 2009 FTC LEXIS 259, at *70. Respondents, in their Post-Hearing Briefs, do not articulate any argument against applying this standard to future advertising claims within the scope of Part III.

f. Miscellaneous provisions

Part IV of the Order, consistent with the proposed order, provides that nothing in the Order prohibits Respondents from making claims that are specifically permitted in labeling, pursuant to FDA standards and regulations. In contrast to Complaint Counsel's proposed and rejected FDA pre-approval requirement, which made FDA standards the minimum substantiation for disease claims, this provision properly gives Respondents a "safe harbor"

against any future FTC challenge to Respondents' advertising representations, by enabling Respondents to demonstrate FDA approval. Substantially the same provisions were entered in the Order in *Daniel Chapter One*, 2010 FTC LEXIS 11, at *4-5 (Part IV) and are also appropriate in this case.

Parts V-IX of the Order, consistent with the proposed order, impose certain record-keeping, notification, and reporting requirements, and properly serve to facilitate administration of the Order. Finally, part X of the Order, consistent with the proposed order, provides for the termination of the Order in twenty (20) years. Respondents assert that a twenty-year period is "unconscionable" given that a portion of the advertising at issue occurred, and according to Respondents ceased, more than five years ago. However, as indicated in subsection 2.a., above, numerous advertisements disseminated after 2006 were found to have made implied disease claims, without adequate substantiation. F. 307-308, 321, 328,344, 365, 432, 580-583, 962, 1143, 1313-1314. Accordingly, a twenty-year duration is not unconscionable for the reason asserted by Respondents. *See also Daniel Chapter One*, 2010 FTC LEXIS 11, at *9-10 (Part XI) (providing for termination of order in twenty years).

5. Conclusion

The Order entered herewith will serve to prevent Respondents from engaging in deceptive advertising practices in the future, is reasonably related to the unlawful acts or practices found to exist, and is sufficiently clear and precise.

IV. SUMMARY OF CONCLUSIONS OF LAW

1. Complaint Counsel bears the burden of proving jurisdiction and liability by a preponderance of evidence.

2. Respondents POM Wonderful ("POM") and Roll Global ("Roll") are corporations within the meaning of Sections 4 and 5 of the Federal Trade Commission Act ("FTC Act").

3. Respondents Stewart Resnick ("Mr. Resnick"), Lynda Resnick ("Mrs. Resnick") and Matthew Tupper ("Mr. Tupper"), are "persons" within the meaning of Section 5 of the FTC Act.

4. Respondents' sales of POM Wonderful 100% pomegranate juice ("POM Juice"), and pomegranate extract products known as POMx Pills and POMx Liquid ("POMx") (collectively, the "POM Products"), are in or affecting commerce, as required by the FTC Act, 15 U.S.C. § 45(a)(1).

5. The Commission has jurisdiction over Respondents, and the conduct challenged in the Complaint, under Sections 4 and 5 of the FTC Act. 15 U.S.C. § 44, 45.

6. Under the Commission's precedent regarding the statutory term "advertisement," the media appearances and interviews by Respondents, challenged in this case as advertisements, do not constitute "advertisements" within the scope of the FTC Act because they were not paid for or sponsored by Respondents. 15 U.S.C. § 45, 52. Respondents do not dispute that the remaining advertisements and promotional materials disseminated by Respondents and challenged in this case (the "Challenged Advertisements") constitute "advertisements" within the meaning of the FTC Act.

7. The POM Products constitute "food" or "drugs," under Section 12 of the FTC Act. 15 U.S.C. § 55.

8. An advertisement is deceptive under the FTC Act if it is likely to mislead consumers, acting reasonably under the circumstances, in a material respect. The determination of whether Respondents disseminated false advertisements in violation of the FTC Act requires a three-part inquiry: (1) whether Respondents disseminated advertisements conveying the claims alleged in the Complaint; (2) whether those claims were false or misleading; and (3) whether those claims are material to prospective consumers.

9. An advertisement is deemed to convey a claim if a significant minority of reasonable consumers would interpret the advertisement to contain that message. Whether an advertisement conveys a claim is a question of fact.

10. To determine whether an advertisement conveys an alleged claim, the first step is to examine the advertisement itself (a "facial analysis"). A proper facial analysis requires

an evaluation of such factors as the entire document, the juxtaposition of various phrases in the document, the nature of the claim, and the nature of the transaction.

11. If, after viewing the advertisement as a whole, examining the interaction of all the different elements in the advertisement, it can be concluded with confidence that an advertisement can reasonably be read to contain a particular claim, a facial analysis is sufficient basis to conclude that the advertisement conveys the claim. However, an implied claim must be reasonably clear or conspicuous from the face of the advertisement.

12. If, after a facial analysis, it cannot be concluded with confidence that a particular advertisement can reasonably be read to contain a particular implied message, the advertisement will not be deemed to have made the alleged claim unless extrinsic evidence allows the conclusion that such a reading of the advertisement is reasonable.

13. "Target audiences," for purposes of interpreting advertising, refer to special audiences who as a group have a greater or lesser capability to recognize deceptive advertising than ordinary members of the adult population or have a distinctive reaction to particular advertising claims. Complaint Counsel has failed to prove that its asserted "target audience" of educated, affluent, health-conscious consumers would be more likely to interpret, or in fact did interpret, the Challenged Advertisements differently than ordinary consumers, or in what manner that group would do so.

14. The evidence demonstrates that Respondents disseminated advertisements that a significant minority of reasonable consumers would interpret to contain an implied claim that drinking eight ounces of POM Juice daily, taking one POMx Pill daily, and/or taking one teaspoon of POMx Liquid daily, treats, prevents, or reduces the risk of heart disease, prostate cancer and/or erectile dysfunction, and/or is clinically proven to do so, as alleged in the Complaint. It is not necessary to demonstrate that every Challenged Advertisement conveyed one or more of the alleged claims. Accordingly, even though the evidence failed to demonstrate that all of the Challenged Advertisements made the alleged claims, Complaint Counsel met its burden of proving the first element of a false advertising claim.

15. Two theories have been used to prove that an advertisement is deceptive or misleading: (1) the "falsity" theory or (2) the "reasonable basis" theory. As to both the alleged "false establishment claims" and the alleged "unsubstantiated efficacy claims," proof of deception requires proof that Respondents' substantiation failed to meet the level of substantiation required. Because whether Respondents' claims were deceptive turns on the nature and quality of Respondents' substantiation, the falsity and reasonable basis theories collapse into the same inquiry: did Respondents possess adequate substantiation to support their claims?

16. To determine whether the challenged claims are false or misleading, it must first be determined what level of substantiation Respondents were required to have for their advertising claims. This determination is a question of fact to be determined based

upon the evidence adduced at trial. Next, it must be determined whether Respondents possessed that level of substantiation. Respondents have the burden of establishing what substantiation they relied on for their product claims. Complaint Counsel has the burden of proving that Respondents' purported substantiation is inadequate.

17. Neither the FTC Act nor applicable case law requires well-designed, well-conducted, randomized, double-blind, placebo-controlled human clinical trials ("RCTs") to substantiate all health-related efficacy claims.

18. The evidence shows that the appropriate level of substantiation for the implied claims in this case that a product can treat, prevent, or reduce the risk of a disease is competent and reliable scientific evidence. Where such claims are made in connection with a food, or food-derived product, that is safe, and that is not being offered as a substitute for medical treatment, well-designed, well-conducted, randomized, double-blind, placebo-controlled human clinical trials, such as those required by the Food and Drug Administration are not required. However, for claims that a food or food-derived product treats, prevents, or reduces the risk of a disease, experts in the field would agree that competent and reliable scientific evidence must include clinical studies, although not necessarily double-blind, randomized, placebo-controlled clinical trials, adequate to show that the product did treat, prevent, or reduce the risk of disease.

19. The weight of the persuasive expert testimony demonstrates that there was insufficient competent and reliable scientific evidence to support the implied claims, made in advertisements disseminated by Respondents, that the POM Products treat, prevent or reduce the risk of heart disease, prostate cancer, or erectile dysfunction, or are clinically proven to do so. Therefore, such claims were false or misleading within the meaning of Section 12 of the FTC Act, and Complaint Counsel met its burden of proving the second element of a false advertising claim.

20. An act or practice is material if it is likely to affect the consumer's conduct or decision with regard to a product or service. Information is material if it is important to consumers.

21. To be material, a claim does not have to be the only factor or the most important factor likely to affect a consumer's purchase decision; it need only be an important factor.

22. The implied claims found to have been made in this case are material because they are health-related and resulted in increased product sales for Respondents. In addition, consumer research of the attitudes and usage habits of POM customers, conducted in the ordinary course of POM's business, shows that such claims are material to consumers. Accordingly, Complaint Counsel has met its burden of proving the third element of a false advertising claim.

23. Because Complaint Counsel has met its burden as to all three elements of a false advertising claim (see Conclusion No. 8, above), liability has been established.

24. Having concluded that Respondents violated the FTC Act, that Act authorizes an order requiring Respondents to cease and desist from such acts or practices.

25. Where one or more corporate entities operate in a common enterprise, each may be held liable for the deceptive acts and practices of the others. POM and Roll are liable as a "common enterprise" and, accordingly, both are held liable herein.

26. Injunctive relief may be obtained against an individual for a business entity's deceptive acts or practices if the individual either participated directly in the business entity's deceptive acts or practices, or had the authority to control them. The evidence demonstrates that Mr. Resnick, Mrs. Resnick, and Mr. Tupper each participated directly in the business entity's deceptive acts or practices, and/or had the authority to control them, and, therefore, each individual is held liable herein, along with POM and Roll.

27. Sole or ultimate control of a company is not necessary to establish individual liability. To establish liability on the basis of authority to control, it is sufficient that Mr. Tupper was part of the inner circle that formulated, controlled, and directed POM.

28. The purpose of a cease and desist order is to prohibit and prevent liable parties from engaging in deceptive acts or practices in the future. The cease and desist order must be sufficiently clear that it is comprehensible to the violator, and must be reasonably related to the violations found to exist.

29. The Commission's authority includes power to issue cease and desist orders encompassing all products or all products in a broad category, based on violations involving only a single product or group of products. Coverage of all products in a broad category is a means of "fencing-in" one who has violated the statute.

30. In determining whether a fencing-in order bears a "reasonable relationship" to a violation of the FTC Act, courts and the Commission consider: (1) the deliberateness and seriousness of the violation; (2) the degree of transferability of the violation to other products; and (3) any history of prior violations. All three factors need not be present for a reasonable relationship to exist. The more egregious the facts with respect to a particular factor, the less important it is that another negative factor be present.

31. A violation of the FTC Act is considered transferable where other products could be sold utilizing similar techniques. In the instant case, this transferability factor weighs strongly in favor of a multi-product order covering any food, drug or dietary supplement, not just the POM Products. Respondents' advertising techniques could readily be employed for any food, drug or dietary supplement.

32. The seriousness of Respondents' violations is shown by the fact that the claims pertained to serious diseases and dysfunction of the body, including cancer, and the inability of consumers to evaluate whether Respondents' implied disease claims were true or actually supported by cited studies. The deliberateness of Respondents' conduct is shown by the consistency of Respondents' advertising themes over the years and by

the fact that Respondents' advertising appeared in a wide variety of national and local media, for multiple years, which facts support the conclusion that the advertisements found herein to have violated the FTC Act did not constitute accident or an "isolated instance."

33. Although Respondents have no prior violations, the strength of the other relevant fencing-in factors, particularly transferability, is sufficient to establish a reasonable relation between the multi-product remedy and Respondents' violations found in this case.

34. The provision in the Notice Order prohibiting Respondents from making any disease claims in the future, unless such claim has been first approved by the Food and Drug Administration ("FDA") (the "FDA pre-approval requirement") is rejected as unsupported by governing precedent and the facts of this case, and is not reasonably related to the violations of the FTC Act found herein.

35. No previous decision by the Commission or any court has required FDA pre-approval as the required level of substantiation for disease claims, including for purposes of a cease and desist order.

36. The required level of substantiation is a question of fact, and the evidence in this case demonstrates that Respondents' implied disease claims require "competent and reliable scientific evidence," which does not necessarily require well-designed, well-conducted, randomized, double-blind, placebo-controlled human clinical trials, such as those required by the FDA.

37. The requirement in the order that respondents possess "competent and reliable scientific evidence" was deemed sufficient to redress unsubstantiated disease claims in *Daniel Chapter One*, No. 9329, 2010 FTC LEXIS 11 (Jan. 25, 2010), *review denied, Daniel Chapter One v. FTC*, No. 10-1064, 2010 U.S. App. LEXIS 25496 (D.C. Cir. Dec. 10, 2010), in which the violations were arguably more egregious than in the instant case.

38. The requirement in the Order in this case that Respondents possess competent and reliable evidence, as defined in the Order, to substantiate their claims is consistent with established precedent, is reasonably related to the violations found to exist in this case, is sufficiently clear and precise to guide Respondents' future advertising practices, and is adequate to prohibit and prevent Respondents from engaging in the same or similar violations in the future.

39. The Order attached herewith will serve to prohibit and prevent Respondents from engaging in deceptive advertising practices in the future, is reasonably related to the unlawful acts or practices found to exist, and is sufficiently clear and precise.

ORDER

DEFINITIONS

For purposes of this Order, the following definitions shall apply:

1. Unless otherwise specified, "individual respondents" shall mean Stewart A. Resnick, Lynda Rae Resnick, and Matthew Tupper, individually and as officers of POM Wonderful LLC ("POM Wonderful") and Roll Global ("Roll").

2. Unless otherwise specified, "Respondents" shall mean POM Wonderful and Roll, their officers, agents, successors and assigns; and the individual respondents and each of their successors, assigns, agents, and representatives.

3. "Commerce" shall mean as defined in Section 4 of the Federal Trade Commission Act, 15 U.S.C. § 44.

4. "Competent and reliable scientific evidence" shall mean tests, analyses, research, or studies, conducted and evaluated in an objective manner by persons qualified to do so, using procedures generally accepted in the profession to yield accurate and reliable results.

5. "Covered Product" shall mean any food, drug, or dietary supplement, including, but not limited to, the POM Products.

6. "Food" and "drug" shall mean as defined in Section 15 of the Federal Trade Commission Act, 15 U.S.C. § 55.

7. "Endorsement" shall mean as defined in 16 C.F.R. § 255.0.

8. "POM Product" shall mean any food, drug, or dietary supplement containing pomegranate or its components, including, but not limited to, POM Wonderful 100% Pomegranate Juice and pomegranate juice blends, POMx Pills, POMx Liquid, POMx Tea, POMx Iced Coffee, POMx Bars, and POMx Shots.

9. The term "including" in this Order shall mean "without limitation."

10. The terms "and" and "or" in this Order shall be construed conjunctively or disjunctively as necessary, to make the applicable phrase or sentence inclusive rather than exclusive.

I.

IT IS ORDERED that Respondents, directly or through any corporation, partnership, subsidiary, division, trade name, or other device, in connection with the manufacturing, labeling, advertising, promotion, offering for sale, sale, or distribution of any Covered Product, in or affecting commerce, shall not make any representation in any manner, expressly or by implication, including through the use of a product name, endorsement, depiction, illustration, trademark, or trade name, that such product is effective in the diagnosis, cure, mitigation, treatment, or prevention of any disease, including, but not limited to, any representation that the product will treat, prevent, or reduce the risk of heart disease, including by decreasing arterial plaque, lowering blood pressure, or improving blood flow to the heart; treat, prevent, or reduce the risk of prostate cancer, including by prolonging prostate-specific antigen doubling time ("PSADT"); or treat, prevent, or reduce the risk of erectile dysfunction; unless, at the time it is made, the representation is non-misleading and, Respondents possessed and relied upon competent and reliable scientific evidence that is sufficient in quality and quantity based on standards generally accepted in the relevant scientific fields, when considered in light of the entire body of relevant and reliable scientific evidence, to substantiate that the representation is true.

II.

IT IS FURTHER ORDERED that Respondents, directly or through any corporation, partnership, subsidiary, division, trade name, or other device, in connection with the manufacturing, labeling, advertising, promotion, offering for sale, sale, or distribution of any Covered Product, in or affecting commerce, shall not misrepresent, in any manner, expressly or by implication, including through the use of a product name, endorsement, depiction, or illustration, trademark, or trade name, the existence, contents, validity, results, conclusions, or interpretations of any test, study, or research.

III.

IT IS FURTHER ORDERED that Respondents, directly or through any corporation, partnership, subsidiary, division, trade name, or other device, in connection with the manufacturing, labeling, advertising, promotion, offering for sale, sale, or distribution of any Covered Product, in or affecting commerce, shall not make any representation, in any manner, expressly or by implication, including through the use of a product name, endorsement, depiction, illustration, trademark, or trade name, about the health benefits, performance, or efficacy of any Covered Product, unless the representation is non-misleading, and, at the time of making such representation, Respondents rely upon competent and reliable scientific evidence that is sufficient in quality and quantity based on standards generally accepted in the relevant scientific fields, when considered in light of the entire body of relevant and reliable scientific evidence, to substantiate that the representation is true.

IV.

IT IS FURTHER ORDERED that:

A. Nothing in this Order shall prohibit Respondents from making any representation for any product that is specifically permitted in labeling for such product by regulations promulgated by the Food and Drug Administration pursuant to the Nutrition Labeling and Education Act of 1990; and

B. Nothing in this Order shall prohibit Respondents from making any representation for any drug that is permitted in the labeling for such drug under any tentative final or final standard promulgated by the Food and Drug Administration, or under any new drug application approved by the Food and Drug Administration.

V.

IT IS FURTHER ORDERED that POM Wonderful, Roll, and their successors and assigns, and individual respondents shall, for five (5) years after the last date of dissemination of any representation covered by this Order, maintain and upon request make available to the Commission for inspection and copying:

A. All advertisements, labeling, packaging, and promotional materials containing the representation;

B. All materials that were relied upon in disseminating the representation;

C. All tests, reports, studies, surveys, demonstrations, or other evidence in their possession or control that contradict, qualify, or call into question the representation, or the basis relied upon for the representation, including complaints and other communications with consumers or with governmental or consumer protection organizations; and

D. All acknowledgments of receipt of this Order, obtained pursuant to Part VI.

VI.

IT IS FURTHER ORDERED that POM Wonderful, Roll, and their successors and assigns, and individual respondents shall deliver a copy of this Order to all of their current and future principals, officers, directors, and managers, and to all of their current and future employees, agents, and representatives having managerial responsibilities with respect to the subject matter of this Order, and shall secure from each such person a signed and dated statement acknowledging receipt of the Order. POM Wonderful, Roll, and their successors and assigns, and individual respondents shall deliver this Order to such current personnel within thirty (30) days after the effective date of this Order, and to such future personnel within thirty (30) days after the person assumes such position or responsibilities.

VII.

IT IS FURTHER ORDERED that POM Wonderful, Roll, and their successors and assigns, shall notify the Commission at least thirty (30) days prior to any change in the corporations or any business entity that POM Wonderful, Roll, and their successors and assigns, and individual respondents directly or indirectly control, or have an ownership interest in, that may affect compliance obligations arising under this Order, including but not limited to formation of a new business entity; a dissolution, assignment, sale, merger, or other action that would result in the emergence of a successor entity; the creation or dissolution of a subsidiary, parent, or affiliate that engages in any acts or practices subject to this Order; the proposed filing of a bankruptcy petition; or a change in the business or corporate name or address. Provided, however, that, with respect to any proposed change about which POM Wonderful, Roll, and their successors and assigns, and individual respondents learn less than thirty (30) days prior to the date such action is to take place, POM Wonderful, Roll, and their successors and assigns, and individual respondents shall notify the Commission as soon as is practicable after obtaining such knowledge. Unless otherwise directed by a representative of the Commission, all notices required by this Part shall be sent by overnight courier to the Associate Director for Enforcement, Bureau of Consumer Protection, Federal Trade Commission, 600 Pennsylvania Avenue NW, Washington, DC 20580, with the subject line *FTC v. POM Wonderful*. Provided, however, that, in lieu of overnight courier, notices may be sent by first-class mail, but only if electronic versions of such notices are contemporaneously sent to the Commission at DEbrief@ftc.gov.

VIII.

IT IS FURTHER ORDERED that each individual respondent, for a period of ten (10) years after the date of issuance of this Order, shall notify the Commission of the discontinuance of any current business or employment, or of an affiliation with any new business or employment. The notice shall include the individual respondent's new business address and telephone number and a description of the nature of the business or employment and all duties and responsibilities. Unless otherwise directed by a representative of the Commission, all notices required by this Part shall be sent by overnight courier to the Associate Director for Enforcement, Bureau of Consumer Protection, Federal Trade Commission, 600 Pennsylvania Avenue NW, Washington, DC 20580, with the subject line *FTC v. POM Wonderful*. Provided, however, that, in lieu of overnight courier, notices may be sent by first-class mail, but only if electronic versions of such notices are contemporaneously sent to the Commission at DEbrief@ftc.gov.

IX.

IT IS FURTHER ORDERED that POM Wonderful, Roll, and their successors and assigns, and individual respondents within sixty (60) days after the effective date of this Order, shall each file with the Commission a true and accurate report, in writing, setting forth in detail the manner and form of their compliance with this Order. In addition, within ten (10) days of receipt of written notice from a representative of the Commission, they shall submit additional true and accurate written reports.

X.

This Order will terminate twenty (20) years from the date of its issuance, or twenty (20) years from the most recent date that the United States or the Commission files a complaint (with or without an accompanying consent decree) in federal court alleging any violation of the Order, whichever comes later; provided, however, that the filing of such a complaint will not affect the duration of:

A. Any Part in this Order that terminates in less than twenty (20) years;

B. This Order's application to any proposed respondent that is not named as a defendant in such complaint; and

C. This Order, if such complaint is filed after the Order has terminated pursuant to this Part.

Provided, further, that if such complaint is dismissed or a federal court rules that Respondents did not violate any provision of the Order, and the dismissal or ruling is either not appealed or upheld on appeal, then the Order will terminate according to this Part as though the complaint had never been filed, except that the Order will not terminate between the date such complaint is filed and the later of the deadline for appealing such dismissal or ruling and the date such dismissal or ruling is upheld on appeal.

ORDERED:

D. Michael Chappell
Chief Administrative Law Judge

Date: May 17, 2012