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April 18, 2007

CONFIDENTIAL TREATMENT REQUESTED

VIA ELECTRONIC MAIL

Representative John D. Dingell
Chairman
United States House of Representatives
Committee on Energy and Commerce
Washington, DC 20515-6115

Representative Bart Stupack
Chairman
United States House of Representatives
Committee on Energy and Commerce
Subcommittee on Oversight and Investigations
Washington, DC 20515-6115

Re: Request to Johnson & Johnson

Dear Representatives Dingell and Stupack:

This letter is the initial response of Johnson & Johnson to the request of the U.S. House of Representatives Committee on Energy and Commerce dated March 20, 2007 ("Request") for certain information related to Erythropoiesis-Stimulating Agents ("ESAs"). As an initial matter, Johnson & Johnson ("J&J") would like to thank the Committee for providing an opportunity to address some of the recent concerns that have been raised about ESAs and for agreeing to give us additional time to prepare this response.

While we respectfully disagree with some of the characterizations contained in the March 20, 2007 letter, J&J intends to cooperate fully with the Committee. We have worked diligently to gather information to respond to the Committee's questions, and we are preserving records as requested. We believe this response is complete, but we will supplement it if additional responsive information comes to our attention.

J&J is a family of operating companies, each of which is a separate legal entity. In responding to the Committee's questions, we have gathered information primarily

from employees of Ortho Biotech, Inc. on behalf of Ortho Biotech Products, LP ("Ortho Biotech") and Johnson & Johnson Pharmaceutical Research & Development LLC ("PRD").

Ortho Biotech markets and distributes epoetin alfa under the brand name PROCRIT® in the United States pursuant to a product license agreement with Amgen, Inc. Amgen manufactures PROCRIT and also markets and distributes epoetin alfa under the brand name EPOGEN®. Amgen manufactures, markets and distributes darbepoetin alfa under the brand name of Aranesp®. PRD is the J&J company responsible for research and development activities relating to PROCRIT. Other J&J operating companies manufacture, market and distribute epoetin alfa under the brand name EPREX® and other names outside of the United States.

PROCRIT has four FDA-approved indications: (1) treatment of anemia in cancer patients on chemotherapy; (2) treatment of anemia in chronic renal failure patients; (3) treatment of anemia in zidovudine-treated HIV-infected patients; and (4) reduction of allogeneic blood transfusion in surgery patients. Based on adequate and well-controlled studies, PROCRIT has been demonstrated to be safe and effective for its intended uses.

In the sections below, we respond to the questions posed by the Committee. We request that the Committee treat this information as confidential and provide prior notice and an opportunity to object before making any information in this letter public.

1. **When did J&J or any of its employees or consultants learn of the suspension of any EPO study (Phase II-IV) that was halted out of concern for the subjects in the study?**

2. **When did J&J notify the FDA of such suspensions and who in the Agency was notified?**

Answers. We have broadly interpreted the Committee's questions to request information about any studies involving ESAs that were discontinued because of an increased risk of adverse events.

We have made our best effort to gather all information that is responsive to these questions from various sources. While we believe the companies' systems have captured all relevant studies they sponsor, we are continuing to verify this. The companies have limited information concerning studies that were sponsored by other companies. We will supplement this response if we learn of other relevant studies or information.

Our response identifies studies that were suspended for reasons that may have included an increased risk of adverse events. We are including: (1) discontinued studies for which PRD or Ortho Biotech was the regulatory sponsor, as that term is defined in 21 C.F.R. § 312.3(b); (2) discontinued studies for which PRD or Ortho Biotech provided clinical

supplies or financial support to another regulatory sponsor; and (3) discontinued studies that we are aware of, but that were not sponsored or supported by PRD or Ortho Biotech. Regulatory sponsors of U.S. studies have an obligation to notify FDA when a study is discontinued because of a safety signal. Regulatory sponsors also have an obligation to report serious and unexpected adverse events to FDA. Aside from the unique reporting obligations of the regulatory sponsors of clinical research for new uses of already approved drugs, companies who hold the marketing license of an approved drug have obligations to periodically report adverse event information about which they become aware through any source.

In February and March 2007, PRD and Ortho Biotech decided to temporarily suspend a number of additional epoetin alfa studies and are currently reviewing and amending study protocols to ensure that they are consistent with the new boxed warnings.

The discontinued studies listed below were designed to explore potential benefits associated with investigational uses, new indications and alternate dosing schedules for ESAs. The results of these investigational studies do not alter the fact that PROCRIT has been demonstrated to be safe and effective in its approved indications and dosing regimens.

(1) Discontinued Studies for which either PRD or Ortho Biotech was the Regulatory Sponsor

EPO INT-76 or BEST Study

PRD sponsored this study. The study's independent Data Monitoring Committee recommended that enrollment and administration of the study drug be discontinued on April 24, 2002. PRD promptly followed that recommendation and instructed study investigators to discontinue the study on April 29, 2002.

Although this study was not conducted in the United States and utilized the EPREX product, PRD notified FDA about the decision to discontinue this study in an April 29, 2002 letter addressed to Dr. Glen Jones of FDA's Center for Biologics Evaluation and Research.

PR00-03-006

Ortho Biotech sponsored this study. On August 20, 2003, the study's Data Safety Monitoring Board recommended that enrollment and administration of the study drug be discontinued. PRD followed these recommendations and instructed investigators to discontinue the study on August 22, 2003.

In a September 5, 2003 letter submitted to FDA's Center for Biologics Evaluation and Research, Attn: Document Control Room (HFM-99), PRD notified FDA of

its decision to discontinue this study. A copy of this letter was sent to Karen Winestock, a Project Manager in FDA's Center for Biologics Evaluation and Research.

EPO-CAN-15 or "LEGACY" Study

Ortho Biotech sponsored this study. The study's Data Safety Monitoring Board recommended that enrollment and administration of the study drug be temporarily suspended on September 29, 2003. Ortho Biotech followed that recommendation and notified study investigators in a letter dated October 1, 2003. The study was permanently terminated on February 23, 2004.

In a December 2, 2003 letter with attachments submitted by Amgen on behalf of Ortho Biotech and addressed to Dr. Glen Jones of FDA's Center for Biologics Evaluation and Research, Ortho Biotech specifically referenced the suspension of the EPO-CAN-15 study.

PR00-06-014 or "CHOIR" Study

Ortho Biotech sponsored this study. The study's Data Monitoring Committee recommended that enrollment and administration of the study drug be discontinued on May 26, 2005. Ortho Biotech discontinued the study on the same date.

In a May 27, 2005 letter submitted to FDA's Center for Drug Evaluation & Research, PRD notified FDA about the decision to discontinue this study.

(2) Discontinued Studies Sponsored by Others but for which PRD or Ortho Biotech Provided Support

PR00-27-024

This was an independent investigator-initiated study. Ortho Biotech provided support for this study in the form of clinical supplies. The study was terminated in October 2001.

We have not yet been able to determine when Ortho Biotech or PRD employees or consultants first learned that this study had been discontinued, or to identify relevant communications between Ortho Biotech or PRD and FDA about this study. An article about the study, however, was published in the *Journal of Pain and Symptom Management*, vol. 27 no. 2 (February 2004).

PR01-04-005, GOG 191

This study was sponsored by a cooperative research group called the Gynecologic Oncology Group ("GOG"). Ortho Biotech provided clinical supplies and

financial support for this study. Based on the recommendation of the study's Data Safety Monitoring Board on September 5, 2003, GOG decided to temporarily suspend enrollment pending a safety review. GOG permanently suspended enrollment and administration of the study drug on September 12, 2003. At this time, we believe that GOG informed Ortho Biotech about the decision to suspend the study on September 12, 2003.

In a September 18, 2003 letter and information package submitted by Amgen on behalf of Ortho Biotech and addressed to Dr. Glen Jones of FDA's Center for Biologics Evaluation and Research, Ortho Biotech informed FDA that enrollment in GOG-191 had been suspended.

RTOG-99-03

This study was sponsored by a cooperative research group called the Radiation Therapy Oncology Group ("RTOG"). Ortho Biotech provided clinical supplies and financial support for this study. Following the recommendations of the study's Data Safety Monitoring Board, RTOG temporarily suspended enrollment and administration of the study drug on September 26, 2003. The study was terminated on October 28, 2003.

To the best of our current knowledge, PRD employees learned about the decision to temporarily suspend the study on October 13, 2003 and about RTOG's decision to terminate the study on October 29, 2003.

RTOG-99-03 was discussed during a October 27, 2003 meeting involving representatives of Amgen, PRD and FDA, but we have not been able to confirm whether the suspension of this study was specifically discussed during the meeting. In a December 2, 2003 letter submitted by Amgen on behalf of Ortho Biotech and addressed to Dr. Glen Jones of FDA's Center for Biologics Evaluation and Research, Ortho Biotech specifically referenced the termination of RTOG-99-03.

EPO-CAN-20

This study was sponsored by a cooperative research group called the Ontario Oncology Cooperative Group and was conducted outside of the United States. Ortho Biotech provided clinical supplies and financial support for this study. The study's Data Safety Monitoring Board recommended that enrollment and administration of the study drug be suspended on November 24, 2003. Ortho Biotech was informed about the Data Safety Monitoring Board's recommendation on the same date. The Ontario Oncology Cooperative Group suspended the study on November 26, 2003.

In a December 2, 2003 letter submitted by Amgen on behalf of Ortho Biotech and addressed to Dr. Glen Jones of FDA's Center for Biologics Evaluation and Research, Ortho Biotech specifically referenced the termination of the EPO-CAN-20 study.

(3) Other Discontinued ESA Trials

Danish Head and Neck Cancer Study ("DAHANCA 10") Study

This study was conducted outside the United States by a research group called the Danish Head and Neck Cancer Group. Ortho Biotech and PRD were not involved in this study. Based on our review of publicly available information, this study appears to have been temporarily suspended on October 18, 2006 and terminated in December 2006.

To the best of our current knowledge, PRD employees first learned that the DAHANCA 10 study had been discontinued in January 2007.

CERA Phase II Dose-Finding Study

Based on publicly available information, it appears that this study was conducted outside the United States and supported by F. Hoffman-La Roche Ltd. ("Roche"). Ortho Biotech and PRD had no role in this study. In a February 23, 2007 press release, Roche announced that it was temporarily suspending enrollment in the study.

PRD and Ortho Biotech employees learned about the suspension of this study on the same date from Roche's press release.

3. Please describe all discussions J&J has had with the FDA or the Department of Health and Human Services (HHS) regarding direct to consumer advertising of Procrit since advising the Agency of any of the adverse events that are cautioned against in the black box warning announced last week.

Answer. We have broadly interpreted direct-to-consumer ("DTC") advertising to include broadcast and consumer print ads, internet advertising, and other media that reaches potential consumers of PROCRIT. Before responding to the Committee's request, we thought it might be helpful to provide an overview of the nature and extent of consumer advertising for PROCRIT over the past eighteen months.

Overview of Recent Consumer Advertising

For business reasons, Ortho Biotech decided prior to 2007 to discontinue both television advertising for PROCRIT and advertising in general circulation periodicals. The last broadcast ads for PROCRIT aired in July 2005. In 2006, advertising in general circulation periodicals was limited to one branded ad and one unbranded ad in *USA Weekend.*

Ortho Biotech has done some advertising for PROCRIT on the internet including banner/display ads and search engine marketing. Ortho Biotech has also maintained a number of websites that contain information about PROCRIT, anemia, cancer and chronic kidney disease. After the new boxed warnings, Ortho Biotech made the content

of most of these U.S. websites unavailable to the public. Exceptions include *www.procrit.com* and *www.orthobiotech.com,* which allow patients and healthcare providers to access important new safety information.

Ortho Biotech has also placed advertisements in specialized subscriber publications. In January 2007, Ortho Biotech purchased an unbranded advertising spot in a special issue of the *Cure* magazine, which is distributed to cancer patients throughout the year by the American Cancer Society and physicians. Ortho Biotech also purchased a branded PROCRIT advertisement in a newsletter distributed by the American Association of Kidney Patients. The company has provided branded and unbranded printed materials intended for display in physicians' offices, such as "Health Monitor Guides" that discuss chronic kidney disease. In addition, from January 2005 through the end of 2006, Ortho Biotech distributed "AnemiaPro Self-Screening Kits" for physicians to distribute as appropriate to patients. The kits contained a FDA-approved home testing device that enabled patients to ascertain hemoglobin levels.

Upon FDA approval of the new boxed warnings, Ortho Biotech immediately instructed its sales representatives not to distribute any promotional materials for PROCRIT until they could be revised to appropriately reflect the new label. Because some of the previously-described materials had already been distributed, they may still be available in limited supply to the public. As a responsible company, it is of course essential for Ortho Biotech actively to educate physicians, and even patients, about the new warning information in the label in a manner that fosters appropriate risk/benefit decision-making. Ortho Biotech has modified some of its physician-directed educational and promotional material accordingly and will continue to support websites and distribute materials that educate patients and healthcare providers about safely using PROCRIT in view of the revised labeling.

Communications with FDA

We interpret the Committee's specific question to be seeking information concerning all communications that Ortho Biotech has had with FDA or DHHS concerning consumer promotional materials for PROCRIT since late 2005 to capture communications preceding and following the adoption of the new boxed warnings. These recent communications are consistent with Ortho Biotech's long history of constructive dialogue with FDA about DTC advertising. For example, FDA reviewed PROCRIT DTC ads in 2001 and 2002 and ultimately agreed that the use of the "Strength for Living" tagline was appropriate after Ortho Biotech made certain adjustments to the ads to make it clear that the reference to strength referred only to the symptoms of anemia associated with chemotherapy, an approved indication for PROCRIT. All letters discussed below that Ortho Biotech has submitted and received from FDA were transmitted through Amgen because Amgen holds the Biologics License Application for epoetin alfa.

On December 1, 2005, FDA's Division of Drug Marketing, Advertising and Communications ("DDMAC") requested that all promotional materials for epoetin alfa be revised to reflect new risk information concerning pure red cell aplasia contained in a revised label. In a letter dated December 13, 2005, Ortho Biotech requested that DDMAC review safety information contained in PROCRIT consumer promotional materials and comment as to whether these statements adequately communicated the new risk information included in the revised label.

DDMAC provided advisory comments in a June 8, 2006 letter. Ortho Biotech wrote to DDMAC on June 19, 2006 that it was revising all consumer print promotional materials to incorporate DDMAC's comments and the new safety information.

In a letter dated August 30, 2006, Ortho Biotech requested that DDMAC review and comment on two proposed broadcast advertisements. DDMAC provided comments on November 16, 2006, but Ortho Biotech ultimately decided not to run those TV broadcast advertisements.

Shortly before February 23, 2007, Amgen informed Ortho Biotech about a communication it had received from FDA requiring the discontinuation of all promotional activities for their ESA products. Ortho Biotech consulted with outside counsel, who later advised Jeffrey Senger, Deputy Chief Counsel, and Sheldon Bradshaw, Chief Counsel for FDA, of the agency's demand. Subsequently, Dr. Richard Pazdur of FDA's Center for Drug Evaluation and Research clarified that the agency was requesting that Amgen and Ortho Biotech voluntarily discontinue promotional activities for their ESA products.

During telephone conferences on February 27, 2007 and March 1, 2007, representatives of DDMAC, Ortho Biotech and Amgen met to discuss anticipated labeling changes. During the February 27 conference, participants specifically discussed DTC advertising. Ortho Biotech informed DDMAC that the company might need to communicate with patients about the important new safety information, but agreed that prior to the May ODAC meeting it would solicit FDA's advice about oncology and DTC promotional materials prior to distribution in an effort to ensure that FDA agreed the revised material would encourage appropriate decision-making by healthcare practitioners. Participants involved in these meetings also discussed the fact that risk information cannot be assessed in isolation and must instead be evaluated together with the benefits of the drug.

On March 12, 2007, DDMAC sent a letter requesting that all promotional materials be revised to reflect information in the revised product labeling and patient package insert. In this letter, DDMAC also informed Amgen and Ortho Biotech that "claims related to the improvement of 'quality of life' or the symptoms of anemia, such as improvement of fatigue or energy, in zidovudine-treated HIV patients, cancer patients on chemotherapy and surgery patients should not be included in promotional materials."

In a letter submitted on March 16, 2007, Ortho Biotech informed DDMAC that the use of all PROCRIT promotional materials had been suspended and that this instruction had been communicated to all relevant personnel, including sales representatives, on March 9th and March 12th. The letter also informed DDMAC that Ortho Biotech was reviewing all promotional materials and would be revising them appropriately to reflect the information in the revised labeling and patient package insert. Ortho Biotech also told DDMAC, that as part of the review and revision of promotional materials, the Company would implement the request to eliminate claims related to "the improvement of 'quality of life' or the symptoms of anemia, such as improvement of fatigue or energy, in zidovudine-treated HIV patients, cancer patients on chemotherapy and surgery patients."

To the best of our current knowledge, Ortho Biotech has not communicated with the Department of Health and Human Services about DTC advertising for PROCRIT. We have made our best efforts to gather information about responsive communications, but it is possible that certain communications have been inadvertently excluded. We will supplement this letter if we obtain additional pertinent information.

4. **Please describe all promotions that J&J undertakes that have the effect of relating the prescription of EPO products to the income of physicians or their practices.**

None of Ortho Biotech's promotions are intended to have the effect of relating the prescription of EPO drugs to the income of physicians or their practices. Rather, prices and contracts given to purchasers of PROCRIT reflect intense competition between Ortho Biotech and its competitors for ESA sales. Depending on the reimbursement methodology used by health insurers and other payors, discounts and rebates for PROCRIT may affect physician and physician practice income.

Ortho Biotech reviews its discounts and rebate programs related to PROCRIT to ensure compliance with applicable statutory and regulatory guidance, including the discounts safe harbor provision set forth at 42 C.F.R. § 1001.952(h). The current contracting system has been in place since 2005, and new contracting strategies are being considered. Ortho Biotech will continue to make every effort to ensure that any discounts or rebates offered are in full compliance with applicable statutes and regulatory guidance.

Ortho Biotech is also committed to making sure that its sales representatives promote its products appropriately. Ortho Biotech sales representatives use tools designed to help explain contracts to physician customers and to assist them in calculating net price and discounts. All sales representatives have been instructed not to discuss profit. Sales representatives found doing so have faced serious punishment, including termination.

If you would like additional details about the information in this letter, we would be happy to discuss your request. We look forward to working with you and your staff as you review this response.

Sincerely,

Lanny A. Breuer/RAR

Lanny A. Breuer