U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES

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FOOD AND DRUG ADMINISTRATION

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RISK COMMUNICATION ADVISORY COMMITTEE

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FRIDAY,
MAY 16, 2008

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The meeting convened at 8:00 a.m. in Plaza I and II of the Hilton Washington DC/Rockville Hotel, 1750 Rockville Pike, Rockville, Maryland, Baruch Fischhoff, Ph.D., Chair, presiding.

COMMITTEE MEMBERS:

BARUCH FISCHHOFF, Ph.D., Chair
CHRISTINE M. BRUHN, Ph.D., Member
JACOB DeLaROSA, M.D., Member
ANNAMARIA DeSALVA, Member
MICHAEL GOLDSTEIN, M.D., Member
PRERNA MONA KHANNA, M.D., M.P.H., Member
MADELINE Y. LAWSON, M.S., Member
MUSA MAYER, M.S., M.F.A., Member
DAVID P. MOXLEY, M.S.W., Ph.D., D.P.A., Member
LINDA NEUHAUSER, Dr.P.H., M.P.H., Member
JOHN E. PALING, Ph.D., Member
ELLEN M. PETERS, Ph.D., Member
BETSY LYNN SLEATH, Ph.D., Member
MARIELOS L. VEGA, B.S.N., R.N., Member

CONSULTANTS:

J. CRAIG ANDREWS, Ph.D.
CHERYL L. HOLT, Ph.D.
GAVIN HUNTLEY-FENNER, Ph.D.
ELAINE H. MORRATO, Dr.P.H., M.P.H.

FDA PARTICIPANTS:
LEE L. ZWANZIGER, Ph.D., Designated /Federal Officer/Executive Secretary
KRISTIN DAVIS, J.D., Deputy Director, Division of Drug Marketing, Advertising, and Communications, Center for Drug Evaluation and Research
AMY O=DONOGHUE, Division of Drug Marketing, Advertising, and Communications, Center for Drug Evaluation and Research
NANCY M. OSTROVE, Ph.D., Senior Advisor for Risk Communication, Office of the Commissioner

PUBLIC COMMENTS:

ELIZABETH FOLEY, Consumers Union
PETER J. PITTS, Center for Medicine in the Public Interest and Manning, Selvage & Lee
KIM WITCZAK

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P-R-O-C-E-E-D-I-N-G-S

8:04 a.m.

CHAIRMAN FISCHOFF: Let's start now. I'm Baruch Fischoff, I'm Chair of the Food and Drug Administration's Federal Advisory Committee Act, and let me welcome the members of the panel, our consultants, members of the audience, and other members of FDA staff who are going to be helping us.

This is the second of two days in which we are discussing the direct-to-consumer advertising for those who weren't here yesterday, to look particularly at the question of, how does direct-to-consumer advertising work with special populations, the elderly, young, and minorities, and so on, in order to see what advice we can provide to FDA for making it work as well as possible in anticipation of -- in order to facilitate a report that FDA is required to provide to the Congress under the FDA Amendments Act of 2007.

Today, we are going to be looking

at another specific question under the general rubric of -- under the general topic of direct-to-consumer advertising, which is a requirement that FDA evaluate a proposal to have an 800 number appear with television ads that will encourage people to report side effects that they have. You'll get -- everyone will get details on that. FDA has been required to produce a report within six months, and there's a proposal for the report that will be presented, so that the meeting will -- none of that was official, so the meeting now officially begins, Lee Zwanziger, the Designated Federal Official, will bring us to order.

DR. ZWANZIGER: Thank you, Dr. Fischoff.

Good morning, everyone. I'm Lee Zwanziger, and I want to welcome, again, the members and consultants of the Risk Communication Advisory Committee, also members of the public and FDA staff, thanks for coming

today.

The following announcement addresses the issue of conflict of interest at this meeting, and is made a part of the public record to preclude even the appearance of such at this meeting.

As Chairman Fischoff just mentioned, today the committee will be discussing design considerations for studying the appropriateness of including in television DTC ads a statement encouraging consumers to report negative side effects of prescription drug ads to MedWatch as is currently required for print DTC prescription drug ads, any study with substantive notes and comment in accord with the Paperwork Reduction Act.

Based on the submitted agenda for the meeting, and all financial interests reported by the committee participants, it's been determined that no interest in firms regulated by the Food and Drug Administration present the potential for conflict or

appearance of a conflict of interest at this meeting.

In general, the committee participants are aware of the need to exclude themselves from involvement in discussion of topics if their interest will be affected and their exclusion would be noted for the record.

With respect to all other participants, we ask in the interest of fairness that they address any current or previous financial involvement with any firm whose product they may wish to comment upon.

We do have a period for open public comment listed on the agenda. If anyone that's not already signed up wishes to speak, please see one of my colleagues at the sign-in table outside.

This entire meeting is being transcribed and the transcript will be posted on FDA's website. It can only contain what the transcriber could hear, so let's all please remember to turn on and speak into the

microphones when you are recognized to speak, and turn them off when you are not speaking.

I'd also suggest that we all turn off cell phones and other communication devices or put them in silent mode. Having forgot that with my own yesterday, I'll say it's pretty embarrassing when it goes off in the meeting.

Finally, I have a couple of extra cords here, if anybody is missing something, please come and see me at a break, and thank you very much.

CHAIRMAN FISCHOFF: Well, let's -- we'll introduce ourselves, and then we'll get to work.

I'm Baruch Fischoff, I'm in the Department of Social and Decision Sciences in the Department of Engineering and Public Policy at Carnegie Mellon University, where I run the Decision Science Undergraduate Major. If anybody has kids thinking about college, see me at the break.

DR. SLEATH: I'm Betsy Sleath. I'm a Professor of Pharmaceutical Outcomes and Policy at the University of North Carolina, Chapel Hill.

MS. MAYER: I'm Musa Mayer. I am a Patient Advocate representing women with breast cancer.

DR. PALING: I'm John Paling. I represent the Risk Communication Institute, and we are dedicated to helping doctors provide patient-focused information.

DR. NEUHAUSER: Good morning, Linda Neuhauser, University of California at Berkeley, School of Public Health. My main interest is in user-designed health communication.

DR. HUNTLEY-FENNER: Gavin Huntley-Fenner. I'm a Managing Scientist with Exponent. My background is in brain and cognitive sciences. I'm an experimental psychologist, and I design warning labels, inserts, some messages on video, et cetera,

and also conduct hazard analyses for products of various types, including pharmaceutical and medical device products.

DR. MORRATO: Hello, I'm Elaine Morrato, and I'm from the University of Colorado, School of Medicine and School of Public Health and Clinical Pharmacy.

My research interest is in pharmaceutical risk management and communication and diffusion of, and adoption of, risk minimization recommendations.

DR. HOLT: Good morning, I'm Cheryl Holt. I'm with the Division of Preventive Medicine at the University of Alabama at Birmingham, School of Medicine. I'm a Social Psychologist in health communication research.

DR. ANDREWS: Good morning. My name is Craig Andrews. I'm Professor of Marketing and Kellstadt Chair at Marquette University in Milwaukee.

My research is on advertising and public policy, public health issues, and ad

copy testing.

DR. O'DONOGHUE: My name is Amy O'Donoghue. I'm a Social Science Analyst with DDMAC at FDA.

MS. DAVIS: I'm Kristin Davis, also from DDMAC at FDA.

DR. OSTROVE: Morning, Nancy Ostrove, with the Food and Drug Administration. I'm the Senior Advisor for Risk Communication.

DR. DeLaROSA: Jacob DeLaRosa, from Idaho State University, cardiac surgeon.

DR. BRUHN: I'm Christine Bruhn, with the University of California at Davis, Food Science Department, and I'm the Director of the Center for Consumer Research.

MS. LAWSON: Good morning, I'm Madeline Lawson, and I'm President and CEO of the Institute for Multi-Culture and Minority Medicine, based in Washington, D.C.

DR. GOLDSTEIN: Hello there, I'm Michael Goldstein, at the Institute for

Healthcare Communication, which is a non-profit foundation that focuses on enhancing clinician/patient communication. I'm also at Brown University.

DR. PETERS: Good morning. My name is Ellen Peters. I'm a Decision Psychologist at Decision Research in Eugene, Oregon. We are non-profit research institution, and I'm interested in how people process various kinds of information and decisions, and how that makes a difference.

MS. VEGA: Good morning. My name is Marielos Vega, and I am a Staff Nurse with the Department of Family Medicine at the New Jersey Medical School.

DR. MOXLEY: Good morning, I'm David Moxley from the University of Oklahoma, Norman, where I share in the school's social work program and social administration and community practice.

DR. KHANNA: Hello, everybody and welcome. I'm Prerna Mona Khanna, a medical

doctor and professional medical communicator. I'm triple Board Certified in Internal Medicine, Public Health and Preventive Medicine, and Occupational Medicine, but I've been a full-time journalist for the last six years, former reporter with the Wall Street Journal and CBS-11 News in Dallas/Ft. Worth. I'm also an emergency aid volunteer with the Disaster Medical Assistance Team and the Texas State Guard, and Associate Adjunct Professor with the University of North Texas, Health Sciences Center, in the Schools of Public Health and Medicine.

CHAIRMAN FISCHOFF: Thank you.

Let me now invite Kathryn Aikin who will tell us about the study.

DR. OSTROVE: And, let me -- this is actually Amy O'Donoghue, Kathryn Aikin is not feeling well, and it would probably not be good for her to be here today, so DDMAC has offered Amy, although she is actually on maternity leave starting yesterday. Amy works

with Kit over in DDMAC.

So, Amy?

DR. O'DONOGHUE: Thank you, Nancy. I'm only hoping I can reach the microphone here.

So, as Nancy introduced, I am Amy O'Donoghue, and I would like to begin by saying that I found out that I would be reviewing these slides and presenting them at 6:30 yesterday evening, so I will do my best to represent what Kit had to say, and we'll go from there.

I'm going to talk about three different issues today, all related to this project that we are all here to discuss. First, I will go into a little bit of detail about the public comment process for Federal research, just to give you some background and idea about what the research process is. Then, I will talk about the current legislation, and other relevant background. Some of you may have heard in the press that

there's a toll-free study that was just completed, there's a new toll-free study, there's been some confusion and I will attempt to clarify that. And then, I will talk directly about the research questions we are here to discuss, and present a draft study design that we have come up with.

You have in your slides this quite complicated slide that I'm not going to go into as much detail as Kit probably would have gone into, I'm going to go over the big main points of it, but I do want to give you some background.

OMB stands for the Office of Management and Budget, for those of you who are not aware, and in 1980, and then in 1995, the Paperwork Reduction Act was passed. This was designed to allow Federal agencies to have more responsibility and public accountability for any type of investigations that they wanted to conduct with the American public. It was designed to do two things, basically,

minimize the paperwork burden on all sorts of people, individuals, small businesses, educational non-profits, other non-profits, contractors, state and local governments, anyone you can think of. So, essentially, you and me, we don't want you to all be burdened with hours, and hours, and hours of filling out paperwork and answering questions for the Government, et cetera, et cetera. So, this was designed to minimize that.

Also, and probably more importantly, it was designed to ensure the greatest possible public benefit from research. So, in another words, this is taxpayer money, we want to make sure that that money is being used in the most valuable way possible.

So, what this did was, it gave OMB, the Office of Management and Budget, review authority over all agency information collection activities, and, essentially, research falls well under that agency

information collection activities, involving nine or more individuals. And, essentially, all of our research involves nine or more individuals, so that usually applies to us.

So, that's the background of why this process occurs, and like I say, I'm going to give you the big points of the process, and not go into the -- let me just get the whole slide up here -- the first thing that happens is that we design a study, and when we design a study we submit it for public comment in the Federal Register. And, this first public comment period is a 60-day period, during which anyone in the public, usually the stakeholders that are interested in the issue, so sometimes academics, sometimes people from industry, sometimes people from consumer groups, will submit comments to us about the design, about the particular topic, about anything related to the research.

We do accept comments after the public comment period closes. We are not

obligated to respond to them, but the whole purpose of this process is to improve the research, and or those of you who are researchers you know that every subsequent discussion that you have, and every subsequent set of eyes that looks at research generally improves it, so we are genuinely interested in improving the research, so we do try to take those into account if we have the option.

But, people, basically, have 60 days to comment on the study. After that period, if no comments are received, which I personally have never been involved in a study that received no comments, but if no comments were received we could turn it right around and put it into a second public comment period, which is a 30-day public comment period.

Usually, what happens, however, is that we do receive comments. In DDMAC, previously six or seven comments was a lot of comments. The latest study that we submitted

for public comment in the fall, which was on the role of distraction in broadcast advertisements, received 30 comments, and so that was quite a lot for us.

Most of these comments are very useful, and they provide important points, and we like to take them into consideration, so the revision time depends, of course, on the number of comments we receive and the complexity of the comments.

When we do get comments, and we've revised the design, we will send it out for peer review, and what this is, is a period where we send it out to -- there's no set number, approximately, three to five individuals who are experts in the field of interest, who usually have experience with research design, often academics, and we will usually give them a month, because they are always really busy and so let's give them some time to respond.

And, when we get back those

comments, we send it out for human subjects review, and at FDA this is called the Research Involving Human Subjects Committee, Risk Committee, and so we do have to go through that process as well.

And then, it goes out for the second public comment period, the 30-day public comment period. The comments that are received to the 30-day comment period do not come directly to us, they go directly to OMB. And, OMB then has another 30 days after the 30 days to comment on the research, and to either approve it, to approve with conditions, or to disapprove the research. And, we often have a working relationship with what we call our desk officer at OMB, where we'll have questions back and forth, just to clarify what we are doing, and to make sure that everything is sensible and makes sense to them.

So, without including any filing or posting deadlines, or revisions, or anything like that, the minimum amount of time that

this process takes is 120 days, and that's just for the public comment and the OMB time. So, obviously, it generally takes longer than that.

So, I'm going to switch gears right now and talk about the FDAAA, Amendments Act of 2007, which I'm sure you talked a lot about yesterday. I was unable to make it yesterday.

The first paragraph up here, basically, is already enacted, and this already mandates the inclusion of a statement in print direct to consumer ads, the statement: "You are encouraged to report negative side effects of prescription drugs to the FDA," and visit either the website or they provide a toll-free number. So, that's already in effect, it's been in effect since the end of March.

The second paragraph demonstrates that Congress wants to know if this is a good idea to put this into television ads. So, what they'd like us to do, and what they

actually would have liked us to do by March, this was six months after enactment of the Act, was to actually conduct a study on whether this would be an appropriate thing to include in a television ad. Obviously, we are not there. We are working diligently on it, and that's why we are here, so that we can get all of your input on it.

So, the main issue that Congress would like us to study, the main question that they'd like us to address, is whether the inclusion of the statement will detract from the presentation of risk information, and, of course, FDA is always interested in making sure that the risk information is conveyed to consumers. It's an empirical question as to whether the inclusion of the statement and the way that it's included would interfere or, perhaps, facilitate the risk information.

And, if it does not impede the risk information, what is the right amount of time to display this phrase? And, I'm going to

come back to that, because that relates to how we have interpreted what Congress is looking for from us, in terms of displaying it. We assume that means they want it to be on the screen in words.

So, I'm going to talk briefly about the other toll-free study that I mentioned before, because you may have heard about it, and there's been some question about it. This study began as a result of the Best Pharmaceuticals for Children Act, which is up there on the screen. Basically, this Act indicated that a statement on certain prescription drug labeling and over-the-counter labeling should include a toll-free number maintained by FDA, so that people have a number to report adverse events or side effects, and that the statement should be clear enough to indicate that people shouldn't use this number to get medical advice. They should actually call their doctor for that, and call FDA only to report it, hopefully,

after the emergency or the situation is over.

On April 22, 2004, FDA published a proposed rule with this proposed side effects statement, and FDA solicited comments on a particular statement that they believed would fulfill the wording, and I don't have the exact wording, but for over-the-counter labeling, for example, it was something like stop use and ask the doctor if you have a side effect. If you'd like to report to FDA call 1-800-FDA et cetera.

So, many of the comments that were received suggested that FDA actually test the wording of the statement, because no one had actually looked at that, and they wanted to test the wording, obviously, to determine what the most understandable wording would be, and in terms of space limitations because this statement would possibly be on prescription drug vials or other small areas, that the most concise wording that was understandable would be desirable.

Also, to evaluate the consumer comprehension of the statement, again, one of the concerns was that people would call FDA with an emergency, looking for advice, and that was something, obviously, you didn't want, and we wanted to make sure that people could understand the difference between mild side effects and severe side effects, in terms of if you take a drug and you have a headache for an hour, probably not something you need to call FDA about. If you experience chest pain, however, that's a very serious side effect, that might be something that FDA would like to know about.

So, it was determined that FDA should conduct some focus groups and some other consumer studies to inform the wording of each of the statements.

In the spring and summer of 2006, we did conduct some focus groups. We had two groups. One included people who had a high school education or less. One group included

people who had some college or more. FDA does not make policy on the basis of focus groups. Focus groups are qualitative research, and as such they are not representative. These groups had, approximately, nine people in them each, so, you know, you pick nine people off the street and who knows what layer of the population they are from, so we use them to develop our quantitative research. So, we will then know what language people use when they are thinking about these issues, if they are thinking about the issues, and what kind of direction we should go when we design the quantitative research from these studies.

But, as such, we did find some interesting findings for what they are worth. Keep that in mind when you look at these. We found that some of the high school educated or less group did think that the statements instructed them to call FDA for medical help. Again, some out of nine, and you can do what you want with that. Some participants in both

groups did understand the statements, but said it's not really enough motivation for me to call the number. I probably wouldn't report it. Some did understand the statements and said, hey, yeah, I might report a side effect to FDA, that's important to me.

The one finding that we did find that was fairly universal, again among these 18 people, was the suggestion of adding a website, because in this particular toll-free statement there was no website as an option, it was just the toll-free number. But, people expressed, you know, I might like to report this over the web, so this might be a good idea.

So, the focus groups were conducted in 2006, and we designed and collected data in a quantitative label comprehension study. We received the data in March, and that is currently being analyzed, so we will have that data soon.

Now I'd like to return to the

research questions at hand that we are all here to talk about today. Based on FDAAA, Congress would like us to study the following questions. Does the inclusion of a toll-free number for reporting side effects in television advertisements, DTC television advertisements, detract from the communication of important risk information, and if the statement does not detract what is the optimal length of time the statement should be displayed in the ad?

So, this is our proposed design in a graphic visual form for you. So, teh consideration that FDA has are two main variables here. One is the appropriateness of the inclusion of this toll-free statement, and the other is the duration of the display in the ad. So, we've defined this is terms of two major independent variables, the placement of the statement, and the duration in SUPER. And, when I have SUPER up here what I mean is superimposed text, that's a text that would be

written across the screen.

So, we are looking at a 3x2 factorial design, plus one, plus one, and I'll describe what we have conceived of as each of the levels of these variables. In terms of placement, it's possible to have the statement -- before the major statement let me go back and just update you on the major statement because some of you are not, obviously, you don't live with DTC advertising as we do, the major statement in a broadcast ad is that part of the ad that you've seen where they'll talk about the indication and then they talk about the major risks in the ad. And, you've also seen reference to the website, or a concurrently running print ad, and a telephone number, and that is called adequate provision. So, as long as people have adequate provision for getting all of the major -- all of the risk information broadcast ads can have just the statement of the most important risk information. And, this is in the audio

portion of the ad. So, a SUPER is always saying these important risks. So, when I talk about the major statement that's what I'm talking about, that particular part of the ad that talks about the major risks.

So, the statement could be placed before the major statement of risks, and it's possible that having the statement up there could cause people to start thinking, oh, if I have a side effect, and then the risk information comes on, we don't know how that will effect their interpretation of the risk information. It could be placed during the major statement of risks, while they are actually listing the side effects. It could be stated there, or it could be after the major statement of risks, in which case people have heard the risks and sort of process them and then they see the statement saying, well, you could report them if you experience them.

So, we are proposing looking at those three placements.

In terms of duration, we've defined this as short and long. We haven't specified exactly how short or how long, that's one of the issues that we'd like to discuss today.

We are also, obviously, going to include a control statement, with no toll-free statement, this type of ad would be similar to what you see today, because there is no statement currently in ads like this. And then, we'd like to also look at a condition of extra comments, and in terms of this we would look at the major statement presented after the risks, and also presented in the audio portion at the same time. So, it would be a reinforcing statement.

In terms of how we would go about doing this, we would recruit a number of participants, and we would have them randomly assigned to one of the advertising conditions. So, in other words, this would be a between subject design, so each person would only see one. And, each person would view the

advertisement two times, and then answer some questions about it. Our primary dependent variable in this case would be comprehension of risk, since that is the issue that we are really concerned about.

And, teh questionnaire probably would not have to take more than 15 minutes. We have left undefined the particular mode of administration of this. In the past, we have conducted studies in something call a mall intercept, in which case our contractor goes to geographically disbursed malls and intercepts people and brings them into a room. We have also considered doing studies on the internet, so that's something that we can all discuss today.

In terms of the sample, we would like to see roughly equal numbers of men and women. We'd like to see ethnic representation similar to the U.S. Census. We'd like a wide spectrum of ages, because these are television ads that are broadcast to a wide number of

people. We would like to have some sort of over sampling of people over the age of 55, because these are the individuals who do typically use more prescription drugs.

In terms of education, we would also like a spectrum. We are particularly interested in having at least 15 percent with a high school education or less, because we are sensitive to issues of health literacy and literacy, and how that will affect the comprehension of the risks and the comprehension of the statement.

So, these again, are the research questions that Congress really gave us as something to study, and we all gave you in the materials the studies -- the issues that we would like you to discuss today. If you are aware of any research that is relevant to this particular study and that could be applied, we would love to hear about it, and also we'd like to know if this approach satisfies -- or it seems like a reasonable way to satisfy what

Congress would like us to do, in terms of the sampling, and the design, and the proposed stimuli.

I didn't mention the proposed stimuli. Basically, what we would do is create mock ads, and the mock ads would be identical except for the placement of the statement, or in the audio in that one condition.

So, thank you for your time, thank you for all coming out here today, and we look forward to hearing your input on this study.

CHAIRMAN FISCHOFF: Thank you very much, particularly, for the emergency.

Could I ask you to put up the slide with the proposed design, because I think we'll probably want to refer back to that, and not everybody in the audience has the handout, and if you'd like to just go from the hot podium to the hot seat for the discussion.

In thinking about this, it occurs to me that I think we are going to have, at

least for the social scientists in the room, we are going -- this is going to be fun, but let me just start with getting something off my chest, which is about the constraints under which you work. I thought this was an admirable description, very nice description of how you function under the Paperwork Reduction Act, and at our first meeting Steven Bradbard gave us another explanation of it. So, I realize this is not meant as criticism, but this is -- let me just, I don't know if this is a comment, this is a question to the extent that I'd like to be corrected if this is wrong.

So, as I understand it, the Congress and the White House passed the Paperwork Reduction Act and it has been implemented, and Congress and the White House -- Congress passed, the White House signed the Food and Drug Amendments Act. One has led, the ladder has said, this is sufficiently important, we need an answer in six months.

And, I don't know the legislative history, there could have been people in Congress who thought people are dying because we are not getting information in the field about these side effects, and there could have been people who say the credibility of the pharmaceutical industry is being undermined because people think that the post-licensing surveillance doesn't exist, there's really no way for people to produce it, and people could have been thinking those or other things.

But, for whatever reason, Congress thought this was urgent enough that it needed to be done now.

And, under another law, Congress and the -- we have a situation where it takes four times longer to get an answer than the Congress or the White House believe it requires to get an answer now.

But, it seems like something is badly broken here, and these are human creations. You know, somehow or other if the

implementation strikes me, as a non-lawyer, non-politician, that the Paperwork Reduction Act has been implemented -- is either written in a way or implemented in a way that is not responsive to what the Congress and the White House believe need to be done in this case, and I imagine other cases where there is some sense of urgency. And, it strikes me that this is a human creation, and somebody needs to be able to -- needs to be able to change it.

So, have I gotten anything wrong in the law?

Okay, thank you.

If anybody would like to talk about this, let's talk about it now, and then we can roll up our sleeves and try to help them with the substance.

DR. GOLDSTEIN: I just have at least one question.

What has been the response to the print ad? What's happened? Do you have any

data on people responding? Has there been a increase, the kinds of people who have called, the kinds of calls?

DR. O'DONOGHUE: I'm not aware of any. It was enacted at the end of March, I believe, so there hasn't been a lot of time to really figure out what's going on.

DR. GOLDSTEIN: Are you collecting that data, though? Is the FDA collecting data about the calls as they come in?

MS. DAVIS: The FDA consistently collects the data about the calls that come in to MedWatch and, you know, to the website, too, so we can look after to see if there's been some kind of bump since March 25th when it went into effect. But, those go to a different group in FDA, but, you know, we can ask them for that.

DR. GOLDSTEIN: And, is the -- just it's a nice way to collect data. Obviously, because of the constraints we want to do a study and plan the study ahead of time, but

you can ask people when they call in whether or not they saw the ad, and that was the reason they called in. Those sorts of questions would be very helpful, if not for this study, in terms of determining what the design is, in terms of future studies.

And, you already have that in place, that would be relatively easy thing to do, relatively easy. Obviously, you have to change the way that data is collected and have those people on the FDA side asking those extra questions.

DR. OSTROVE: Yes, and I think it might -- you know, we can certainly look into doing that, because I think that is a very -- that would be a very useful piece of information, at least with regard to telephone. But, if they go to the website and decide to report something there, I think that would be a little bit more complicated, because it would involve changing the form that you used, and I hope I'm not misspeaking

here, that form was approved by the Office of Management and Budget, and you need to go through a process in order to change the form.

So, you know, maybe there's some other way of doing it, but we can certainly look into that.

MS. VEGA: I took the opportunity to visit MedWatch, to go to their website, and I was very surprised to see that currently, and I don't know if this is going to change in the future, the website is only available in English.

And, as we were sitting here, I took the opportunity as the presentation was going on to contact the 1-800 number right here, and it is also just in English. There is no -- the message is very lengthy, so, I mean even though they give you the website and some of the information, and it's not only lengthy, but the speed of the message is too fast for someone -- like I would have to dial back in order for me to -- or go back to the

message to really capture all that information.

So, I think that that's something that should be looked at, in terms of reaching vulnerable populations, because it's only reaching a small percentage of the people we are interested in.

DR. PETERS: With the current data that's being collected, even if you were not able to change some of the questions, I wonder if there's something that could be done with the data as is, in terms of doing some rough coding at least, taking a look at, are they appropriately reporting the kinds of side effects that you think that they should be? Are they inappropriately reporting side effects maybe that are so minor, like, you know, I had a headache for an hour, the example that you pointed out? Are they inappropriately asking for help?

To Mary Marielos' point, if you have -- if you collect any demographic

information on them, it may be that people who are older can't hear this very, very fast telephone message, so you may find that there -- well, they may actually hang up and they give up, so I'm not sure if you can collect that.

But, you may be able to do something with demographics, at least in terms of what type of reporting that they are doing.

MS. LAWSON: I had a question about the focus groups. You said there were nine, and how many, if it were nine, how many persons in each group?

DR. O'DONOGHUE: No, there were two focus groups, and each focus group had about nine people in them.

DR. BRUHN: I have a question about the whole concept of reporting adverse effects. The people are supposed to go to their physician if they are experiencing, you know, a negative effect that might be really serious.

And, I assume the physicians are being asked to let people know, to let FDA know. Do you know how many physicians are actually responding? I mean, do you feel you have a good rapport with the physicians? I believe that physicians are often overburdened and seeking ways to work more efficiently and may not actually do all that reporting. Is it facilitated, for example, by those physicians who do records on the computer now, so that they could just click something and a note can go to -- a flag could be put to report something about an adverse effect?

I value the idea of opening it up so that the public also knows they can communicate, but if our goal is to enhance information, because now we have a large number of people taking a drug, whereas, in the trials it had been small, it seems that the physician avenue should also be explored and facilitated, made easier, so it's more likely to be more comprehensive.

DR. O'DONOHUGHE: I personally cannot address that, because all of those issues are outside of DDMAC. I don't know if Nancy can address some of that, but that's a different division.

DR. OSTROVE: That's -- Amy's absolutely right. I mean, it's a group, and, in fact, the MedWatch group itself has been moved around a little recently.

We have been doing more outreach to healthcare providers. There is a MedWatch Partners that I don't think we've really had the opportunity to talk about that in detail during the first meeting, but I think, you know, MedWatch is one of the things that I mentioned as one of our programs. And, outreach has increased.

However, that doesn't mean that everyone knows about it, and, in fact, I believe that DeLaRosa admitted that he didn't know about MedWatch until we had talked about it the last time around.

We are in the process of just -- I'm just in the process of pretesting and, hopefully, fielding a survey of physicians that will be looking at how they get emerging risk information, and we'll be getting, in fact, feedback, we'll be getting data on their knowledge of MedWatch.

So, we will be getting some data on that, hopefully, fairly soon, but I don't believe that we really have those numbers now. The point is a very, very good one, and we are cognizant of the need to get more of that information.

But, I believe that Congress has also kind of indicated its interest in making it easier for not just healthcare providers, but for consumers to be a source of reports about adverse events, with the requirements in FDAAA.

MS. DAVIS: Amy just had to -- she'll be right back, but if you have any general questions that DDMAC or that Nancy can

answer we are happy to do that, but she will be right back if you have questions about the study design.

DR. ANDREWS: I did, so maybe I need to wait.

Can I ask those now, Kristin?

MS. DAVIS: Unfortunately, I'm not really qualified to answer the study design questions, but Amy will be right back. I'm sorry about that.

DR. ANDREWS: Oh, okay.

DR. KHANNA: So, within media, if we roughly break down the different vehicles in three broad, broad categories, electronic, which is television and radio, print, such as newspapers and magazines, and then now online media, we know with pretty good certainty that of the three very broad categories that the groups which are more likely to be vulnerable and express and exhibit health disparities would be the ones who would be most likely to be watching TV and listening to radio, as

opposed to reading the New York Times or the L.A. Times, et cetera, or going on line, which really attracts people with higher educational levels.

So, the less affluent, lower socioeconomic class, and really people with, perhaps, more time on their hands, would be more likely to respond to television prompts than print prompts.

And so, my concern is that we may be now targeting a group with more time on their hands, and a group that, perhaps, might call the 800 number and expect to speak to somebody about the medicine, and talk about emergencies, and may report minimal side effects, diarrhea, headache was already mentioned, et cetera.

And so, I think we need to take that into consideration, because of the specific outlets that we are now addressing, is that we may get people who may be more likely to report less serious adverse effects

with broadcasting.

DR. ANDREWS: I had a few questions about the design. It is -- actually, I want to put my reviewer hat on, not tough reviewer, but the extra prominent one is fantastic. We did some research, actually, I mentioned it yesterday, in journal public policy in marketing back in 2004 with Mariea Hoy on clear and conspicuous disclosures, and what was interesting is that on a modality issue a lot of the research points to the dual modality as being very effective, so it's good to see it up there.

I didn't see audio only, that is -- and I know there are expense issues in designing these things, but it's clearly better than just the SUPER, which is the worst of all the categories.

Some other things that we found going back, actually, FTC goes way back on this fact, to 1970, they recommended a duration rate of five seconds. I don't know

where you come down on, they were translating that into as far as words per minute that would be adequate for consumers to be able to see. So, I don't know exactly.

DR. O'DONOHUGHE: Well, let me address both of your points. Actually, the first one, we could certainly add an audio only condition. The reason that we didn't initially is because of the wording in FDAAA, it seemed to indicate that they wanted to know about a display. This is why we did not, but, certainly, adding a condition would be valuable.

In terms of the duration, with the five seconds, is that considered an adequate duration, or a long duration, or would that be more on the short end?

DR. ANDREWS: I think that was viewed as adequate. They were -- again, I'm not an expert on this, but they were citing 132 words per minute that were optimum to 180 on the translation of that, but I'm sure they

would have more information on that.

The other issue I had is, I looked back at our article, and there's always other factors lingering that can affect the results. And, especially, when you use mock ads. And, I'm assuming that it's a fictitious product, which --

DR. O'DONOHUGHE: Yes.

DR. ANDREWS: -- we have erred on having real products and using brand familiarity as a covariate occasionally on that, to give some realism to it, and maybe multiple real params.

The other bigger issue, I think, is there are some other factors on the design of this that could play a part, contrast, and background, type size, distraction, all of these are additional factors that can sometimes confound the results.

The other issue, it's interesting you mention on the data collection, I know we've always been wrestling with this over the

years. For years, we used mall intercept studies. They are extremely expensive now, but I would, probably for the seriousness of this, would kind of err to that. We've also used online studies as well. You have questions as far as the participation of folks on line, and, you know, digital divide issues, but also a lot of them may be on line to get other incentives, let's say, rather than, you know, being, you know, a true consumer.

So, I guess, you know, there's tradeoffs on that. So, anyway, that's it.

CHAIRMAN FISCHOFF: As a general point, we've been asked to provide references, so anything would be welcomed by their office.

DR. ANDREWS: I can provide this article. I don't know --

DR. O'DONOHUGHE: Thank you.

CHAIRMAN FISCHOFF: And, perhaps, the FTC guidelines, if you've got that.

DR. KHANNA: I just had a follow-up on that point. I think audio only is

absolutely not a consideration, because without a warning or a prompt that a phone number is coming up I think there are very few people who are going to be sitting down and watching TV with a piece of paper and a pencil in their hands.

So, just a thought.

Probably except for the group that I mentioned earlier, who may be less -- more likely to unemployed and watch TV all day, you don't have this in your proposed design, but I might -- I might throw this out for your consideration, and that is, when I was doing my reports often times at the top of the report in the intro I would say, get a piece of paper and a pencil handy, because I'm going to give you a website at the end of this story, that you might want to go to for further information and future reference. You may want to consider that.

Otherwise, again, what might happen is, since most people don't watch television

with a piece of paper and a pencil in their hands, is five seconds, ten seconds, even 15 seconds, may not be enough time for them, even if there is a SUPER as well as audio, or just a SUPER alone may not be enough time for them to run to the kitchen and grab those things to write the number down, they may have to wait til the next ad, you know, whenever it airs.

So, that may be a consideration also, to let people know that a phone number is coming up later in the commercial.

DR. O'DONOHUGHE: So, are you suggesting in the actual ad or in our testing? So, when we actually do the study you suggest that we tell people ahead of time, or are you suggesting that somehow in the actual ads, when the ads are run, that they should have some kind of warning?

DR. KHANNA: I would leave that up to you all to discuss and decide what you think would be most beneficial.

DR. O'DONOHUGHE: In terms of, I'm

not sure that we could, because there's nothing in the regulations saying that there's this warning part coming up.

DR. KHANNA: Right.

DR. O'DONOHUGHE: I'm not sure that we could implement that.

DR. KHANNA: Okay.

DR. O'DONOHUGHE: In terms of the research itself, what we are primarily interested in is the understanding of the risk information, and I'm concerned that if we were to tell people ahead of time, okay, there's a number coming up, that might skew the results, because the people watching home on TV, who didn't have this warning, would not have that, and so that would be a different viewing situation. We'd like to keep it as similar as possible.

DR. KHANNA: No, I understand completely, just for your consideration, really.

DR. O'DONOHUGHE: Thank you.

DR. HOLT: Thanks very much.

I have a couple design questions, I guess, but I wanted to go back to a couple of the issues that have been mentioned about just the feasibility of putting this information in. I think that it should be done, but I don't think it's going to be the only or optimal place to put this information.

You know, when I was reading this in preparation for the meeting, my major reaction was people aren't going to be able to do this, people aren't going to call. And, I thought that for somebody to be able to call you've got to make it real easy for folks, you know, to be able to report this information.

I also thought that the physician really was probably the most appropriate place where this information should be reported, but in addition, you know, if you are going to be reporting it, if I'm going to report it, I'm going to need that written on my pill bottle. You know, I'm going to need it written in the

materials that I get with, you know, it's got to be -- I'm not going to be able to get it on the ads, you know, because it's just too far of a disconnect from where these things happen, I think.

But, I think it's a good idea, you know, it should be done, just because it's one more, you know, tool in the arsenal, but probably not going to get it where you want the reporting to be all the way.

Design questions I have are just nuts and bolts type questions, of course, involving things like recruitment and sample size, and I wondered about the viewing of the ad two times, and is that -- that seemed to me to be artificial, although maybe that is really what is going on in terms of people viewing ads, you know, they come on twice during a 30-minute program or something of that nature. So, maybe that was the explanation behind that.

DR. O'DONOHUGHE: In terms of

artificial, unfortunately, that's always something we struggle with when we are designing our research, the tradeoff between the realism of the situation and the experimental control.

In terms of viewing the ad twice, that is the typical standard used in research right now, in looking at advertising. So, that's what we've used in terms of when people view it once it tends not to be quite enough, viewing it twice seems to be enough to be able to get information out in the experimental design.

CHAIRMAN FISCHOFF: I just, for the committee, I have ten people on the list, and I'm going to push up the people, just put the rest down for the one perfect moment that everybody is wanting to speak, and I'm going to push up the people who haven't had a chance to speak yet.

So, not relying totally on my peripheral vision, Gavin, please.

DR. HUNTLEY-FENNER: I want to echo Cheryl's comments, and I do have additional concerns about the design.

The thing I'd like to ask about, well, first I'd like to make just a brief comment, this extra prominent condition I think is going to be important, certainly when you have the video or what's on the screen echoing or reflecting what folks are getting auditorally, that you'll tend to get more attention to the message coming in through multiple channels.

But, that having been said, there is this deeper question of, well, what do you do if this works, just as someone might hope it does. And, I think the one thing I'd like to ask about is detectability, with respect to existing data. That is, the degree to which increasing the quantity of data of uncertain quality would potentially leave you no better off than the status quo.

And, I'm asking, I'd like to know

whether you know how detectable important side effects are as a function of where the information comes from, whether physicians are reporting it, hospitals, manufacturers, consumers, and what would be the effect on overall detectability if you increase the number of responses or calls in from a single source, given what you know about the quality, the background quality, of that source.

DR. O'DONOHUGHE: To clarify, your question is in terms of the telephone calls that we get to the MedWatch system already, do we track them, and is there a way to determine how many of them are related to what they see, or --

DR. HUNTLEY-FENNER: Right now you've got data from multiple sources. And, I happen to know that if you go look at your data, and you divide it by source, you'll see some interesting differences. So, for example, physicians reporting in are going to give you data that looks different than sort

of a man in the street reporting it.

And, if you look at all of those data, in order to come to a conclusion about, well, I think we have a problem here with this particular class of devices, or this particular class of medicines, then you are going to have to do some kind of statistical analysis that involves detectability.

Now, what happens when you change the proportion of responses coming from one subset? Given what you know about the quality of the data, existing data from that subset, would it leave you better off?

DR. OSTROVE: That's a fair question, and it's not one that we can answer here. Basically, it's not -- Congress has kind of indicated its desire, and we are responding specifically to that.

What you are asking is a very important question that gets to a different system within FDA, because all we are doing is looking, in this particular -- I mean, it is

an important question, and I'm not trying to undermine the importance of that, it's just not one that we are qualified to even address.

So, what we can do is take it back to the right people, which are the people in the Office of Surveillance and Epidemiology within the Center for Drugs, and others who are doing the same kind of work, and say that this has been raised as an issue by our committee.

Is that --

DR. HUNTLEY-FENNER: Well, the reason it bears -- that's a fine response, I understand that you are limited in what you can do given the charge that you have received from Congress, and your internal resources, organizational structure, but it bears -- it bears on the question of the design for the study, because what you communicate to people has direct relation to what it is you get in.

And, you'll want to, ultimately, design a message that's going to help you --

help you get high quality, higher quality data than you've been getting so far.

And, I'm not sure that -- I think part of the problem is getting the message out there, so that there's awareness that you can report in, but part of the problem is the quality of the intake process, and what you do when people call in. What kinds of question do you ask? How do you -- let's suppose you need to filter out the less serious side effects, how do you ask those questions differently, depending on the type of issue that they are calling about? I mean, those are -- I don't know, I want us to be thinking about those issues as well, because that's going to help you assign a risk score to each of the scenarios you are considering.

DR. OSTROVE: Absolutely, and what you are pointing out is that this is not -- you can't consider what we are doing as an isolated process, that it needs to be looked at, you know, in terms of the Gestalt of how

the information is coming in and how the information is getting used.

I completely understand, and again, we will bring this up, and it probably makes sense for us to, you know, be working together with other groups within the agency who have a stake in this.

But, the other thing that we have to keep in mind as well is that Congress, specifically, gave us a statement that at least as part of this we need to look at, and it may not be the optimal way of doing things, and one of the things that I think we can add into the design is, perhaps, a different statement that would get at the intent in a way that would be more useful in terms of the outcome that we end up getting from the public.

DR. HUNTLEY-FENNER: And, the other reason I raised the question is, it has to do with power, statistical power. So, given the types of differences that you might expect,

and the sort of variation in responses you can expect, how many subjects would you have to test to understand whether the messages are going to effectively communicate to the populations and have the results you want?

And, that's something that -- it's not clear to me that the design of the current study is going to have sufficient power. And so, I suppose your contractors will tell you exactly how many subjects you need to test in order to start to see differences between duration X and duration Y, but that would be something that you'd want to take into account.

DR. O'DONOHUGHE: That's, obviously, extremely important. We have not done a power analysis for this yet, because we knew we were coming here and the design would most likely change in numerous ways, so we haven't discussed exactly the sample size and the power issue.

I do want to comment, your issue is

so important, as Nancy said, but the mandate that we've been given, that we have to study, is not so much -- and this is sort of ironic -- not so much the understanding of the statement itself, and will people call, and will people understand the statement, but, really, will the presence of the statement affect the communication of the risk information in the ad. So, it's a little strange, because the whole purpose of today is to talk about the statement, but really the purpose of the study is to look at whether the presence of the statement influences the understanding of the risk information in the ad.

CHAIRMAN FISCHOFF: I'd like to -- so, on deck we have Elaine, Musa, and then Betsy, and then seven other people.

Let me just pick up, I'd like us to come back to this topic later on, and let me suggest, because these are absolutely critical topics, and let me suggest a bureaucratic or

legal framing in which I think it's our obligation to help you with this, and maybe we can put it in the back of our minds as I understand it.

So, basically, you have, what Gavin is calling for is a signal detection theory analysis. That is to say, what's the -- it's not a risk analysis, it's what's the discrimination ability that people are giving you recognizing that some give you -- will have different -- will look at different -- have different thresholds for reporting.

So, you are going to get a signal there, and then one could design this study in a way that helped you to understand what that signal, the properties of that signal are, just as Ellen and other people were -- and Mike, and other people were suggesting, you could design, with proper OMB approval, the recording form. At MedWatch, that would give you an inference on that signal. I think you have people here who could help you with that

design.

And, why is that a matter of this business? This came up when the Commissioner visited us last time, that by this activity, either by doing it or by not doing it, the Food and Drug Administration will be changing the signal that it has to provide to the American public about the safety of the drugs in general, and of specific drugs in question here.

So, it will be -- I mean, the simple message is to say we don't want to know about it, simple message, and people will infer whatever they want to infer, or they are going to say, as the Commissioner said, we are lowering our threshold for reporting things, more information is going out, we are changing the properties of the signal that we are giving out, and so my response to him was, you had better have, your communication system ought to be ready to explain to people what this different signal is, otherwise, it's

going to take a couple of years for people to equilibrate and there will be lots of stuff that you don't want that's going to go on.

So, this is creating a new signal, this will be essential to the FDA's communication to the American public, and I think it would be remiss if it didn't do everything it could to do the signal detection theory analysis to characterize that signal, so that you could then incorporate that in the communications about the safety of the drugs and side effects. This is an opportunity to begin that process, and I'd like to see us come back and talk -- give you some advice on how to do that.

Elaine, Musa and Betsy.

DR. MORRATO: My questions and comments are along that same line.

How long have consumers been able to report in adverse events? Is this just new as of March, or there's a running history? No. Right, so there's at least some baseline

data that could be analyzed, not just, you know, what's happened last month, to Dr. Peters' point.

I used to manage a 1-800 line, in terms of the analysis for a consumer product company with over-the-counter products, and people are trained to consider these as, here's my chance to call. So, you are absolutely right, you should be expecting -- and I don't know if that's the quality that you are getting right now, so it relates to that, too.

But, my comment is on the verbiage, negative side effects, and I know you may not have the ability to change that as part of the test, because that's been mandated to you, but at minimum I think there should be questions in the survey that's trying to get at comprehension of what does negative side effects mean.

I can't imagine that the average person knows what that means, and so, you

know, whether it could be a listing of possible kinds of reasons why you might call and get some reaction to whether or not they are going to call for those kinds of things, some way to grade along that I think would be useful.

Also, in some of the background material, you've provided other questions that you would be including, things like willingness to ask a doctor, I'd include willingness to ask a pharmacist. I think some patients may be more likely to have the conversation with the pharmacist. I think Dr. Holt is absolutely right, that most people are going to be looking at a 1-800 number on a bottle, not necessarily, as was mentioned earlier, running to the kitchen to get a pencil.

So, you know, maybe these are not directly related here, but kind of part of the general.

The other is, we are looking at the

primary questions around the impact on communication of the risk information. I think there should be built in some questions on impact on the likelihood of reporting as a question, to try and differentiate. That sort of relates to what are they likely to report as well.

And then, with regard to the sampling, given yesterday's discussion around sort of special sub-populations, I think the study needs to be designed in size to be able to address ability to communicate with those subgroups.

So, you mentioned oversampling over 55, that doesn't quite match up with what we were talking yesterday in terms of what elderly is, perhaps, but whatever the definition that's being used for elderly in the other report for DTC you should be using here, and making sure that there's enough sample to talk it.

The same I think you mentioned

about race ethnicity, and that the goal here was to get the similar distribution. In terms of, since that's a focus area on ability to communicate, I think it needs to be over sampled to be able to talk to that.

And then, since we also were talking about pediatrics, some questions in here that get at whether or not there's children at home, or, you know, some way to be linking, are these caregivers of children, and whether or not this might affect it, so that this research gets linked in with the other report on how do we better communicate to those special populations.

Just a few points. Thank you.

MS. MAYER: I think based on Institute of Medicine reports and meetings, that I'm aware of, the FDA is very aware of the limitations of passive adverse event reporting. And, I know that there are plans in the works for the future, and, hopefully, the near future, on using large databases to

get much more accurate post-marketing safety information.

So, it's not as if MedWatch is the only, or even best, source, it never has been, it's always, as I understand it, been plagued with those kinds of problems. So, I think the over sampling of minor side effects is probably not really teh issue here.

It occurs to me that the over-arching message that's going to be sent by having this information in every single TV ad that is selling a drug is that drugs have side effects that should be taken seriously. And, I think consumers in the United States consistently seem to believe that FDA-approved drugs are safe and effective, right off the bat, and, particularly, the ones that are being advertised which are recently approved drugs that are still under patent and may not have a lot of significant safety record attached with them. So, I think it's an important message, an important corrective

message to send, and I have no doubt that that's part of why Congress mandated this.

I think that the impact of seeing, you know, multiple ads with this message every day, and that's what most Americans will see, is that the message will not really, for that reason, and also because of the time disconnect, in other words, let's say a person is not taking a drug and is, in fact, alerted that they may have a health problem, then goes to their doctor, then starts taking the drug, then has the side effect, I mean, there's a time disconnect there, obviously.

So, I think that this message will turn out not to be really drug specific. It is a way of alerting the public to, yes, here's a place to report a significant side effect, and it will become common knowledge.

I don't think we need to worry about people having a pen and paper in hand, because they'll probably be able, within a few weeks or months, to recite the phone number

from memory or recall the website.

But, the thing that concerns me about the study is that the study doesn't take into account the impact of this kind of repetition on specific perception of side effects for a given drug. I mean, it's measuring it as for the first time or the second time, and not the continuous repetition of it, and I'm not sure what you do about that. It's just that I think it's important to be mindful that the division of attention that people may experience the first couple of times they are exposed to this may not persist. In other words, people may have more attention free to give to the specific side effects that are being listed after hearing this 100 times than they will the first or second time.

DR. SLEATH: I was going reemphasize what Dr. Morrato said about race and ethnicity. There seems to be a disconnect with what we talked about yesterday, but I'm

even more concerned with your educational distribution of your sample. It says 15 percent with high school education or less, and to me that seems low, and I might consider having a certain percentage with high school and then a certain percentage with less than high school, because that may be the group where the number detracts from the risk communication information more.

DR. O'DONOHUGHE: I'd just like to make a comment about, it did say 15 percent. I know that in our past research we've used 30 percent high school education or less. Does that sound more like what you were thinking of?

DR. SLEATH: It sounds more like what I was thinking of, but in my own research I break it down, because I think people with less than high school can be very different than people who have graduated from high school. So, I would consider having a certain percentage of each, and I'd be interested in

what others think on the panel.

DR. O'DONOHUGHE: Thank you.

DR. NEUHAUSER: First, I want to say that I agree with everything that's -- the important comments from my colleagues, and I want to preface my remarks by a little bit of background.

I spend a lot of my time designing large-scale communication with and for diverse audiences that have a lot of challenges, either low literacy, language issue, or a disability or something else. And, a lot of the work I do relates to designing communication in which people are directed to an 800 number. It's print, it's not television.

But, the main thing I have learned out of doing this is, the most efficient way to do that kind of work well is to have a lead time of doing qualitative work before getting into a randomized study.

So, I would strongly, strongly,

strongly recommend starting with useability testing or other types of qualitative approaches, in which you take the target audiences that you've described here and which my colleagues have made comments about and work with them on alternate message designs. When you feel like the message you have is testing well with the vulnerable groups that you are interested in, then I would start the randomized trial. Otherwise, you may find that you just have to go back to square one, save a lot of money, much more likely to get you the result you want.

So, I would recommend doing useability testing in an iterative way with at least three sets, three iterative sets of the vulnerable groups you want to go to. This is just a very short statement. We can talk more about that.

The second thing is that, and this goes to what Dr. Sleath was mentioning, I would say that your main group of interest

here might be people who are low literate, so the lower half of the U.S. population that could cover, obviously, overlap with age, so 61 percent of people 65 and over are considered low literate, and various other groups.

I agree with Dr. Sleath's comments that just saying high school or less will not necessarily get you the group that you want. So, my strong recommendation would be here to say people who test as low literate using the test of functional health literacy. I would suggest the short version there. And, testing at 16 or below.

So, if you find those people, because you can have people who have graduated from high school who are highly literate. You can also have people graduating from college who are not very literate. So, that is -- I would suggest using them in your useability testing or other qualitative, psychographic and cognitive research, and I believe that

what you will find is, if you do the up-front work with groups for whom you actually measure their health literacy, and that you will start out your quantitative work with the kind of messaging that you are interested in.

My last point has to do with a comment made by Dr. Khanna about, can't use audio only. One of the reasons is, a lot of people depend on seeing text, so there are 32 million deaf and hard of hearing people in the United States who depend on captioning or other ways to get information.

And, I have a specific suggestion there, that when the statements are developed that you look at the FCC regulations about captioning. I think it's CFR 103, but I could find it for you. And, those captioning regulations for emergency communication require that the captions do not sit over any other important test information, and there's other guidelines there.

But, I think that would be

important, and you might seek a subgroup here of people who have challenging hearing and need to use captioning when you do your qualitative work, at least that. You may not want another subgroup.

And, the final thing was to mention, as others have, that the sample sizes are large enough to, you know, detect these differences for your target groups here.

DR. O'DONOHUGHE: May I ask a question? In your research, I'm curious, you recommended the TOFHLA. We've used the REALM in the past, do you have a preference for the TOFHLA, and do you have any experience with both of them?

DR. NEUHAUSER: Yes, my read of the literature, and my own research, show that I'd say a strong conclusion in the health literacy research world is that the REALM is an inferior test, because often what it is testing is a person's experience with words, health words. That goes up over time, so an

older person may have below health literate but have familiarity with health words, just cognitively might not be able to put them together in a risk statement.

So, I strongly recommend using the TOFHLA, and using the short form which is highly validated.

CHAIRMAN FISCHOFF: Thank you.

AnnaMaria, Ellen and Mike, and Marielos and Christine.

MS. DeSALVA: Okay, thanks.

I've had just a recurring thought in this discussion, and that is that, you know, the advertising is frequently, or mostly, intended to raise awareness of a condition and of a potential treatment among people who need to be newly diagnosed, or who need to initiate or maybe re-initiate treatment.

And, this question is really for people who, obviously, have been using the therapy, and actually may have an adverse

event to report.

So, for me there's just sort of a fundamental disconnect in terms of the audience. It's sort of, you know, combining messages that are really meant for two distinct audiences, and in that sense it's opportunistic because it sort of presupposes that people who have been on a therapy for a long period of time are paying to the ad and will sign up, you know, to participate in MedWatch, or to respond to the call to action.

And, for me, there's just a fundamental question is, is there enough up side there to justify the down side, and the potential down side is for the people who are initiating therapy, or thinking about initiating therapy, or seeking diagnosis for the first time, they are having to, obviously, consume all that benefit/risk information and put it together, and then you are adding in this third element.

So, I'm just wondering, and I'm not

a researcher, some of my colleagues here will know far better than I do, but I'm just wondering if there's any merit in adding into the study design some sort of a question that looks at, you know, is the hypothesis a valid one, and are people who have been on the therapy for a long time, are they close enough to be advertising, are they paying attention, is it relevant, is it a relevant channel for them.

And, if it's not, if we are able to show that it's not really enough, and that there is also, you know, this confounding effect, in terms of the risk information, then it can become a very clear recommendation, because certainly there are, as others have said, there are probably more relevant moments, and touch points,and channels to reach someone who, you know, may be suffering from an adverse effect. And, this is sort of more opportunistic, and sometimes more is more, but sometimes it's not.

DR. O'DONOHUGHE: You bring up an interesting point, and the research as designed, as you've mentioned, is, essentially, because it's a fictitious drug. It will be approximating people who have never heard of it before. This is a new treatment, oh, might this be right for me, let me look at the ad and discover the risk/benefit information.

In terms of I think what you are addressing, what we could do is have an existing ad and draw in people who have the condition, so they are familiar with it. Maybe they are on medication for it, and also whether they see the statement or not.

That does bring us in a completely different direction. If the committee is interested in that, in discussing that, we can certainly consider that. That's an interesting point.

CHAIRMAN FISCHOFF: Ellen.

DR. PETERS: I wanted to continue

what Ms. DeSalva started, in terms of what kinds of questions might you want to ask. So, not just the design itself, but what might you want to ask of people who have been watching this fictitious ad or real ad.

The idea that Congress has that adding an additional piece of information may detract from other information is a very good point, and you should be looking, not just at comprehension of the MedWatch statement, but also at comprehension of the other required elements, not just risks, but, perhaps, benefits, and if there are other required elements that you think are important pieces of information that people should comprehend you should test if it detracts from that, that the idea of less is more is an important one, and you are going to get this balance between completeness of information provided and the comprehension of that information.

Second, I would look at, I would measure people's risk perceptions separate

from their benefit perceptions. Part of what you might find here is that by having the statement, and this goes back to something Musa said earlier, by having the statement you may increase risk perceptions, and in addition to that decrease benefit perceptions. Now, whether that's good or bad is an entirely other question, but you should know what's happening.

Also to Musa's statement, you may end up doing -- I wonder if you are going to end up doing multiple ads here, if you are going to show people multiple ads. And, if you are showing people multiple ads, this kind of generic messaging that Musa suggested may go out with this, that side effects need to be taken seriously. You could start to get a little bit of a handle on that question, if you asked at the very beginning, before you showed them any ads, risk perceptions of medications in general, benefit perceptions of medications in general, and then repeat it

again after you've shown all of the ads. It doesn't get exactly to the point, but it might begin maybe to answer it.

In terms of other things to measure, I'd also -- I might consider asking things that are beyond comprehension and risk perceptions, and I think maybe Michael could speak to this better than I could, but maybe ask about what would you intentions -- if you were diagnosed with this condition, what would your intentions be to take the drug, so ask something a little closer to behavior, even if you can't quite get to behavior.

Dr. Morrato brought up the idea of asking about the likelihood of reporting. I would ask it, maybe I might ask that generally, but I think I might ask it a little more specifically, too. If you experience this little minor side effect of a headache would you report it? If you experience this other major side effect of heart palpitations, would you report it? I would get a little

closer to the behavior.

And then, in terms of sort of more a Gestalt kind of thing, we are all focused on communication here, and we've talked a lot about the need to start the communication process earlier, and this is an opportunity, potentially, to do that. What about asking these people, what do you want to know from this? What would you want to know, given that MedWatch exists, what would you want to know from this? Do you want this early data? And, you need to be able to describe, not just that it's early data, but the quality of the data. So, in some senses I might almost ask, do you really want this early data that may or may not be correct? And, I'm not sure I'd word it quite like that, but you'd want to give an idea of the quality of the data.

Would you prefer results from patients -- would you prefer -- if you'd like to see these results, would you prefer to get some of these results that are based on

patients who have called in, who have been on the medication for a long time, or who are new users, or from physicians, or from pharmacists, or from somebody -- or from the manufacturer, or from somebody else, but you can actually start to get a feel for the communication process itself now, at the point where you've just started to test the messages.

DR. GOLDSTEIN: That was great, lot of great ideas, and I could probably spend a whole bunch of time just resonating with what has been said before.

I want to pick up on this last point about motivation, and it gets through theories. We heard about -- yesterday, about motivation being an important determinant of whether the message is received. So, I do think it's really important to consider the population that you are targeting. And, you are going to get more relevant information if you ask people who either have a condition

that the drug is being targeted for, or they've actually had some adverse events before so they know what an adverse event is, and are more likely to report it, and then you can see the effect more clearly of that sub-population drug for them, because they have the condition, they've had adverse events themselves, of whether you are going to have enough of a signal to noise ratio to make it worthwhile.

So, of all the things that may help you to detect that signal, to look at a population that is more ready to hear the messages about calling, and also more likely to have a need to know what the risk information is for this new drug, or this new product.

I do think, just to resonate with some of the things that have been said, taking that time initially to do some of the qualitative testing will save you a lot in terms of, the sample size has gotten enormous

now because we have all of these cells now, and we have all of these sub-populations, and they are over sampling, and I do think it's important to do that, but you might be able to save a lot of time by doing some initial pre-testing and do the qualitative work to maybe eliminate the cells, like the short and long for instance.

Just another suggestion in that regard.

CHAIRMAN FISCHOFF: Marielos.

MS. VEGA: I still want to have some clarity about you recommend a strategy and how you are going to do that, and I have recommendation but I want to hear first the recruitment strategy.

DR. O'DONOHUGHE: Well, the recruitment strategy has not been decided at this point. Actually, we were waiting to discuss this with you all. It depends on the mode that we use, so if we use a mall intercept, or if we go by the internet, or

some other method, each method has a tradeoff in terms of who you are getting and who you are losing, and what kind of weighting you have to use and things like that. So, it hasn't been determined.

If, say, we go with a mall intercept experiment, typically, what is done -- one of the things we often do in our research, and I'm afraid I can't see everybody's name, but the gentleman that just spoke, we usually, or often, do take people who have some experience with the condition for the very reasons that you mentioned, because they tend to be more motivated to look at the ads.

But, the contractor will use geographical malls across the country, they will recruit in terms of their methods, and I can't go into detail right now because we don't have a contractor that is working on it right now, and we don't have exactly the mode of administration that we are going to use,

but if you do have recommendations then please do share.

MS. VEGA: Well, the reason why I asked that question is because I have experienced -- organizations who use contractors to do these, and what they have focused in base mall geographical areas to do the recruitment, and I just don't think that is correct.

My recommendation will be to use what others have already done. The NCI has something called, "Special Population Networks," and they have -- I am involved with Hispanic, with the National Hispanic Network, but this is specifically for cancer, but they have, it's called SPN Networks, they have one for Native Americans, for Hispanics, for Asian Americans, and for African Americans, and I think even the contact information at the NCI, the person who runs this network, because they already have a relationship. They already know in these communities, so I think in terms

of recruitment, I don't like the idea of going into malls and doing the type of recruitment, I just don't think it represents, really, teh people who might -- a lot the vulnerable populations don't have the money to go to malls. The elderly may not be able to get to malls. So, I just don't like the idea.

I think in terms of one of the very important questions, in terms of diverse events, then it should be asked where this medication was obtained, and if the adverse event was the result of the medication, and somebody was in China or other country, and are you measuring the cost effectiveness of this program?

DR. O'DONOHUGHE: You mean in an economic sense?

MS. VEGA: Yes.

DR. O'DONOHUGHE: That's not in our design, that's not ours.

MS. VEGA: And, the other thing I think is very important when it comes to the

1-800 number, is I have seen in FDA brochures, pamphlets, or whatever, that they use like 1-800-FDA, they use the letters as opposed to the numbers, and especially for immigrants, they have never been exposed to this. I had that experience myself when I first came to this country, it took me a long time to figure out on the phone where the letters were. So, I think to make sure then you do put the numbers, you can use both ways, but make sure that, so people don't have to start looking for the numbers on the phone.

That is my comments.

CHAIRMAN FISCHOFF: Okay, thank you.

Christine, and then Elaine and Gavin.

DR. BRUHN: You know, the nice thing about coming later is you can pick up on all the great comments other people have said.

I had been thinking that your design states, want to see it including this

statement about calling an 800 number is going to distract from the list of risks. I think, if anything, it's going to increase sensitivity to risks. So, right now your statement is written one sided, you know, just going to see if it makes risk less prominent. when you are looking at this statistically, you should look to see if it increased as well as decreased sensitivity.

I feel that you need to tell people why you want them -- well, first of all, two things about the calling, you are already stating is there going to be confusion, do they think maybe they should call the FDA when they are in the midst of heart palpitations, when they should be calling their physicians. That is, indeed, a consideration for your phraseology, but I believe you also need to motivate the people as to why to call in. And so, you might use focus groups to explore the wording of that motivation, and you might use something like the FDA is actively monitoring

responses to all medications. So, you are not pointing your finger at any specific one, and you are also presenting the FDA as open and actively seeking responses, and, perhaps, include another phrase about why it's important that if you are experiencing a major side effect to contact FDA. So, explore the motivation to call concept.

Someone was mentioning the 800 number on the bottle, and, indeed, this is not specific to your project, but I think it's an important piece of advice anyway. It does need to be on the bottle, and not on that insert that goes with the medication. I am sorry, I know a lot of people who get their medication and throw the insert away right away, and they might experience a side effect two or three days later, the trash is gone, they don't have the number anymore. It's got to be on the bottle itself, attached to the medication.

And then, I really like Musa's

comment about this is now going to be so prominent, these ads with the side effects to report to the FDA, it's going to become common knowledge.

And, while I agree with your statement about sometimes words are hard to find the numbers when you are dialing on the telephone, I believe that words can be clever and make it a number that you always remember.

So, I just noticed that you could 1-800-SIDE EFT, that might be harder for a non-english speaker, but that tells me side effects for an English speaker, so that might be a cool thing.

With all the comments you've received, you are going to have to change your design, and I suggest omitting the providing the number before the major statement of risks, because you are giving them a number and then you are telling them why you should call. You should tell them why they should call, and then give the number. You've got to

motivate them first and then give the number.

So, I think that's all the ones that I had down. Thank you.

CHAIRMAN FISCHOFF: Let's see, Elaine, Gavin and Madeline.

DR. HOLT: It came to mind, has there been any thought or consideration on how -- what's a minimal clinical meaningful difference, or a threshold for when you are trying to measure detract from the communication of important risk information in the ad, because at the end of the day if there is a change then you are going to get argument as to as is it a meaningful change or not.

So, has there been any discussion