U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES

+ + + + +

FOOD AND DRUG ADMINISTRATION

+ + + + +

PROPRIETARY NAME REVIEW CONCEPT PAPER

+ + + + +

PUBLIC WORKSHOP

+ + + + +

FRIDAY,
JUNE 6, 2008

+ + + + +

The workshop convened at 8:30 a.m. in the Kennedy Ballroom at the Crowne Plaza Hotel, 8777 Georgia Avenue, Silver Spring, Maryland.

FEDERAL PARTICIPANTS:

GERALD DAL PAN, Director, Office of Surveillance and Epidemiology, CDER, FDA
KATHRYN AIKIN, Division of Drug Marketing, Advertising, and Communications, FDA
LESLEY FRANK, FDA
CAROL HOLQUIST, Director, Division of Medication Error Prevention, Office of Surveillance and Epidemiology, FDA
CARRIE NEWCOMER, Division of Drug Marketing, Advertising, and Communications, FDA
PARIVASH NOURJAH, Agency for Healthcare Research and Quality
LANA PAULS, FDA
ELLE IBARRA-PRATT, Branch Chief, Advertising and Product Labeling Branch, CBER, FDA

FEDERAL PARTICIPANTS: (cont.)

MICHELLE SAFARIK, Division of Drug Marketing, Advertising, and Communications, FDA
KELLIE TAYLOR, Division of Metabolic and Endocrine Drug Products, Office of Surveillance and Epidemiology, FDA
DENISE TOYER, FDA

INDUSTRY PARTICIPANTS:

ANDREW EMMETT, Biotechnology Industry Organization
KATHY GANS-BRANGS, AstraZeneca
STEVEN HARTMAN, Novartis
STUART HOBBS, GSK
DAVID KORN, Pharmaceutical Research and Manufacturers of America
BOB LEE, Lilly
MAUREEN McGIRR, Merck
UNA ORTELL, TAP

TABLE OF CONTENTS

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

(8:33 a.m.)

DR. DAL PAN: Ladies and gentlemen, please find your seats. The meeting is about to begin. Okay. Good morning. Welcome back to day two of our meeting on proprietary name review. For those of you who didn't attend yesterday, welcome. My name's Gerald Dal Pan. I'm the Director of the Office of Surveillance and Epidemiology at CDER at FDA. We're going to continue our ongoing discussion.

This morning we're going to hear from our colleagues in the Division of Drug Marketing, Advertising and Communication about the promotional aspects of the evaluation of proposed proprietary names. We'll have a panel discussion following that and a short open public hearing. And then this afternoon we'll turn to logistics of the pilot program and a discussion of that. So let me turn it over now to my colleagues in DDMAC.

MS. FRANK: Okay. Good morning I'm Lesley Frank, Senior Advisor Regulatory Counsel for the Division of Drug Marketing, Advertising and Communications -- that's DDMAC -- in the Office of Medical Policy and CDER. I'd first like to take this opportunity for the panelists if they could introduce themselves. I'll start with Mr. Emmett.

DR. EMMETT: Good morning. Andrew Emmett with BIO, the Biotechnology Industry Organization.

DR. McGIRR: Maureen McGirr with Merck and Company.

DR. ORTELL: Una Ortell, Promotion and Advertising at TAP.

DR. HOBBS: Stuart Hobbs, GSK.

DR. LEE: Bob Lee, Lilly.

MS. PAULS: Lana Pauls, FDA.

MS. HOLQUIST: Carol Holquist, FDA.

DR. AIKIN: Kit Aikin, FDA.

MS. SAFARIK: Michelle Safarik, FDA.

DR. NEWCOMER: Carrie Newcomer, FDA.

DR. DAL PAN: Gerald Dal Pan, FDA.

MS. TOYER: Denise Toyer, FDA.

DR. KORN: David Korn with PhRMA, the Pharmaceutical Research and Manufacturers of America.

DR. GANS-BRANNGS: Kathy Gans-Brangs, AstraZeneca.

DR. LOWREY: Tina Lowrey with the University of Texas at San Antonio.

DR. ZUCKERMAN: Ilene Zuckerman, University of Maryland School of Pharmacy.

DR. DAY: Ruth Day, Duke University.

MS. FRANK: First of all, I'd like to thank the panel members for joining us here today. Yes, this is Panel Number 3, Promotional Review of Proposed Proprietary Names. We are here today to solicit information, to solicit views on the agency's proposed method for sponsor-led testing of proposed proprietary names from a promotional

perspective. Today we're going to ask you to describe the strengths, the limitations of the proposed approaches. Those will be outlined by Dr. Kathryn Aikin here. And we're also going to ask you to identify alternate approaches and methods that possibly could be used as an adjunct to this method and what they can offer.

Now I'd like to introduce our FDA speakers. First up will be Michelle Safarik and Dr. Carrie Newcomer. Michelle Safarik is a Regulatory Review Officer at DDMAC, and Dr. Newcomer is a Consumer Promotion Analyst with DDMAC, and they will be presenting an overview of the current process of a proposed proprietary name review from a promotional standpoint. Michelle?

MS. SAFARIK: Good morning and happy Friday. As Lesley mentioned, my name is Michelle Safarik and I'm a Reviewer in the Division of Drug Marketing, Advertising and Communications, or DDMAC, in the Center for

Drug Evaluation and Research at the Food and Drug Administration. My colleague, Dr. Carrie Newcomer, and I will be presenting an overview of the current promotional review process for proposed proprietary names in DDMAC.

There are two objectives for this presentation -- the first is to provide an overview of how DDMAC in CDER is involved as a consultative division in the review of proposed proprietary names, and number two, to discuss the process of how DDMAC evaluates proposed proprietary names from a promotional perspective.

The review of proposed proprietary names from a promotional perspective in CDER is a consultative and collaborative process which is organized into two parts -- review divisions in the Office of New Drugs consult at the Division of Medication Error Prevention to evaluate proposed proprietary names from a safety perspective. The Division of Medication Error Prevention, in turn, consults

DDMAC to evaluate proposed proprietary names from a promotional perspective.

The DDMAC consultative team leads the review of these proposed proprietary names in DDMAC. The DDMAC consultative team consists of DDMAC reviewers, social scientists and regulatory counsel. All DDMAC reviewers are given the opportunity to comment on proposed proprietary names from a promotional perspective. These comments can either state that the reviewer has no objection to the proposed proprietary name from a promotional perspective or state that the reviewer has an objection to the name with the rationale as to why.

DDMAC evaluates proposed proprietary names using the same analysis as an employee's for its review of promotional materials. For example, does the name overstate the product's efficacy? The fictitious name, Cureitpred, for a prednisone produce is an example.

Does the name minimize its risk? An example would be the fictitious name, Safepred.

Does the name broaden its indication? An example would be the fictitious name, Predforall.

Does the name include unsubstantiated superiority or comparative claims? An example would be the fictitious name, Betterpred.

And finally, does the name appear overly fanciful. An example would be the fictitious trade name, Superpred.

In determining whether proposed proprietary names are misleading, because of the reasons cited on the previous slide, DDMAC compares the sounds and words formed by the proposed proprietary name to the proposed indication and other information provided by the Division of Medication Error Prevention. For example, dosage form, recommended dosing and how supplied.

Additionally, because proposed proprietary names may contain embedded medical terminology and Latin that is understood by healthcare professionals, DDMAC reviews embedded Latin terms. For example, the fictitious proposed trade name, Boncore can be broken down into two parts, bon and core, bone meaning good and core meaning heart. Thus, this name may be misleading for a cardiac drug.

Proposed proprietary names may also form sounds and words in the Spanish language. As prescription drug promotion may be targeted toward the Hispanic population and as more non-English-speaking individuals become familiar with common Spanish words, proposed proprietary names that contain elements of the Spanish language could be misleading. For example, the fictitious proposed trade name, Saludeye, can be broken down into salud and eye, salud meaning health or healthy and the English word, eye. This may be misleading for

an ophthalmic drug.

I will now turn over the microphone to Carrie for the remainder of this presentation. Thank you.

DR. NEWCOMER: Thanks, Michelle. So after the DDMAC reviewer receives in put on proposed proprietary names from other DDMAC reviewers and the DDMAC consultative team, the DDMAC reviewer will list which proposed proprietary names are unobjectionable or objectionable. A rationale accompanies those names which are objectionable.

This statement is used when DDMAC objects to a proposed proprietary name with the exception of an overly fanciful objection, which is presented on the next slide. When DDMAC objects to a proposed proprietary name because it is overly fanciful, the objection is accompanied by this statement. An example of a proposed name that DDMAC would consider to be overly fanciful would be a prednisone project with the fictitious proposed trade

name of Superpred. Prednisone is a common substance. It's an analogue of cortisone that has been around for many years. And when Superpred is listed by its established name, the limitations of the product are clearly recognized.

Our consult is forwarded to the appropriate Review Division in OND. If the Review Division subsequently objects to the proposed proprietary name, the Division of Medication Error Prevention does not begin reviewing the proposed name from a safety perspective, and the sponsor is notified by the Review Division that the proposed name is unacceptable from a promotional perspective.

If the Review Division does not object to the proposed name, the Division of Medication Error Prevention begins to review the proposed name from a safety perspective.

Once the sponsor is informed that DDMAC has objected to the proposed proprietary name, the sponsor may either submit an

alternate name for review if it has not already done so, or it may submit a rebuttal along with any supporting documentation to DDMAC's objection. The DDMAC consultative team, along with other pertinent DDMAC personnel, review the rebuttal and any supporting documentation to determine whether or not we will maintain our objection to the proposed name.

The Review Division then notifies the sponsor of the agency's position on the promotional nature of the name.

In summary, DDMAC serves as consultants to the Division of Medication Error Prevention and the Review Divisions in OND in evaluating proposed proprietary names from a promotional perspective. DDMAC evaluates proposed proprietary names using the same analysis it employs for its review of promotional materials and enlists social science and legal perspectives in its evaluation.

This concludes the overview of the current promotional review process for proposed proprietary names. I will now turn the microphone over to my colleague, Dr. Kathryn Aikin.

MS. FRANK: Dr. Kathryn Aikin is a social science analyst with DDMAC, and she will be discussing the proposed study for assessing perceptions of trade names from a promotional standpoint. Dr. Aikin.

DR. AIKIN: Good morning, everybody. It's a pleasure to be here this morning so very early. As Lesley mentioned, my name is Kit Aikin. I am a Social Science Analyst in the Division of Drug Marketing, Advertising and Communications in the Office of Medical Policy in CDER. And today I'm going to be discussing our proposed design for evaluating proposed trade names from an empirical perspective.

Just a quick outline of my presentation. I'm going to very quickly

review the legislation that got us to where we are and then talk about our draft study design. The Food and Drug Administration Amendments Act of 2007 reauthorized the Prescription Drug User Fee Amendment, and as part of that, the FDA committed to increasing timely consistent review of draft names to prevent name confusion. And this statement is from a draft plan that's available on the FDA website at the website listed below.

As part of that draft plan, we committed to having a public meeting which is where we all are today. So we've heard about the evaluation approach that we take. We have a two-part approach, an approach from a safety perspective which we heard about yesterday. We also look at trade names from a promotional perspective, and my colleagues, Carrie and Michelle, have gone over that. I'm going to talk about our proposal for obtaining data on potential promotional aspects of trade names and how we can obtain data on this through

empirical measurement.

We are proposing a method in which the proposed trade name be evaluated in the context of two control names, a neutral control and an extreme control. The way we conceptualize a neutral control -- it would be one in which it is pretested to ensure that it makes no representations at all from a promotional standpoint, i.e., it's neutral from a promotional standpoint.

The extreme control would be one in which it is pretested to ensure that it makes clear and extreme representations or misrepresentations about the drug, again from a promotional standpoint.

We are proposing and envision a methodology wherein both control names, having been pretested, could be used in all research on proposed names. This methodology will add control and continuity to the studies so that they could then be evaluated after the pilot program as a whole.

Our design for our pilot -- we are proposing a crossover design in which the proposed trade name is evaluated in the context of both a neutral control name and an extreme control name. This involves splitting a sample into two groups, both of whom will evaluate the proposed name but in a different order from each other. Both groups will respond first to questions about the neutral control name.

Next, half the sample respondents will respond to extreme name first and then to the proposed name. The other half of the sample respondents will respond to the proposed name and then to the extreme control name.

Responses to the proposed name will be compared with responses to the neutral control name. The extreme name will serve as a positive control to ensure that the individuals in the sample can identify names that make representations about either

efficacy or safety.

This methodology will require a different sample for each proposed name but will require fewer individuals per study than other designs, for instance, a straight experimental design in which each condition is separate, because all subjects would see the proposed name and the control names. So in other words, this is a within-subjects design rather than a between-subjects design.

We suggest using a combination of both open-ended and closed-ended questions in the protocol. Open-ended questions are those that allow for free response from participants. For example, what does drug x say or suggest about its use or effectiveness in treating condition y. Closed-ended questions are those that use a bounded scale or predetermined response choices. An example would be how effective or ineffective do you think drug x would be in treating condition y where one equals very ineffective and five

equals very effective. Again, these are examples and we hope to have good discussion about this.

Things to watch out for designing questions are, leading questions in which the questions are worded in such a way as to lead the respondents to one response choice versus another. We also suggest avoiding yea-saying in which all the questions are worded so the response is always yes or always at one end of the scale, and this is not a complete list of questions or problems to avoid but it's an example.

So what type of questions should be asked? We recommend that the questions cover the same topics as those considered in the promotional review, questions about efficacy, questions about indication, questions about risk, safety, implied superiority, and fanciful or the implication that a common substance has some unique or special qualities, as my colleagues mentioned.

In terms of choosing a sample, we recommend that you choose a sample that's relevant for your product's intended use. If your product is going to be used by family practitioners, we suggest that you include them in your sample. Similarly with specialists. If for example radiologists are going to be the primary prescribers, we suggest that you include them in your sample.

Also, we suggest that you consider consumers in your sample, especially if your product is intended for OTC use, but it's not irrelevant for a DTC as well, as DTC is causing more prescribing choices on the part of the consumer.

Now again, because we're advocating the establishment of standard, neutral and extreme control names to be used across all tests, we do recommend that sponsors use a different sample of respondents for each proposed test name to avoid contamination between tests, and that is, if your sample

that you're testing is already seen your neutral and extreme control, that may bias their responses.

That concludes my presentation. I look forward to a great discussion by the panel. Thank you.

(Applause.)

MS. FRANK: Thank you very much. Now, do any of our panel members have clarifying questions for any of the FDA presenters? And I would like to remind panelists, please, before you speak, please state your name for the transcript. Why don't we start at that end of the table? I see you're all jumping up here. Dr. Day, do you have any comments?

DR. DAY: That was short, clear, understandable, and wonderful, and I don't need any clarification at this time.

MS. FRANK: Any other questions? Dr. Zuckerman?

DR. ZUCKERMAN: Hi. Ilene

Zuckerman, University of Maryland. That was a really clear presentation. I have some clarifying questions on the current process, just so I can better understand the process. And then I have a question -- I'm not sure if it's clarifying or if it's -- well, I'll ask it anyway. You can tell me if I should be asking it later.

On the current process, can you tell me -- you talked about this team that evaluates the name for promotional bias, I guess. What -- can you tell me about that team, the reviewers, the internal reviewers, the number of people, the composition of that team?

MS. SAFARIK: Michelle Safarik. So currently, Carrie and I are the DDMAC Reviewers that evaluate proposed trade names in consultation with the Division of Medication Error Prevention. My specific background -- I'm a Reviewer who reviews promotional materials directed towards

healthcare professionals. And Carrie is a Consumer Promotion Analyst who reviews promotional materials directed towards consumers. The other members of the team are Lesley Frank and Marissa Chaet who are two regulatory counsel in DDMAC, and they have expertise in the Act and its implementing regulations in regards to promotional labeling and advertising. Does that help?

Oh, and social scientists. I'm sorry, Kit. And then we also have Dr. Kathryn Aikin and Dr. Amie Odonoghue as well, our two social scientists. I apologize.

MS. FRANK: And I'd also like to add that the names are provided to all DDMAC Reviewers, so those who are especially familiar with the drug area, the drug class are invited to submit their thoughts, objections, non-objections, their rationale, and they're very good about it.

DR. ZUCKERMAN: Thank you. That was my next question was, does every team

member have the opportunity to review. And then I have a question on the proposed pilot. What was the rationale -- well, a couple of questions. One is, will the participants in the pilot be given any information about the drug as far as its -- the indications or any other information about the drug, the proposed drug?

DR. AIKIN: Well, that's a point we'd like to discuss with the panel, that sometimes the proposed names are evaluated before indication and safety are known. So in those cases, we don't get that information either. But sometimes we do know that, and I think we'd like some discussion from the panel whether that information should be provided or not.

DR. ZUCKERMAN: Okay, thanks. And can I ask one more question? On your design, what was the rationale for not varying whether you start with an extreme or proposed name as well and starting with just the neutral name?

DR. AIKIN: The rationale was that we felt starting with the test name might bias responses more than starting with a neutral control. You can also think about the neutral controls, starting there, as practice and that gives them a chance to practice rating names in a way that we don't expect would bias their responses, because the neutral control is not supposed to make any representations. That was the rationale but, again, we're happy to discuss that.

DR. LOWREY: Tina Lowrey, UTSA. I have just a few questions. One is on the make up of the extreme control. You said that it makes clear representations or misrepresentations. Are you not going to suggest one or the other? In other words, if an extreme control makes clear representations that are truthful, it's a very different testing environment than if the extreme control has misrepresentations in it.

DR. AIKIN: That's a very good

point. Kit Aikin, FDA. When we're evaluating from a promotional standpoint, we're looking for overstatement of efficacy, minimization of risk, so, I guess, probably the more accurate way to think about it would be misrepresentations about the product characteristics, and that is something that implies something that it does not have. So that's a very good point. Thank you for bringing that up.

DR. LOWREY: And then also, the issue about the order. Are you going to be having participants rate the neutral control before they then get exposed to either the extreme control or the proposed name, then they rate that and then move on? Or is it an exposure to all three names and then the rating of just the proposed name?

DR. AIKIN: We envision that they would be exposed to the neutral control, rate it, exposed to the proposed or extreme, rate it and exposed to the extreme or proposed and

rate that. So they would rate it three times on the same measure.

DR. LOWREY: Okay. And then also, I wanted to know how many participants you would suggest that a sponsor use, both on the consumer side and on the healthcare professional side?

DR. AIKIN: We did not suggest a number. The way we worded it in the concept paper is that we suggest that the sponsor or the person writing the test consult a statistician in order to get an adequate sample size to achieve the power to detect differences, but we did not suggest a number.

DR. LOWREY: Okay. And then my last question, and I don't know if this, maybe, would be more appropriate for the comment stage, but I understand the desire to use the same names throughout all studies so that you can compare, but one of my concerns about that is that the names may differ so much from the proposed name in other ways than

just the representation or suggestions about the product. They may differ in phonetic ways and orthographic ways, et cetera, which we talked about a lot yesterday.

And so I'm wondering if it might be a better idea to develop neutral controls and extreme controls that are very similar to the proposed name and only differ on the degree to which they offer representations?

MS. FRANK: I think that question really does go -- that does go to the first question, but right now we're going for clarifying questions. But if we could hold that, that is an excellent question, and we'd like Dr. Aikin to address it. Any more clarifying questions? David?

DR. KORN: David Korn from PhRMA. Just one question. In the first presentation, there were examples given of the kinds of names that you thought might fit into particular categories. Do you have examples in mind of a model to think through the

neutral control and the extreme control? Perhaps -- there's that example in the concept paper -- you can use that one or something else?

DR. AIKIN: I think the example we used in the concept paper of an extreme control would be fungus-free. We did not have an example for a neutral control. We had hoped that one would be established through pre-testing. We want it to be established through a scientific method.

DR. KORN: Is there a way that you could explain how -- I guess the question is how far away from the extreme control, if you start with that idea, would a neutral be, whether it would have to be completely removed from -- would almost be a different name or whether you would think in that context? It would be fungus-something else? What kind of a concept?

DR. AIKIN: Well, I think this gets back to Dr. Lowrey's point about making the

name related to the proposed name, which we had not envisioned and, perhaps, would be an alternative suggestion. We are proposing that the neutral control be pre-tested to not make any representations whatsoever and then could be used across multiple studies.

If we are envisioning a design in which the neutral control has to be pre-tested to be neutral but still similar to the proposed name, that's a different design that I think the panel should discuss.

MS. FRANK: Clarifying questions from the other side? Mr. Lee? Dr. Hobbs?

DR. HOBBS: Stuart Hobbs. Regarding the neutral control, are you proposing that the neutral control, the one that's proposed be used by every sponsor for every test, or would sponsors come up with their own neutral controls?

DR. AIKIN: Well, we're open to both. We had envisioned one in which it would be used by everybody, because then that

facilitates evaluation of the pilot program testing across all tests, because then you have similar variables. But we're open to hearing other ideas.

DR. HOBBS: One more question. You told us who's on the team at the FDA that evaluates names for promotional purposes. Can you tell us a little bit more about whether you use a questionnaire, whether it's a yes or no, whether it's a visual analogue scale type questionnaire and how you make decisions based on that, if you do?

MS. SAFARIK: Michelle Safarik. Currently, we don't use any questionnaires or visual analogue scales. We just use expert judgment by the various disciplines.

MS. FRANK: The name, along with all information provided by the Division of Medication Error Prevention -- I hope I got that right -- acronyms change so much these days -- but we have all the information provided along with the name, and that is

circulated to the entire review staff along with those on the review team. And they evaluate it from their various expertise, and they bring that to the table, and basically, internal discussions are held and a consensus is formed.

DR. HOBBS: Just so I understand, I guess I would suppose that maybe they'd come back and say it's okay or they say, no, we don't agree and the reason they don't agree. Is that --

MS. FRANK: Typically, we'll get emails that will say we have no objection, and it's internal discussion also and can be oral discussions. But it's -- basically, it's the matter of the names are vetted, and a consensus of our internal experts reaches a conclusion which is then forwarded.

DR. ORTELL: Una Ortell, TAP Pharmaceuticals. I have a question. I don't know if you have the answer to this here today. What percentage of names get rejected

for a promotional aspect?

MS. FRANK: You're right, we don't have that information. I'm sorry.

DR. ORTELL: So given that we don't have that information, would you say just from your day-to-day working, you know, business ,that more often than not, you reject, or is that too --

MS. FRANK: I honestly can't say.

DR. ORTELL: Okay.

MS. FRANK: We're just -- we're part of the process and we provide -- we're a consultative body, and we provide our consult to the -- ultimately, it's the Review Division, currently, who makes the assessment to object or not.

DR. ORTELL: And then my second question is also a clarifying quetion on the process. Does the promotional review, and I'm sorry, I -- you addressed it, I think, in your presentation, Carrie, but just for clarification, does the promotional review

take place before all the extensive safety reviews go on?

DR. NEWCOMER: Yes. If DDMAC objects to a proposed name because of a promotional implication and the Review Division also objects to it, the Division of Medication Error Prevention does not begin the review from a safety standpoint and then the sponsor is notified. When DDMAC does not object to a name, that's when the safety review begins.

DR. ORTELL: Okay. Thank you. No further questions.

DR. McGIRR: Hi. Yes. I had a number of questions. My first --

MS. FRANK: Name, please?

DR. McGIRR: Oh, sorry. Maureen McGirr. I had a number of questions. My first follows up on Stuart Hobbs' question about the -- whether or not you have a set methodology or a set questionnaire that goes out to the reviewers and a standard process

for collecting that back. I guess -- I assume you get a variety of opinions back from different reviewers and my question is around how you collect those together and assess those opinions and what kind of standards, if any, you apply.

So for example, do you have a standard that you're trying to accomplish? Are you trying to get back that a hundred percent of people had no concern with the name? Or is it okay if some people had some level of concern with the name and then you determine whether or not that's a reasonable concern or not? Is there -- how do you resolve the fact that you're probably getting a number of different subjective opinions back, and do you need to have unanimous agreement?

MS. FRANK: Well, I'd like to -- Lesley Frank -- I'd like to add that, as mentioned before, this is a collaborative process of people who are very experienced in

various fields, and they contribute, sort of, to the mass, to the discussion. And ultimately, from that comes our recommendation to object or not object, and it really is that process. But what we want to do is -- and that's why we have this pilot program -- is to increase the transparency of the program and to afford the sponsors the opportunity to participate by generating data and submitting to us for our evaluation.

And that said, sponsors have always had that opportunity to submit data on their names, but this really, sort of, formalizes in terms of the pilot program a way to do that through a methodology that we're here to discuss.

DR. McGIRR: In terms of the review process that DDMAC -- for promotional review of the names -- is there a specific time frame that you apply for that review knowing that you have to leave a certain amount of time for the DMETS review process to be taken?

DR. NEWCOMER: Yes. We provide our comments within -- I think the email goes out on a Friday afternoon, and we always respond back to the Division of Medication Error Prevention by Thursday at 10:00 o `clock at the latest, so we are -- the DDMAC review is within a week that we provide our comments.

DR. McGIRR: And if DDMAC rejects a particular name and the company submits a rebuttal, I'd like to have a better understanding of what that process is like. Is there a specific time frame for vetting that rebuttal? Who's involved in that assessment of the company's rebuttal, and is it the same reviewers who did the initial review? Are there other parties who are involved? Is the Office of Chief Counsel involved at all?

MS. SAFARIK: Michelle Safarik. We don't directly communicate with the sponsor. Everything goes to the Review Division, so if the sponsor does choose to submit a rebuttal

from a promotional perspective, we get that communication from the Review Division. Once it's received, usually, as far as a due date, the Review Division determines that. And usually, they give us adequate time to review the name, so all the rebuttals, at least in my experience, that we've received are additional data from the sponsor.

So again, as with the regular review, the DDMAC consultative team -- so again, that's the DDMAC EPD reviewers, regulatory counsel and social scientists will meet to discuss the sponsor's data.

If we feel that we need additional input, we will get that. We had a case where our evidence review team was involved because there was a patient-reported outcome claim embedded in the name. So we call upon whoever we feel additionally is needed and then provide our comments on whether we're going to maintain our objection or not to the Review Division, and then that's communicated to the

sponsor.

DR. McGIRR: I'm sorry, I didn't follow that. You said an evidence review team?

MS. SAFARIK: Yes.

DR. McGIRR: Is that in the Review Division or --

MS. SAFARIK: No. We actually have a team within DDMAC who reviews patient-reported outcome claims from a promotional perspective.

DR. McGIRR: And then, is the APLB process the same as the DDMAC process or is it different?

MS. FRANK: Elle Ibarra-Pratt, would you care to comment?

MS. IBARRA-PRATT: Hello. Yes, it does. Our process is similar to DDMAC. As I mentioned yesterday, with exception of the fact that we are a much smaller group, we currently have five reviewers. So when names come into our branch, it gets reviewed from

both a safety perspective and a promotional perspective, and everyone in our group is involved.

DR. McGIRR: Thank you.

MS. FRANK: Mr. Emmett, any clarifying?

MR. ELLISWORTH: No.

MS. FRANK: Okay.

DR. DAY: Dr. Frank, may I ask a clarifying question at this time?

MS. FRANK: Be my guest.

DR. DAY: I had passed before -- thanks -- Ruth Day -- giving everybody else an opportunity here. So there are basically five variables of concern to DDMAC: efficacy, indication, risk, superiority, and fancifulness, that should not be overdone in the names

Are you recommending that all of these be tested systematically? For example, a proposed name might be bordering on one of these, but the other names tested might only -

- the extreme one might be looking at one of the other variables. So are there five types of trials that should be included here? So I'm asking a semantic question here about what's being tested.

DR. AIKIN: Well, DDMAC looks at all of those variables in its review, and, for lack of a better term, failing on any one of those variables might be enough to get it rejected from a promotional standpoint. So we would envision each of those variables being tested within the study. The extreme control name might only be extreme on one of those, but again, it might be enough to get it rejected from a promotional standpoint.

But the comparison is with the neutral name. You're not comparing the proposed name to the extreme name. The extreme name is there to make sure that you're sample can actually detect that particular extreme name.

DR. DAY: Correct. So that would

be good to put in the revision of the pilot proposal whether they have to test on all five and how that works. One other question. I do understand in the results, you're going to be looking at different scores. I presume, for the dependent variables, there'll be a look at the type of coding that's done on the open-ended and then the usual measures for the closed-ended questions of means and standard deviations and so on. And I know you're going to do a different score, so it would be comparing the neutral to the others and so forth. But are there absolute levels that might be of interest as well?

DR. AIKIN: Kit Aikin, FDA. We suggested both methods in the concept paper that perhaps one level or perhaps a different score might be appropriate. This is an issue on which we really wanted input from the panel and the relative strengths and weaknesses of either approach.

DR. DAY: Thank you.

DR. McGIRR: I have another question.

MS. FRANK: Maureen?

DR. McGIRR: Maureen McGirr. So in the proposed pilot, where there's a comparison between the names, what is the standard of assessment that you're seeking to achieve there? Are you seeking to achieve that the proposed name gets the same level of and type of responses as the neutral name, or can it vary from the neutral name? How much can it vary from the neutral name? Can you give us some sense for what you're going to apply in terms of assessing those differences?

DR. AIKIN: Kit Aikin, FDA. Again, as I just stated, we're looking for input on both. We would expect -- I mean from our standpoint, we're looking for differences of a p less than .05 level, traditional levels of significance. As was discussed yesterday, it would be helpful for us in the pilot program to see not only names that pass from

promotional perspectives but those that are close or don't pass, because we're using this to compare to our current process, and it's useful for us to have information on both those that pass and those that don't pass to see if the pilot program is mirroring or is, in fact, better than our current process.

DR. LOWREY: I have one more question that goes back to Dr. Day's question.

MS. FRANK: Dr. Lowrey?

DR. LOWREY: Oh, I'm sorry. Tina Lowrey, UTSA. Are you viewing the extreme control as a manipulation check of a sort just to see that people can respond in the way that you intend for them to?

DR. AIKIN: Yes. Another way to look at it is what our Office Director, Dr. Temple, described as assay sensitivity.

MS. FRANK: Are there any other clarifying questions?

(No audible response.)

MS. FRANK: Okay. Our first agenda

item is a discussion of the strengths and the limitations of this proposed method. Let's open up the discussion. Who would like to comment? Dr. Lowrey, would you like to bring forward your comment from earlier?

DR. LOWREY: Sure. So my concern with using the same names, even though I understand the rationale behind it is that, if a name differs from the proposed name on more than one characteristic, you're not necessarily going to be able to pin down exactly why the differences and the ratings exist. So just as an example, one of my areas of research is the phonetic symbolism of brand names which basically just implies that the sound of a name can convey attributes.

So just as an example, an ah sound conveys attributes such as largeness, slowness, dullness, et cetera. And an ih sound conveys speed, sharp, you know, small size, et cetera. And so, if both your neutral control and your extreme -- but I'm, I guess,

a little bit more concerned about the neutral control that you're doing the direct comparison to -- if it differs from the proposed name on vowel sound or consonant sound or length in addition to the fact that it varies in terms of the fact that it doesn't make any representations or suggestions about the product, then you may be introducing some confounds into the ratings of these two names.

So I'm not sure what the easiest way would be to alleviate that, given that your desire was for all sponsors to use the same names so that you could compare across all of these tests. But you might -- I don't know if it would be a good idea to also include in the study design not only your current suggestion but maybe one more group of participants that respond to the proposed name against a neutral and extreme that are very similar to the proposed names. You can tease out whether the proposed name in the current study design, if the results are viable.

In other words, what I'm saying is the results from both of those two very different tests are similar, then you can have more confidence in the results of your current proposed design. Does that make sense?

DR. AIKIN: Could I ask a clarifying question?

DR. LOWREY: Sure.

DR. AIKIN: On what characteristics would you suggest that the control and neutral be similar? Just on sound-alike, orthographic similarity or some other characteristic?

DR. LOWREY: As similar as possible is all I'm saying. I realize it's very difficult because some of the prefixes and suffixes that are used to convey representations about a product obviously differ on which disease its intended to treat, et cetera. This whole medical field is very new to me. I do all my research in the consumer behavior domain, just regular packaged goods and products of that nature.

So I realize there are constraints just in the fact that these are names designed to communicate very specific issues of treatment, but if you could get a neutral and an extreme that is as close to the proposed name as possible while still providing the test conditions that you're looking at, I just feel like it would allow you to have more confidence that the differences between the proposed name and the neutral control are based only on the issue of how much representation of attributes is being provided.

MS. FRANK: Dr. Lowrey, would you be suggesting, possibly preliminarily, a test of the two pathways, if you will, to see which one, pardon the expression, gives you what you want in terms of results? Or would that be just an interesting side light?

DR. LOWREY: No. I don't even want to suggest that you're looking for results that give you what you want. What I'm saying

is that, if the results from your proposed design differ greatly from the results of a much more tightly controlled study in terms of surface attributes of the words, then you're not sure with your proposed study design what's causing those different results.

If the results are very similar from both studies, then you know that you're results from your proposed design are much safer. You can have a lot more confidence in them.

MS. FRANK: Lesley Frank. Does this mean that maybe if there are differences that there should be certain testing to isolate those differences --

DR. LOWREY: Yes.

MS. FRANK: -- and then to try to perfect the methodology to account for them?

DR. LOWREY: Right. In other words, in the pilot study, if you kept getting significantly different results from the two study designs, you might be worried about the

proposed study design because it may be introducing a lot of bias because of the use of that same name -- same neutral name and same extreme control name throughout all of the studies.

MS. FRANK: Thank you. That's a very interesting point. Are there any other comments? Dr. Day?

DR. DAY: That's a general comment that I have, is the potential for confounds and now knowing what's driving results that you get. And I think that's similar to what Dr. Lowrey is talking about right now and what I was talking about before about what are you testing for with the other names, whether it's for efficacy, indication, risk and so on. So the reviewers will be looking at that. But I think that a very careful look at the selection of the neutral and the extreme names is going to have to be looked at to see what are we going to be able to conclude versus not.

Otherwise, you know, if, say, the proposed name does not give good results on one of these tests, it could just be that there was one of these variables that was involved and the name might be modified in a small way to meet that rather than tossing it out and starting all over with another name. So it would be good to look at the selection of all these other names in a more controlled way.

MS. FRANK: Dr. Zuckerman?

DR. ZUCKERMAN: Ilene Zuckerman, University of Maryland. I'm not sure, Dr. Lowrey and Dr. Day, if this would add or make this a more robust pilot, but what if we could -- if they could test the names, use their design but use more than one neutral name for each drug, and then you could compare those results as well as to the current methodology and maybe have a bank of neutral names and a bank of extreme names that could be used over and over again with different drugs?

MS. FRANK: Dr. Aikin, would you care to comment?

DR. AIKIN: I actually like that idea. No, and the reason I like it is because the danger in having -- I mean although there's significant advantages in having one neutral and one extreme across all studies, the disadvantage to having that is that you are continually reducing your potential subject pool. And if you have a number of neutral and a number of extreme names, then you can vary back and forth. But that assumes that all neutrals and all extremes are equal across all studies.

DR. ZUCKERMAN: But they don't have to be equal because, if the ultimate goal is to compare the ultimate decision of whether this drug -- the promotional aspects of this drug's name agree with the current process, then it shouldn't matter which neutral and extreme you use. So for any one drug that you're testing, if you have more than one test

with more than one neutral and more than one extreme, theoretically, you should get the same results.

DR. AIKIN: Well, again, I think this goes back to the issue of pre-testing and I'll let Dr. Day --

DR. DAY: I was almost going to suggest the same thing for those five variables, that even within an within-subject design, you could have these extremes for all five -- efficacy, indication, risk, superiority, fancifulness and so on, and then just have independent random orders for each person. So you can test everything, still within the same number of subjects. So I was almost going to suggest that, but I'd also like to comment on these neutral names.

And there is value, as you propose, in having a neutral name across all proposed names for all sponsors. But you could also have a neutral name that's -- or some of these other names that are specific to this proposed

name, so there's general-general across everybody versus general within this category for this proposed name. And I know it sounds like the three of us are here increasing, increasing what needs to be done, but I think it's all doable with the same number of subjects in the same testing session, and it's just a matter of having independent random orders and setting it out right. And I think it would be much more informative.

I think it's a very clear and wonderful design. I like it very much. I'm just concerned about what can be concluded given that there's only three names.

MS. FRANK: David?

DR. KORN: I have a couple of general comments not on the specifics of the design. PhRMA has some questions with the proposal to include promotional testing within the scope of this pilot program as constructed. While proprietary name review has been the subject of intensive debate for

the past several years and the subject of numerous public meetings back to 2003, the focus of that debate has always been on FDA's safety review, that is, the testing procedures for sound-alike and look-alike names that were discussed yesterday.

There's been little, if any, public discussion or development of the testing methodologies for promotional testing or public discussion of any statutory or First Amendment considerations.

PhRMA's concerned that including the promotional testing within the scope of the pilot program may shift the focus away from the safety aspects and issues of the pilot project that it was designed to address and were discussed yesterday.

In addition, it would add separate costs and uncertainty to the process because of the added testing, and this would add additional costs for companies as well.

For these reasons, we suggest

considering how the pilot program is constructed overall, and I suppose we might talk about that this afternoon, but just wanted to raise that in the context of this discussion.

MS. FRANK: David, thank you for your comments. They are actually a little beyond the scope of this discussion which is really on the methodology, the attributes, possible limitations, and ultimately, we're discussing alternatives. That said, I think we can all agree that we're here collaboratively to avoid medication errors and misleading names, and this is consistent with the safe and appropriate use of prescription drugs.

Remind you that yesterday you stated that PhRMA definitely supports the concept that proprietary names should not suggest a drug is safer or more effective, and I think we can wholeheartedly agree on that but let's move forward. And are there any

more comments or questions on the question at hand, the strengths and the limitations of the FDA proposed methodology?

MS. PAULS: In addition, I'd like to request that PhRMA present those comments in a formal presentation to the docket. That would be very important because we do want to take those comments into consideration, although we don't want to expand on them here.

DR. KORN: As noted yesterday, we do intend to do that.

MS. PAULS: Okay.

DR. KORN: I have a sort of follow-up that is related to the design here, but it is again general and it's just a point. You noted that one of the factors that's examined is whether a mark is overly fanciful. And the regulations, as noted, do have a definition that addresses the question of that, and it's a comparison about whether it's overly fanciful and suggesting something which is different than an ordinary product.

It's an important role of trademarks and proprietary names to identify and distinguish products, and fancifulness is something that's, in general, sought after. And so we hope that any discussion of fancifulness is not discouraging the use of a fanciful mark in general and is focused on the regulation. How is that accomplished?

MS. FRANK: Well, absolutely everything we do is -- will be consistent with the statute, the regulations. And again, I'd like to reiterate Lana's comment. We really look forward to PhRMA's participation and submission to the docket, which will be thoroughly reviewed at that time. Thank you. Dr. Zuckerman?

DR. ZUCKERMAN: Hi. Ilene Zuckerman, University of Maryland School of Pharmacy. First of all, I just wanted to comment that one of the strengths that I liked was that it is empirical, and so I compliment you on that. However, it's still not clear to

me -- you know, I understand the design, but what's not clear to me is the data collection and analysis component, you know, that you would have a questionnaire or something asking about each of the five attributes of the drug, and you talked a little bit about that.

And I would recommend that that be a little bit more fleshed out as to, you know, maybe some sample questionnaires, how those questionnaires would be developed and tested, et cetera, and then how those data would be analyzed and how those data would be used then to make the ultimate decision. Because ultimately, it's a yes/no, and correct me if I'm wrong, that you'd be comparing to the current methodology. Is that correct?

MS. FRANK: Dr. Aikin?

DR. AIKIN: Yes. Ultimately, the conclusion reached from the empirical data would be compared to the current process. And we envision that the person analyzing the data would not also be on the other team. And

fortunately, we do have two social scientists at this time, and we can switch them back and forth, because we are concerned that anyone that's on the collaborative team and then reviewing the data or vice versa might introduce bias to the other system.

DR. ZUCKERMAN: So it's two separate evaluations which I was --

DR. AIKIN: Yes.

DR. ZUCKERMAN: -- and assuming that --

DR. AIKIN: Yes. And then at the end, we would compare our conclusions.

DR. ZUCKERMAN: Right. So I'm just recommending that in the next version of this, it be a little bit more clear as to, you know, the analytic component of this and that the analysis plan will be consistent, which brings me to my next question which is somewhat clarifying. For the pilot, the FDA staff is going to be doing both arms? Is that correct?

(No audible response.)

DR. ZUCKERMAN: And is the ultimate goal then to have the applicant take this methodology and implement it as part of their application?

DR. AIKIN: Please correct me if I'm wrong, but it's our understanding that the applicant would take the methodology, those that want to participate, and then apply it. I do have a question for the panel that I would like them to discuss. We did not put forth a detailed questionnaire in the pilot -- I'm sorry -- in the concept paper for the very reason that we wanted to give sponsors the opportunity to be creative in the way they might approach these problems.

Do you think that our putting forth a detailed questionnaire would inhibit people from developing their own questions that might be better?

DR. DAY: Well, everybody's looking at me.

MS. FRANK: Dr. Day.

DR. DAY: Since I made that comment yesterday about, are we going for standardization so we can all compare versus flexibility, the answers are yes and yes, I think we need to do both. So I think some samples on some parts with open encouragement of additional ways to do it would be great. But without some sample, it can leave different sponsors kind of up in the air not knowing which way to go and being anxious about it and then going a pathway that wouldn't work.

I think you've already specified quite a bit when it comes time for suggesting new approaches, some of us may have some additional things to contribute on that.

MS. FRANK: We invite submissions to the docket. Dr. Zuckerman, did you have a comment?

DR. ZUCKERMAN: Yes. I wasn't here yesterday, so I didn't have the opportunity to participate in that standardization versus

flexibility discussion, but reading the concept paper, that was one of my concerns was, I would think you'd want this to be reproduce-able and so it should be standardized. That would be my recommendation, although I do appreciate and understand that you want to give the applicant some flexibility in creating their own methodology and, you know, for their needs or whatever. But when I look at this as purely from a, you know, methodological perspective, I would recommend that the questionnaire be standardized.

MS. FRANK: Dr. Day?

DR. DAY: Can I just comment further on that? That comment from yesterday is that there should be some elements that are standardized and that everybody does. It's not here, standardize, then go do what you want. It's here are things that everybody would do that are core things to do that'll be in informative no matter what and that are

relatively easy and inexpensive to do as much as possible they can get done and then in addition, other things are not precluded but encouraged. So it was do both.

MS. FRANK: Are there any comments or questions? Maureen?

DR. McGIRR: Yes. I think, Kit, you had asked the question of whether we had a point of -- whether any of us had a point of view around whether the reviewers in DDMAC should be given information about the uses of a product or not. And I guess just responding, my reaction to that would be yes, from a legal standpoint, in order to assess if something's false and misleading, you need to assess that against the data supporting the application for the product or any proposed uses.

I suppose that, you know, if it's an outrageous name like Cure-All or something like that, then you can, on its face, think -- you can assess that. But for the most part,

to assess whether it's false or misleading, you're going to need some information about the product's uses to be able to assess whether or not there's an overstatement of efficacy or overstatement of safety.

DR. AIKIN: If I could just clarify. I think my question to the panel is whether the participants in the pilot should be given that information, not the reviewers in DDMAC but thank you. That's a very good comment.

DR. McGIRR: Thank you.

DR. LOWREY: Can I speak to that? I think that that's going to be necessary for the consumers and healthcare professionals also to judge on these issues. So I think that the participants of the study should be given some information about the product. Otherwise, how can they rate that it's overstating or not what it can do?

MS. FRANK: Dr. Lowrey, I had a question. You brought up consumers and do you

think it would be useful to test subgroups, identifiable subgroups of consumer population, and I also open this question up to industry. In your current testing, do you test subgroups of population with proprietary names? Do you think that should be added into the methodology, Dr. Lowrey?

DR. LOWREY: Are you asking me whether consumers should be tested or whether certain subgroups of consumers?

MS. FRANK: Certain subgroups.

DR. LOWREY: I think it depends on the drug under question, so if it's an OTC drug that could be purchased by anyone, I think just a general sample of consumers should be consulted, but if it's some sort of a drug that's extremely specialized and only people with a certain rare disease may be even aware of it, then I don't think you need to do a general sample, but pull from patients of that particular disease.

MS. FRANK: Any comments on that

point from industry?

MS. GANS-BRANGS: Just a comment. This is Kathy Gans-Brangs. Just a comment about trying to pull from patients with that particular disease. If you're in the pre-market setting, there might be all sorts of issues in trying to even identify those kind of patient populations. So I just want to say that might be difficult.

MS. FRANK: If there are no more comments. Oh, Dr. Day? Sorry.

DR. DAY: This question about giving the indication or not, I think it's an empirical question, and I think some pre-testing or, if someone could do a study giving and not giving an indication and see what happens, that would be very interesting. And I do have a suggestion for an alternative task on this. And I guess I should save it for when we get to that part.

MS. FRANK: Well, unless we -- if -- oh, David? Sorry.

DR. KORN: I have a question on the design that's in the concept paper. It wasn't specifically mentioned here. You're focusing on the data that was going to be developed here, but there was an evaluation session in the draft concept paper that talks about how companies should evaluate the data, and it has specific types of groups within the company that you would hope would be evaluating it. And I'm assuming that there's flexibility; you're not looking for that kind of specificity for companies to have gone through and that you're looking more toward the data that is going to be there?

For example, it refers to social scientists with expertise in consumer psychology. And are you looking more toward a social -- are you looking more toward having the social science aspect built into the study?

DR. AIKIN: Are you referring to section one under B?

DR. KORN: Yes.

DR. AIKIN: We're describing our review.

DR. KORN: Okay. And you're not reflecting how it's going to be evaluated by the companies?

MS. FRANK: Well, we certainly encourage companies to look at this, look at the name prior to their testing. They're going to have to set up the -- establish the methodology, consult their statisticians. But I think -- are you saying maybe the name should not be vetted internally through your promotional experts but instead just tested?

DR. KORN: No. I'm just asking exactly what you're thinking of for the submission in terms of how much -- whether it's simply going to be a name and a data package or whether you're looking at a whole type of review.

MS. FRANK: What we're looking for is to test the standard process that we use in

the pilot program. The methodology, once we receive the results from that, to assess the method itself, the data collection, the results. And then when we have both groups, essentially having looked at that information from both names, we will basically get together and make a determination.

I think I now understand your question. I apologize. What we would expect is for the company to submit enough information for us to adequately evaluate the methodology protocol, the data, the results. So anything that would be required for us to evaluate it from that standpoint. Are you suggesting that we should include that more specifically in the concept paper?

DR. KORN: No. I'm just wondering whether this suggests more. And if you're just looking more at is there a methodology presented to justify the data package, that's -- that would be different situation than justifying -- than trying to prescribe how a

company would do it internally.

MS. FRANK: Are you asking if the company should submit their internal practice?

DR. KORN: No. I'm just asking whether this is being prescriptive about how companies should undergo the testing or whether it's simply a description of a way that a company might approach it.

MS. FRANK: Well, one thing I'd like to say -- nothing in here is etched in stone, and nothing in here is prescriptive. That's why we're here is to discuss all the parameters involved, the strengths, the limitations, you know, other -- we've gotten some valuable information here of considerations, everything from the methodology to cost to how to conduct the trial.

And it's really a matter of, you know, I don't think you should look at this and say we have to do it any one way. This is just the draft of our concept paper. The

final concept paper will be out later in the year, and this all addresses all the parts of the substance, the criteria to be used by the agency in its evaluation and the logistics of the program. This is not final.

DR. ORTELL: I have a question, Lesley.

MS. FRANK: Una?

DR. ORTELL: Una Ortell. The pre-testing of the neutral control, there's no elaboration on how that would occur. And I was just wondering, is that something we should be talking about here and -- or did you have some ideas.

DR. AIKIN: I was hoping we could discuss it here, and I'm sure that we are going to have lots of suggestions for how that should proceed. Our basic criteria that we laid out that it should, during pre-testing, be established that this name does not make representations on any of the five standards that we use for promotional review.

DR. ORTELL: So as we're moving forward, then we probably should put some meat around some of these topics. And so I was wondering, did anybody have any ideas about, you know, what would be acceptable. For example, would it be sufficient to get a panel of about 15 or 20 professionals together to ask them to assess a name? And if everybody says -- you know, is the proper way to say does this make a representation or not, is that sufficient?

Or do you need to have a series of questions, say does this make an indication about this disease and have maybe ten questions of varying different diseases, for example? And then if you get an equal distribution of answers, then does that represent a neutral name?

So I guess my point is, maybe we should talk about what's a good way to get a bank of neutral names so then we have that in our back pocket.

MS. FRANK: Do any of our academicians have any good ideas here?

DR. DAY: I keep wanting to say what I'm going to propose for alternative approaches and save it for when it would come in here. I've used the following methodology. Make up a drug name or get a drug name and test it in open-ended and closed-ended right away. First thing, you give the name and you say, what do you think this drug would be used for and people write it down. And then you do the typical semantic analysis, clustering them into categories.

Right after that, for the same people, you ask to what extent do you think it could be used for treatment of fungus, pain, diabetes, da-di-da-da, and then it's a checklist. So the open-ended, if you don't ask that, you don't know what things come up because you pre-selected. But with the other categories, you actually have your target category in for the indication plus those

other things, and then you can see in a directly quantitative way. And I was going to suggest that as another way to get at and to test for indication and so on later on, but it could be used to evaluate these neutral names or any of the proposed names to begin with.

DR. ORTELL: Una Ortell. So once we would go through a process like that, I guess my question to FDA is would you take on that task of actually doing the pre-testing so that you could provide industry with a list of neutral names that they can use as they go forward in the testing of their own drug names? And maybe even also do the same for extreme names so that there's a bank of neutral and extreme? And then we have some starting points. Just a question. Or would you want somebody to take the lead as industry generates a neutral name, that neutral name can be added to the pot so to speak? I don't --

MS. FRANK: I think that's a very

good point. I think you've given us a lot to think about which we really need to take back and discuss, but we thank you for that. That's a good point.

This may be a good time, either to take a break or to go on to the second question, because it sounds like possible alternative adjunct approaches is really the way to go here for the next part of the discussion. But would you like to take a break? I'm seeing nodding. Okay. We'll take a short break now. We'll reconvene --

MS. PAULS: If we could reconvene at 10 a.m., please?

(Whereupon, the above-entitled matter went off the record at 9:48 a.m. and resumed at 10:07 a.m.)

MS. FRANK: Okay. I think we're missing a panel member here or two. So, okay. Thank you. Our last agenda item is a discussion of alternative methods to the proposed pilot program method regarding the

evaluation, again, of proprietary names, proposed proprietary names from a promotional standpoint. And I ask that when you discuss alternatives or possibly methods that could be used as an adjunct to the current - to be used in conjunction with the current method, that you be as specific as possible.

Let's open up the discussion. Dr. Day, I believe you had a possible alternative method?

DR. DAY: I'm not sure whether it's an alternative method or an adjunct, but I offer it for consideration. First of all, I like this simple design, the way that it's laid out, but what concerns me is what's being done in each part of the design with the, you know, the proposed name and all the other names. So it's nice to have open-ended and close-ended, but what I like to do is have the open and the closed both for the same information, the same semantic module, so to speak, if you'll pardon the terminology.

So what I was proposing before just illustrated the indication, although it could be for any of those other five variables - the efficacy, indication, risk, superiority, fancifulness as you think would be appropriate - asking the open-ended question, "What do you think this drug is used for?" and take down verbatim what they say. And there are certain semantic coding procedures that can be done to identify the core term and get frequency plots by different semantic categories.

And then right after that - with the same people - say, "Here are some possible things that..." - do you think - okay, you can have a list of indications that it could be. So fungus, pain, diabetes, heart problems, so on and in a closed kind of test. But there's a couple ways you do that. You can say, "Which one do you think it's most likely?" and they can check one of them. Or what you can do is to have the five point scale; how likely is it that this drug would

be used to treat fungus or pain or diabetes? And that way you get information for a bunch of them rather than just they happen to pick one and it was totally random, or they pick one but they were really deciding between two, and so on.

So that little methodology - what is it used for? - open-ended; could it be used for? And then having the multiple choice either where they choose or the multiple array where they rate the likelihood. So that would explicitly test for, in this case, indication. But this methodology can be used to test for any of those other variables that I just mentioned or anything else.

Now this could be either the main part of original testing, or it could be an adjunct to other kinds of things you want to do. Or it could be a follow-up. So say, for example, FDA raised concerns about implied superiority or something about the indication and was going to reject the name and went back

to the sponsor, and the sponsor could perhaps follow-up with this and to see in an open-ended and closed way what people thought about the issue that was raised. So this could be an additional follow-up testing method.

So that's one of the tasks. I don't know exactly what to call this, but it's a specific semantic focus asking, what is? Or, how effective? I mean it can be translated into effectiveness. So how effective do you think this drug would be? In the open-ended, they write down whatever they write down. And for the closed part, it could be very effective down to not effective at all versus can't tell. And it would be nice to get a response of can't tell, you know, a high frequency of responses there.

So it's a little methodology that can be applied to different semantic categories. So that's what this thing is.

The other thing I wanted to mention that I touched on before is using multiple

drug names in the same testing with the same people, if you want to test for any of these variables specifically as well, and then just putting them in independent random orders for each person or a few random orders. And it doesn't change the design, the order of those three things that are being tested. Or what you can do is collapse all of them into the same list so you have the neutral and then you have the test items or you can have all together in one thing, and do whatever test you want to do, but this little procedure I'm talking about - what is it, such and such for and the open and the closed.

So I'd like - and as a matter of fact, the sponsors could include their two potential names in this. I guess that would be the between subjects, but it wouldn't be bad to consider that being within subjects as well. So there's a lot more information that can be obtained without extra - any measurable extra time and testing and with more focused

conclusions about the different things that might be of concern. So that's the second thing I want to say.

And the last thing is some pre-testing before whatever goes out goes out would be very good. Things have been suggested about pre-testing the neutral names, that everybody might use and so on, but even this methodology, if you stayed with that design that Dr. Aikin showed us, it would just be good to do it and just see then what the challenges are in data analysis and interpretation. And there might be some things that might need some tweaking. So I would recommend a pilot test of the pilot test.

MS. FRANK: Thank you for your comments there. Well, there are limits. Do you think this could be used as either a screening process or just really as an adjunct or a parallel?

DR. DAY: You mean the pre-testing

the pilot?

MS. FRANK: Dr. Day, yes.

DR. DAY: Well, I was suggesting right now, do it now and find out how it works for anything. You know? And I'm particularly interested in what the data are going to look like and then whether you're going to use absolute or relative measures and so on and just try it out before asking those sponsors who want to participate in the pilot to use the methodology. And then it can be used to do other things as well, like testing these neutral terms that everybody might do.

MS. FRANK: Thank you. Mr. Lee?

DR. LEE: Yes. I had a question, a follow-up. On these various surveys that would be taken, whether we're talking about the ones this morning or the ones you would suggest, is there a sense of how many respondents we would need, a range of the kinds of numbers?

DR. DAY: Well, I support Dr. Aikin

that a statistician should be consulted and so on, but what you want is sufficient data that can be obtained by either having lots of observations on fewer people or fewer observations on lots of people. And I believe that Dr. Aikin comes from - has her PhD in social psychology where there are certain ways of doing this and that are similar to what I do from cognitive psychology that don't seem to be the same as the way clinical trials are done.

So if you submit something to JAMA or New England Journal and if you don't have, you know, hundreds of people, it looks funny even though you may have adequate statistical power. And if there was a way to do some education on this so that we could have crossover of these two research traditions, it would be great.

DR. LEE: I'm sorry. It was Bob Lee. Just a real quick follow-up. If you were to do more than one name, as you

suggested, do you need a separate set of respondents for the second name?

DR. DAY: I think that question should be directed to Dr. Aikin.

MS. FRANK: Dr. Aikin?

DR. AIKIN: So are you asking if we use Dr. Day's methodology, whether a separate set of respondents would be needed?

DR. LEE: Either. If we wanted to test more - we typically would test more than one name at a time. So in either event, would you need different - or in which situation would you need different sets of respondents?

DR. AIKIN: Well, from the methodology that we're proposing, we have two groups, one in which the proposed name is tested against the extreme and neutral. If you were testing an additional name, you could add a third and a fourth group in which you have a second name so each group would be a different set of respondents. If you wanted to use multiple names within the same study,

as Dr. Day is suggesting, I would probably defer to her, but it seems to me it would be the multiple names, fewer subjects approach where you would test multiple names but you wouldn't have different subjects in each group. Does that answer your question?

DR. DAY: And if I can comment further.

MS. FRANK: Dr. Day?

DR. DAY: If you were trying to test five names that your company is interested in, it would probably be unwise to put them all in with the same people in this methodology. I mean you could but then it depends upon how similar the names are, so if it was "Abilify" and "Abilification" and "Abilifi-something" or you know, "New Outlook" and "Outlook Improvement" - I don't know - I'm just saying that the semantic similarity of all of those would tip off sort of what the domain is, so you'd have to be careful.

MS. FRANK: Are there any other

proposals for alternates or adjunct methods? Dr. Zuckerman?

DR. ZUCKERMAN: Ilene Zuckerman, University of Maryland School of Pharmacy. I would just like to reiterate and agree with some of the comments that Dr. Day made with regard to pre-testing. It's written in my notes as well in that the pre-testing phase - I know it's like pre-test on a pilot - you know, it may sound somewhat redundant, but in that pre-testing phase, you could get more information on the process measures that you also are probably interested in such as how long it takes to do the study, the variability in the responses, and that would give more information about sample size estimates, because you are going to need some variance in the responses.

And also in developing and testing and validating the questionnaires that would be used - I think that's really key and important.

Another suggestion I have that may sound off the wall is in the development of this bank of neutral and extreme names, is it possible perhaps to include existing names that we supposedly know passed the test in previous evaluations and possibly use names that did not pass, you know, that were rejected? I know there's probably all kinds of issues around that that make it not doable. So that would sort of be like a, I don't want to use the term "gold standard," but a standard that could be used. And so I guess that's really my comments for right now.

MS. FRANK: Dr. Aikin?

DR. AIKIN: I just wanted to ask one clarifying question but also to say the idea of using names that might have been rejected in the past is very intriguing as sort of a double-check to see how sensitive the methodology and questionnaires are.

My question was in using existing names for either the neutral or extreme

control, how do you propose testing for prior knowledge and experience?

DR. ZUCKERMAN: Yes. I thought of that. I don't - that would be, you know, a potential confounder, so we'd have to think more about that, but maybe they could be - and again, in the development of this bank of names, maybe the could be thrown in as part of that testing process to see, you know, how well your test of neutrality and extremism is measured.

So more maybe just sort of as a check but, yes, the existing - and that also brings up the issue of - again, this has been discussed before - in this testing process, should the participants have knowledge about the indication and everything that's, you know, information about the drug, the indication and whatever else is known.

And I would suggest that that knowledge, the participants should have the same level of knowledge that the current

reviewers have, if possible, to make the two processes comparable.

MS. FRANK: Dr. Day?

DR. DAY: I'd just like to repeat that it's an empirical question about which way to do it, with and without the indication. And I think that there is some value in nobody knowing anything to begin with. You get more information about what competing indications might be than if you told people, and then have a follow-up where you do it where that is known. I think there is some potentially really important problems that could exist doing it one way versus the other, and I think that it's really important to know.

And also, you might consider healthcare providers versus consumers. So healthcare providers, you know, what is it you're trying to get - are you trying to have both of them do exactly the same thing, or should one group have more information than

another?

And another comment about the subject population. Should you have special groups or not? Well, there's two points about that. When there's special groups, they may know they've been selected because they're special, because you contacted them in a certain way, and then they wouldn't be blinded as to the purpose perhaps.

But the other thing is since we're talking about promotional things, even if it is targeted for oncology patients, if there's going to be any promotional aspects, then the general public's going to know about it, and you want to make sure that it doesn't sound like - I don't know why I'm focusing on fungus today, somebody else brought it up, but - if it's for toenail fungus that if that seems to be an indication by the name or something that other people won't be interested in it as well. So those are my comments.

MS. FRANK: Are there any other

comments?

DR. HOBBS: Yes. Stuart Hobbs.

MS. FRANK: Dr. Hobbs?

DR. HOBBS: It sounds like we're going down a road to trying to define what we're going to do. And I guess one question I have is - because I'm naive in consumer research and trade name testing - but I have yet heard any discussion on testing for validity of the test, reproducability, et cetera. And I was wondering if anyone would like to comment on that?

MS. FRANK: Dr. Zuckerman?

DR. ZUCKERMAN: Ilene Zuckerman, University of Maryland School of Pharmacy. I think there was some discussion about that in, you know, the pre-testing phase, testing the validity of the questionnaires, testing the validity of the names. And it may not be much of - somewhat of a validity question, but more of a reliability question, as you point out, but I think those are really important points,

and they should be included in the methodology.

MS. FRANK: Dr. Day?

DR. DAY: Ruth Day. Reliability will be taken into account by having some neutral names across all. There's one way. And that's basically like a test/re-test kind of thing. The validity - that's why that little paradigm that I suggested could be done up front - what is this used for, and you get an open-ended and closed-ended, could it be used for this, this and the other thing. Actually, if you prefer to go back to the kind of testing that was originally proposed, that could be done first, so you at least know that the extreme names that you've selected have some validity because, don't know, 60% of the people thought it was for diabetes or something of the sort. So that's one way to know something about the items that are selected.

And again, I think that knowledge

of the other items in the test is really important, and data on it before being used is really important.

MS. FRANK: Dr. Hobbs, did that answer your question? Okay. Thank you. Other comments, questions?

DR. LOWREY: I have a suggestion.

MS. FRANK: Oh, Dr. Lowrey, I'm sorry.

DR. LOWREY: Sorry. Tina Lowrey, UTSA. So the study seems to be getting more and more complicated, I'm sure, to - I know, I know - and there's this issue of respondent fatigue.

So one of the things I was thinking about in terms of my concern about confounds with the neutral names and extreme control names that might differ on attributes other than just the representation of the product is to do, if we're going to create a bank of potential neutral names and a bank of potential extreme control names, would be to,

with a completely different group of people, not part of the actual studies that the sponsors would be conducting, would be to have a sample of people rate each of those names along - there's a standard manipulation check which is quite lengthy, but that could be then part of a data set that you could go in and pick a neutral control name that is as similar to the proposed name on all of these different attributes so that you can rule out those potential confounds.

So it would be things like heavy/light, sharp/dull, quick/slow, et cetera. All of those things that the sound of the word might convey separately from its semantic meaning. And so then you would have this bank of names that you could pick from rather than having to add an additional cell in your study design where you included a name that was as close to your name as possible. So that's another sort of an alternative way to alleviate some of the respondent fatigue that

might occur having to go through too many names at one point in one study.

MS. FRANK: Thank you. Kathy?

MS. GANS-BRANGS: Yes. Kathy Gans-Brangs, AstraZeneca. Just a quick follow-up. How large would the experts here envision a bank being that would be really a useful bank?

MS. FRANK: Dr. Lowrey?

DR. LOWREY: Tina Lowrey, UTSA. I really don't know because I believe that given the number of different diseases that could possibly be treated and the number of different prefixes and suffixes and stems that are typically used in coming up with drug names for these different categories, it might be that there needs to be a bank for drugs that treat cancer and a bank for drugs that treat diabetes, because I assume those names are very different from one another, because you tend to pick certain kinds of syllables that convey meaning semantically. So I think it might be sort of context specific.

DR. DAY: Ruth Day. I think there are some that are neutral semantically. We've come to learn about them. I hate mentioning specific ones that just might come to my mind today, but there are some that, you know, sound - Tina keeps coming back to phonetic symbolism, you know, the sound over and beyond the nature of the health condition and so on. And we can control for those kinds of things or manipulate them. But there are some if you hear a drug name that's already out there, you don't necessarily know what it's for.

And so think that there are - we can make up names and test a bunch quickly, and just know that they're neutral. So I think neutral could be neutral both in semantics and all these other things. And I appreciate the idea of going into different health conditions and so on, but I think it's going to be unrealistic to do that. So neutral is neutral. And the only ones that are really semantic is the indication. I mean

all the others with efficacy and risk and superiority, you can do neutral on it. So I bet you we could test, you know, a dozen of them and get a subset of, you know, six or five that are neutral on all of those things.

MS. FRANK: Dr. Lowrey?

DR. LOWREY: Do you think that's true, though, for the extreme control? In other words -

DR. DAY: No, no, no.

DR. LOWREY: Okay. So extreme control might be more content specific.

DR. DAY: Right. But there probably are some names we can make up to be extreme on efficacy like "superpred" or, you know, things like that. So I think that that's not hard to figure out, but some of the others might be.

MS. FRANK: Thank you, Dr. Day. Further comments? Una?

DR. ORTELL: Una Ortel, TAP. I just had a clarifying question and then I have

an alternative approach I believe. And I'm not sure, David, if you brought up this question earlier. Is the proposal that the people who are going to be involved in the tests, that they be kind of experienced in the promotion and advertising regulations? And this is section b(1) where it talks about evaluation. So are we going to get a naive group of doctors to do this evaluation, or is it - I think what you're saying is people who know what they're doing in this regard in terms of marketing, regulatory affairs, et cetera. So that's my question. And then I have a comment.

MS. FRANK: Dr. Aikin, care to respond?

DR. AIKIN: We had envisioned the sample being a group of healthcare professionals that are the relevant target population for prescribing. They don't necessarily have to be experienced in promotion, but that they would be a relevant

target population for when the drug is marketed. So for instance, if it's a product that you expect to be prescribed by general practitioners, they should probably be included in your sample.

DR. ORTELL: So I think then that that point is not clear, doesn't clearly come out in the pilot paper, so maybe just having a look at that to ensure that it is clear that you're talking about people who aren't actually experienced in promotion and advertising regulations. So I do agree with that. That's good.

My alternative approach - I was going to just bring up something, and that is just to take into consideration the resources needed to, you know, come up with names. These days it's incredibly difficult and burdensome in terms of time and other resources. So I'm wondering if DDMAC would consider using this approach where there is a dispute. So for example, the current approach

at DDMAC works well. The experts review it. It's the same as the approach for reviewing commercials which, of course, have a very broad reach, et cetera and for all other promotion and advertising materials. And so I think from that perspective, it works well.

If DDMAC says that a name is rejected, an alternative approach would be then that name could possibly go into this pilot program and data could be generated to either support the company position or DDMAC's position. So I just would like to bring that up for consideration.

MS. FRANK: Dr. Aikin?

DR. AIKIN: Thanks. Thanks for the alternative approach, and I'm really glad that you're generating alternative approaches here because that's what we want. My question back for you, and it's just a question - one suggestion that was brought up yesterday and that I tried to reiterate again today is that we would like to see not only the successes

but also the failures.

And in your approach, in cases where DDMAC might reject the name for a promotional standpoint based on our expert collaborative process, and the company decides to participate in the pilot and gather data, and the data confirm DDMAC's conclusion, do you think that we would still get to see that data or those data?

DR. ORTELL: I think it would be critically important to provide that negative data from the company's perspective to DDMAC as well, because I think we are in a pilot environment. We're trying to generate some good information. And from my perspective, I think absolutely, once you go and do the study, it would be very important, either positive or negative, to give the results to DDMAC for evaluation.

MS. PAULS: Lana Pauls, FDA.

MS. FRANK: Anybody else like to comment on this?

MS. PAULS: Yes. I was going to ask the other industry members to please comment on Una's, in regard to providing the negative data.

DR. LEE: I wasn't going to comment on that. I had another question. I just didn't want the session to close before I had a chance to ask it.

MS. PAULS: Yes. Can I please ask the industry panelists to comment on Una's question? Then we'll go on to you, Bob. Thank you.

DR. McGIRR: Yes. I'd be happy to comment. Maureen McGirr. I agree completely with Una's suggestion. Of course, if you entered the pilot, you should provide the negative data. I like the scenario that Una is suggesting with, you know, using this as an alternative approach. I think that there is, of course, a question around timing and how that would work, you know, assuming it takes time to do the testing and you're under time

constraints.

MS. FRANK: Would you see this ultimate goal, though, of essentially turning over the process to industry to do the analysis and then ultimately to increase the transparency, predictability, and then, of course, we would do the analysis of all the information, the methodology, the statistics, et cetera, and that that should be the ultimate goal? Or do you think that should just be an adjunct to the current process?

DR. ORTELL: Lesley, you were directing your question to me?

MS. FRANK: Open question.

DR. ORTELL: Oh, okay.

MS. FRANK: Una?

DR. ORTELL: I'll comment. Una Ortell. You know, I think that, ultimately, what people want to get at is the right process and the correct way to move forward. So as you generate the data in the pilot, it may demonstrate that, in fact, the one-week

review at DDMAC achieves just as much as, you know, months worth of collection of data and that, therefore, you know, the process is good. Or it may show that, in fact, generating all these data is preferable in that you get, you know, better results once we define what "better" is. And so I think we have to go through the process with the goal being to come out with a good process.

MS. FRANK: Because I think, ultimately, if we can come up with the process and that we have the methodology and that industry can then - essentially partners, in a way that they do now anyway, of submitting data to the agency for our review, that hopefully, this would expedite the process. And we've heard word out there that people would like that process sped up where they would like increased transparency.

So that's what we were hoping to do through this pilot program - to see, you know, if the method that, at the end of the day,

hopefully companies will participate and use, if that will contribute to that. And as Lana said, would industry care to comment on this proposal, the alternate or possibility of using this as an adjunct now? Because frankly, we have always encouraged industry to submit data, and some companies do that now anyway, and we're very happy to review it. So this is just a formalized process, developing this pilot program. Mr. Emmett?

MR. EMMETT: Andrew Emmett with BIO. Again, thank you for the opportunity to comment on this very thoughtful proposal. And, of course, BIO is extremely supportive of the overall overarching goals of the pilot program to reduce medication errors.

I just want to echo some of the sentiments expressed earlier that, you know, the promotional review at this time may be a little bit beyond the scope of the pilot program as envisioned under the PDUFA IV technical proposal. But at the same time, we

believe that of course, FDA should continue to have the ultimate authority over the promotional review.

And I've really enjoyed this discussion of the methodologies, and perhaps it would make more sense to take some of this discussion of the social science methodologies and techniques and bring them in-house into FDA's reviews, standardize them a bit more, make them more transparent so there's an understanding between FDA and the sponsor of what the expectations are. And hopefully, that will improve the overall first cycle approval rate of reviews of trademarks.

But my concern is, by linking the promotional review to the safety review within this pilot program, that some discomfort with the promotional review among industry may inhibit participation in the overall pilot program, and we may not have robust enough participation in the pilot to really achieve the goals for the safety review and the

medication errors. And perhaps that's something we could assess further in the logistics panel in the afternoon.

MS. FRANK: Thank you for your comment. Other comments? Dr. Aikin?

DR. AIKIN: This is just a follow-up on your proposal that companies participate in the pilot program if the name is rejected. And I fully recognize this may be an unfair question to ask you at this point. Do you envision companies using the methodology described in the concept paper or to incorporate the methodologies that have been described here this morning, the more advanced with the multiple control and extreme names and perhaps a different approach?

DR. ORTELL: I think, ideally, a company would have discussions with DDMAC about how to move forward, and it would probably be, you know, some combination of what's in the pilot, what has been discussed here and perhaps some other additional

thoughts. But ideally, DDMAC would approve the design prior to moving forward.

MS. HOLQUIST: Carol Holquist, FDA. I just have a question. I just want to clarify something. The names that are submitted under the pilot will still undergo a proprietary name review, I mean the promotional part of the review, because that is part of our assessment of a name overall. So whether we use this methodology or not, any name that is submitted under the pilot will still have that component of the review in it.

DR. HOBBS: Stuart Hobbs. Let me make sure I understand. The DDMAC is going to continue while we're doing the pilot, if that occurs, to do the same process you're doing now?

MS. FRANK: The pilot program will have limited participation, so we will continue, of course, to review promotional names as they are submitted, the proprietary names, sorry, from a promotional perspective

as they are submitted to us.

DR. HOBBS: Okay. If we, as a sponsor, participated in the pilot program and we did all this work which seems to be empirical testing, validated procedures, and we said, yes, it meets all the requirements of being a good trade name, and your testing came back and said it didn't, and your testing is I think what I heard is you send out information and people send back a yes or no and maybe a qualifying -

MS. FRANK: Well, it's actually a little more than just a yes or no, because the people who are responding to the proposed proprietary name, they're trained. And when they come back with an objection, there's usually a detailed response as to why.

DR. HOBBS: Okay. So just to follow on with that, it's unclear to me how the outcome would be negative from the pilot project if the pilot - I'm no sure what the measure for being successful is in the pilot.

Is it agreeing with what the FDA review is? Or is it some measure within the test itself? That's the concern I have because I'm not sure I can agree that there's a scientific approach. There's an expert approach and I think that's a valid way to look at it. And one of the proposals is we think that expert approach with DDMAC now is sufficient most of the time. But that's not the same as a scientific approach.

MS. FRANK: Dr. Day.

DR. DAY: Ruth Day. I have a shocking suggestion, and pardon any toes that get stepped on. Would it be of interest to you if the DDMAC reviewers, at least for a few examples, acted as respondents in the study so that DDMAC would do its usual review but for a subset, they would take the questionnaire. And so if we're going to use something like "What do you think this drug is used for?" when they don't know what the indication is and write it down, and could it - do you

think it's used for and give the alternatives and so on - they went through all of that, would that be of interest to you?

DR. HOBBS: Well, let me make sure that-

MS. FRANK: Stuart Hobbs, sorry.

DR. HOBBS: Stuart Hobbs. I'm not questioning the ability of DDMAC at all. I'm just questioning the difference between the process being one that's less scientific versus more scientific from a science perspective, hypothesis-testing perspective and how you make decisions about the outcome between those two. That's really what I'm asking.

MS. FRANK: Mr. Lee?

DR. LEE: Yes. That gets to the question that I wanted to ask on the range between neutral and extreme. In assessing whether the test name is neutral or extreme or somewhere in between, someone has to make a judgment as to where along that range it is,

and I'm assuming that it does not have to be neutral, that something more than neutral is still an acceptable name. So if the DDMAC panel were to take the test, you'd get a sense of where they started to rate the name between neutral and extreme. It still doesn't tell you where acceptable is.

DR. DAY: That would be the next step, but it would be something that would be easy for them to do, and you'd have some preliminary information about it.

MS. FRANK: Dr. Zuckerman?

DR. ZUCKERMAN: Hi. Ilene Zuckerman, University of Maryland School of Pharmacy. I'd like to comment on Stuart Hobbs's comment, because I had the same question about the overall, and not just the promotional aspects but the safety as well, that I was going to bring up this afternoon in the logistics, the same issue of what is the objective, what is the overall goal of this program.

And my understanding from reading the concept paper was that the objective was to develop some methodologies for the applicants, for the industry to be able to use to do their own evaluation as part of the PDUFA requirements, that they would be now doing this, but they have to submit enough information to the FDA to make sure that the process was reasonable - I know you want to say valid, but reasonable - and the current process is different.

And so my concern is - I share some of the concerns - is, is the overarching objective of this whole pilot to examine the concordants between the current decision and the decision that the industry would be making, using some standardized methodology, or is the objective to develop a validated methodology? And I think they're very different, and I think that's sort of somewhat the confusion that I hear and I share right now. Because if the overall objective, as I

understand it, to see if the industry can come up with the same answer as DDMAC would have anyway, then that's, you know, a different approach.

I mean think everything we've talked about still holds, but it changes what the overall objective is that I've heard discussed so far.

MS. FRANK: Well, what we're trying to do here is develop a methodology, so really, it transfers over to becoming a sponsor-led program, a sponsor-led method, a development of data, research on these names in a regulatory framework, of course, that then gets submitted to the agency. And we would review it just like we would review any NDA submission. So I mean that's where we're looking at, and we're looking for transparency in the process.

We're looking for the submission of data, and we need a pilot program to find out how well this works. We need to understand.

You know, we're here now to get comments as to the methodology. We're hearing some wonderful suggestions, and we need to take that back to develop a possible final method, if you will, that could then be used. We could evaluate it, and if need be, perfect further. But this is really no different than what we do with respect to other submissions to the agency that the sponsor is responsible for. So we're looking to that to help also increase the transparency but to sort of shift to the sponsor.

DR. ORTELL: Lesley, Una Ortell. Just one difficulty with this is that, of course, as mentioned yesterday, we don't have all the names that may be tentatively approved. So the bigger question is not having all the names, does that completely invalidate the testing, because if you're trying to, you know, make sure that you're not making - well, I suppose it's more on the safety side. I'm thinking as I'm speaking.

Sorry.

Let me change that question to say does it - do you think it makes a difference if we do all this testing, the fact that we don't have all the information on names that are currently approved, are tentatively approved? Do you know what I'm talking about? No.

MS. FRANK: You're asking about names in the pipeline?

DR. ORTELL: Yes, names in the pipeline that are tentatively approved. Yes. Do you think that makes any difference here, or is it more on the safety side? It's probably more on the safety side.

MS. FRANK: Carol Holquist, would you care to comment?

MS. HOLQUIST: I think there will be a number of things that you might not be aware of, not just names in the pipeline. I think you might also not fully have a good understanding of some of the contributing

factors to some of the errors that we have learned through our post-marketing experiences. That's why I think just like any review that's done with FDA, you know, we set out some sort of methodology. We hope to follow it, but then the experiences of the reviewers at the FDA may have a different viewpoint based on lessons learned from other applications or whatnot, and that's just how the science is going to grow. And we hope to be transparent about some of those discussions and decisions so that we can all learn from it, and then it won't be, you know, just at FDA.

So I think it's going to be a process that grows over time, and that's why we hope in this pilot that we can - you know, much of this is going to be discussed this afternoon - that we hope that we can share these experiences across the people and we won't be held to these standards of confidentiality or proprietary, that, you

know, we'll be able to tell one sponsor versus the other, like, this is what's going on. And we need feedback this afternoon on, you know, how can we do all of this.

MS. FRANK: Mr. Lee?

DR. LEE: Yes. In the interest of transparency, what is DDMAC looking for after this methodology would be exercised and you'd have all the data and you would take a look at it? What are they looking for in terms of neutral versus something that has meaning versus something that has an extreme meaning in terms of acceptability of a name?

MS. FRANK: Dr. Aikin?

DR. AIKIN: Well, I think that's part of why we're here is to decide or at least to discuss what the markers would be. As described in the concept paper, we describe an approach where either the proposed name is compared to the neutral name in terms of differences or that there's some point at which it becomes acceptable or not acceptable.

But I think that's why we're here is to discuss the relative strengths and weaknesses of those two approaches.

And just to clarify, we are proposing an approach in which the proposed name is compared to the neutral. It is not compared to the extreme. The extreme is used as a control to see if your participants can tell whether names have some sort of promotional aspects.

DR. LEE: Does that suggest that what you're looking for are neutral names, that test names should be neutral?

DR. AIKIN: I think we're looking - we are testing to see if the names proposed have any promotional implications, and if they don't, that would be an acceptable name.

DR. LEE: Isn't the ultimate test, though, false or misleading? So that if it does have a meaning but it's not false, it's not misleading, would that be still an acceptable name?

MS. FRANK: As long as the name we're looking to is, it's truthful, it's accurate and consistent with the statute and regulations. That would be acceptable.

DR. DAY: Ruth Day. A major stumbling block for participating in the pilot program will be the expense in time and money to conduct the studies. And there's no way to say how long it'll actually take, but I've heard people commenting, oh, we go through months of doing this and then that happens and so on. If the procedure can be pared down so that it's quite brief, two things will happen. I think that the entire testing can be done in a half an hour, and I think group testing is possible.

Now I have gone and watched as some companies do their testing in these testing centers where they have these panels of people who come in and get tested on all kinds of products. And there you have one interviewer and a person, and maybe they're looking at a

package, and they're asked questions. It goes on and on and on. For this, people can probably answer this within a test booklet, as long as they are multiple pages and they can't see ahead. Or something can be put up on the screen, each question at a time with the answers in the booklet that they can check off.

You know, it still depends on what methods are used and the different tasks that have been proposed, but I think this can be conducted in a half hour, and if it was done right, you could do it, you know, in a day. I know that sounds outrageous, so let's say a week. I mean I don't think this is months and months of recruiting people.

I think you have the gift certificates or whatever it is you're going to pay them, and people come in a room, and we haven't settled how many people and so on. We don't want to say numbers, but a room of 50 people once or twice or some other combination

of that.

I don't see this is as prolonged. You're not getting them to pronounce anything, so it's all either orally presented by the interviewer- well, I wouldn't even say the interviewer, the experimenter and then with answers that can be written. As long as people can write and you can read their writing, I think it can be administered that way, and I'd like to hear comments from Dr. Aikin whether she thinks that's possible.

MS. FRANK: Dr. Aikin?

DR. LEE: Well, I think that's a very interesting approach, and certainly I can see that working for consumers. I don't know the viability of getting a group of healthcare professionals in one room. They are traditionally rather difficult to recruit. I would like to hear comment from the panel on whether they think this methodology could be administered over the internet.

DR. DAY: I'll bet it could be.

DR. AIKIN: I'd also like to hear from industry who does often do these type of studies what sort of success or failures they've had with recruiting and administering tests over the internet to healthcare professionals.

DR. ORTELL: Una Ortell. I think, Ruth, just to clarify my comment about months and months, really talks to the process from the beginning to the end and not the actual testing. So you develop the booklets, you, you know, get the budget to do the whole shebang. And it probably could be administered over the internet I would think. Any other comments here?

MS. FRANK: Mr. Lee?

DR. LEE: No. I was going to say that I don't have the experience in that. I'd offer it if I had it.

MS. FRANK: Well, are there any other comments or questions? Ruth Day?

DR. DAY: Ruth Day. I appreciated

your comments and I knew there were the other things in it, but even the planning for it and what are the questions and all that, I mean, if a simple approach is saying - I don't mean to keep pushing this one way that I recommend or I offered today, so it's not the be all and end all necessarily - but it's very simple, because then you don't have to have lots of other questions.

What is this used for? Open-ended. You type it in in the internet box if that's the way you want to do it. And then could it be used for this, this, or to what extent do you think it's for this indication? And it comes up. And I've used some of these software tools before, and they just enter the number from 1 to 5, and there's not much planning for that. You just have to figure out what are the names you're going to use.

And, you know, if you want to do other questions as well, fine. But if those were the core questions that everybody used,

it's already made. You know? You have to think of what are the foils, what are the health conditions you're going to use. I suppose everybody could have some standard health conditions and, you know, like take it from FDA advisory committees. You know, there's cardiorenal, there's oncology. You know, take some subset of ten things or so on. So anyway, I think that even the planning for the testing instrument itself can be greatly compacted in time and energy and cost.

DR. ORTELL: Thank you. Una Ortell. Actually, the more DDMAC can, you know, provide some such guidance in this next revision, I think it would be very helpful. And additionally, if we were to go with the suggestion that I had which was that DDMAC approve the design of the study before doing it, then we would just ask that DDMAC would have some very tight timelines to fit in with Ruth's one week suggestion.

MS. FRANK: Thank you for your

comments. I think we need to focus on well, there are some short-term concerns here, there is a long-term goal that we're going for, and that is the generation of this data, this information to ultimately have the sponsor be the ultimate producer of the study, of the information of the data to submit to us for review, which I think would help the whole process. And that's what we're trying to do so that in the short-term, you know, there may be some added cost but for the long-term benefit. And we're trying to address that in terms of the type of study.

Do we, you know, decrease the number of participants, you know, increasing the, of course, the number of questions we're going to have to ask. But it's a matter of, you need to talk to your statisticians about design, but we'd be happy to, you know, work with companies on this.

DR. ORTELL: Una Ortell. Just to get back to Stuart's question earlier, and it

may be premature to ask this question, but presuming we do this study and industry submits the data to DDMAC and then DDMAC does their own review and comes up with a different conclusion, do you have any, you know, comments on how you will address that in the review process?

DR. AIKIN: I'm sorry, I got distracted. Do we -

DR. ORTELL: I can repeat the question if you like.

DR. AIKIN: Yes, could you repeat the question for me, please?

DR. ORTELL: Sure. Una Ortell. So if we assume - let's just assume industry does this testing, and they come up with a certain conclusion, and let's assume it's a positive conclusion just for the discussion, and blind to that data, DDMAC does their own review and comes up with a negative conclusion on the answer to the question, what process will you have for determining which way to go in that

case? And I think that was kind of your question earlier, Stuart?

DR. AIKIN: This is Kit Aikin from FDA. Well, we haven't proposed a dispute resolution process in the concept paper. To the extent that we review the methodology and questionnaire and data and find that we come to a different conclusion because of perhaps some deficiency within that, we would, I would guess, communicate that to the company to see if that can be rectified.

To the extent that it's a difference in statistical analysis results, again, we would communicate with the company to see where the differences lie. Perhaps it's an error on our part. Perhaps it's an error on that part.

But are you suggesting that we should propose a process for points where we disagree with the conclusions of the data analysis?

DR. ORTELL: Actually, my question

was more towards - I mean assuming that if DDMAC did the analysis of the data and came to the same conclusion as the industry, my point was actually to your original process which is, you know, sending the name around to all the reviewers and having input from legal and the social scientists, et cetera.

So my question was if the current process gave you a different answer versus this new data-driven process, what would you do?

DR. AIKIN: That sounds like actually a very good question, but it's probably more suited to this afternoon's discussion or the logistics of the program so that we'd -

DR. ORTELL: Okay.

DR. AIKIN: - be happy for you to bring it up then.

DR. ORTELL: That's fine. Thank you.

MS. FRANK: Are there other

comments or suggestions?

MS. PAULS: Okay. If there are no other comments or suggestions - this is Lana Pauls from the FDA - I can't say I've ever facilitated a meeting before where we've been 45 minutes ahead of schedule. That being said, we're going to go ahead and start with the open public hearing, and if we have additional time, even though we will most likely end a little bit earlier and then convene a little bit earlier, what we will do after the registered public comment is we will go ahead and open it up to the audience for questions or comments for a short period of time.

So, in regard to the Panel 3, we have one registered participant. Her name is Nancy Globus. She is the Director of Med Errors. Nancy, if you could please join us at a mic?

DR. GLOBUS: Good morning, everyone. My name is Nancy Globus. I am the

director of operations at Med Errors, and you heard from my colleague, Susan Proulx, yesterday. And Med Errors does not have any particular expertise in these methodologies nor do we propose to.

However, we do feel that there are some places where safety and promotional aspects of a trademark may intersect and agree that there should be some form of looking at the name for those five areas that were put forth. For instance, there may be some aspects of the name that do not strictly fall under look-alike or sound-alike or any other name pair similarity but still may render a trademark to be misleading to patients or practitioners.

And an example of that may be, for instance, if you have a particular letter string that is often associated with a particular class of drugs but is not a USAN stem - for instance, if you have the letter string v-a-x, most people, most practitioners

and possibly patients may think that that is a vaccine. And where would that get flagged if not in the safety review? That is likely to get flagged in the promotional review.

Another example may be a letter string t-r-i, tri, also not a USAN stem for any particular pharmacologic class but could lead patients or practitioners to believe that the product contains three ingredients. So there are some aspects that are safety-related that are likely to get caught under a promotional review. And we just wanted to state that and they may get caught under a promotional review without the elaborate methodologies that we have been discussing this morning.

I do have a question overall - is that if the purpose of this entire pilot is to reduce the risk of medication errors, if it's a safety concern, then do the questions that are being asked in the more elaborate methodologies that were put forth, do they

answer questions that will relate to medication safety? And to us, that is the ultimate goal here, reduction of medication errors from whatever source, but we have to think long and hard about will all of this elaborate methodology lead to decreased medication errors or increased reduction of medication errors.

And my other question which I think may already have been discussed is DDMAC still will do, under the pilot, their normal review in parallel like was discussed yesterday with the safety review, like the regular safety review will occur and the proposed? So DDMAC will still do their regular review before the safety review starts?

MS. FRANK: We will do our regular review, that's correct.

DR. GLOBUS: Before the safety review starts?

MS. FRANK: The timing, I believe that would be the same.

DR. GLOBUS: Okay. Carol, did you want to answer that? Okay. Thank you. That's all I have and Med Errors looks forward to working with sponsors as well as the agency in this pilot program, and I'll take any questions if anyone has. Thanks.

MS. PAULS: Are there any clarifying questions for Nancy from the panel?

(No response.)

MS. PAULS: Okay. Thank you, Nancy.

DR. GLOBUS: Thank you very much.

MS. PAULS: Like I said, we're still significantly ahead of schedule, and we need to make sure that the hotel is prepared for a mass influx for lunch. So, what I'd like to do is take the opportunity to ask if there are any people on the panel that either want to speak up or anybody from the audience that would like to make a comment for any of the sessions. If you would, please come to one of the mics and we will address you at

that time. Please make sure you state your name and your affiliation.

DR. HARTMAN: Steve Hartman, Novartis. I have a practical sort of observation or comment. And in some way, it's directed to the panel and the FDA. In another sense, it's also directed to the vendors. If I understand Dr. Aikin's suggested proposal in its simplest form, let's suppose that I want to test 10 names and the proposal requires, for statistical reasons, 100 respondents. I'll just pick that just for mathematical simplicity. If I want to do now 10 names, I either have to use the same controls but 10 different panels, a total of 1,000 respondents, or I can use the same 100 respondents, but I have to use 10 different sets of controls, 10 different neutrals and 10 different extremes, if I understand you correctly.

But in either event, as a vendor, because it's not Novartis that is doing this,

it's a vendor that's doing this - in either event, the vendor's pool of respondents that it uses for testing has been re-depleted in some combination of controls they can use, because once one respondent has been exposed to one control, that respondent can never in any other study ever be exposed to that control again.

So once that respondent has been used for one or more controls, he or she can never be used again for those same controls. So there's a reduction, as a vendor, in my pool of respondents. And in the pilot, we want to have 25 to 50. So now I have now multiplied my 10, this experiment 50 times. As a vendor, I've now significantly reduced the respondents. What I have to do is I have to either continually find new respondents, one option. Or the alternative is that we have to continually have a growing pool, a constantly growing pool of neutral and extreme names.

And that's my comment. Just as a practical consideration, we're not going to have a pool that's going to stay the same and change. We're going to need to constantly replenish these things which you just need to consider. And it's not just for the pilot, but if we're ongoing with more than just pilot members, we're going to constantly need these new pools of names. And that's something you ought to just take into consideration. That's my comment. Thank you.

MS. PAULS: Dr. Aikin, do you want to give a first response to that, please?

DR. AIKIN: Yes. I think that we - and in my comments, I acknowledged that was one of the weaknesses of our design, that it does continually reduce the available subject pool if you use one single neutral and one single extreme name for all the studies. It does aid in looking at studies across the pilot, but again, you do reduce your potential pool of participants. I think that some of

the alternative approaches proposed here today address that concern. But I would like to hear from the panel about their reactions to this weakness of the design that we have proposed.

And just the practicalities of engaging in this sort of research, whether it just is out of the reach of the industry or whether it is a feasible approach to looking at proposed trade names from a promotional perspective.

MS. PAULS: Ruth?

DR. DAY: Ruth Day. I think there can be a bank of neutral names. There can be a bank of extreme-on-specific variables so there can be alternatives so that new ones don't have to be generated all the time. But in terms of the question about whether the participant pool gets depleted and so on is a valid one and needs to be taken into account.

MS. PAULS: Are there any additional people from the audience?

DR. BRASS: Yes. Hi. Eric Brass from UCLA. As I listened to the discussion this morning from the perspective of a physician and investigator, I heard various things that, simply, I had trouble lining up. I heard the existing process described within the agency as one that seemed very streamlined, very quick, and where there was a fair amount of confidence that decisions were being made in a reasonable fashion. On the other hand, I heard a reasonable, attractive suggestion that if we could go from a subjective, no matter how good, process to an objective scientific process, that would be a better informed decision-making.

But I did not hear a clear domain, and Mr. Lee's comment about what is it we're measuring if not simply neutrality. And Dr. Day suggested there were five dimensions which we might be able to quantify that were relevant. But I did not hear a scientific instrument that would measure, in a reliable

way, each of those five domains in a way that would allow an interpretation.

And I came away with, what we need is a panel of ten knowledgeable cynics who would look at the promotional names and make an informed judgment, and in the meantime, work to develop scientific tools which might objectify that. But again, just like I commented yesterday, substituting the appearance of science is not a solution to anything. We either have to have confidence that we're providing reliable metrics that are going to improve the system or we should not do it.

And I also was struck by, given the description of the existing system, we're going to add substantial man hours of review time to the agency to go through this additional data compared to the very facile. So that's why I was also struck by the rationality of a dispute resolution mechanism where if it could not be resolved, perhaps

additional data might help persuade one side or the other. Thank you.

MS. PAULS: Any response from the panelists or from FDA to Dr. Brass?

DR. AIKIN: This is Kit Aikin from FDA. Those are all very thoughtful comments and I do appreciate them. Thanks.

MS. PAULS: Okay. Over on - Dr. Day?

DR. DAY: I agree with Dr. Brass's concerns. I do think that the new methods tested can target each of the five dimensions and that maybe we don't need to have a whole lot of testing of the extreme names, because if you focus on what is it used for, open-ended, and then closed-ended, could it be used for this, this and this, and do that for each of the five, you're done. So you can target each one.

Otherwise, for the extreme - for the - if you do it with having other items, those have to be pretested and validated and

so on, and you have to make sure that they really work. This is a direct and that's sort of more of a contrasting method. So I do think that among all these suggestions are scientific ways to find out about these five dimensions.

But in the case proposed, you would have to have the extreme representations or the extreme cases that tested each one of the variables. So I agree with that, with Dr. Brass. So that would mean you'd have to have one for each five, but you can get around that by asking in the more direct way that I've mentioned.

MS. PAULS: Thank you. We have a question over here?

DR. ORTELL: Una Ortell. Just to address your comment or your question about whether we would feel it would be difficult to continually come up with naive respondents. I think that that may be addressed this afternoon from a logistical perspective. But

I do think it should be considered which is why the dispute resolution proposal might actually be a reasonable one. Thank you.

MS. PAULS: Okay. Now we have a question over here.

MR. BREEN: Thank you very much. This is John Breen from Interbrand Wood. I just wanted to offer two comments. The first is a simple one regarding the methodology for conducting there assessment with health professionals, a face to face environment in a room of people or online. I just wanted to make the comment for the record that the majority of the work we do today with health professionals is done online successfully and does offer a lot of convenience factors in terms of recruitment, things like that. So I know it's a very simple and basic point but just wanted to make sure it was addressed.

The second point is kind of in terms of the approach itself. And, you know, many times, you know, in creating names and

assessing names, it's some of the, we call them fanciful claims, inappropriate communications, are quite obvious in nature. A lot of the times you can tell whether or not a name has a very overt communication. So perhaps a good approach, and I think it's been raised by the panel, would be to have a sequential approach where there's a level of preliminary screening that eliminates obvious names. Perhaps that could be submitted to the division. Then if there is some conflict whether or not there is that problem, then we go into the more extensive testing which will allow us to kind of reduce some of the practical implications, because we can focus in on names that are more viable and, again, go through a more scientific process that way.

So those are my comments and if there are any questions, I would be happy to answer them.

MS. PAULS: Any questions or clarifications for Mr. Breen?

(No response.)

MS. PAULS: Okay. Last call for questions from the audience. Okay.

DR. SALEM: Mohammed Salem, Boston. My question is more on the general process which is going to be used. I think we've alluded today that some of the things which are done right now normally from the division, the information is passed over to DMEDS, and then DMEDS technically passes it over to DDMAC to review the information before it comes back for the safety review. Could you at least tell us what is the timing for those kind of processes which occur right now and then compare those with what will be happening in the future for the pilot programs?

MS. HOLQUIST: Typically, right now what happens is the review division consults our division for review of the proprietary name. So weekly we prepare an agenda and in that agenda has all the product characteristics of every name that's come in

for review for the week. Then we forward that by email to the DDMAC reviewers who are representatives on our expert panel.

And then within about a week, we get a written response from them stating whether or not they think the name is acceptable from a promotional perspective or not. And if it's not, they give us the rationale why not. Then we forward that rationale directly back to the review division who gives us an opinion whether or not they agree with them or not. And if they agree with them, we close out the consult and the sponsor is notified. If they have an alternative name in-house, we move to the review of the alternative name.

However, if they don't have it, we ask the sponsor can you submit alternative names so that they can be evaluated right away. We went to this model.

Previously, we used to go through the entire review process and then at the end

of the safety review notify people, and we might have been okay with the name from a safety perspective, but the promotional aspects of the name still killed the name. That wasted a lot of time in the review cycle.

So it was our opinion that if we found right up front that the name was not going to be viable, why review it and go through this extensive safety review if indeed it was going to be a problem. So that's why we went to that methodology.

Now under the pilot, that's part of logistics we'd like to discuss this afternoon is that we probably - I don't know - I think we would have to do the safety review of the data that comes in through the pilot in parallel to what's being reviewed for the promotional aspects.

We'll still - I don't want to talk about what we plan for the pilot, because that's going to be the next discussion panel. But we would do our - what we're planning to

do is - or what we're proposing are parallel reviews, that we conduct our review as we normally do and then a second, you know, very separate team looks at the data that's submitted just from the agency.

So that's what we're looking for feedback this afternoon, is how do we operationalize a lot of these things.

DR. SALEM: Can I ask one other - with the original question I had in terms of the current process. So the current process, some of us sponsors also submit our research to the agency. How is that research being reviewed currently?

MS. HOLQUIST: For promotional or for safety?

DR. SALEM: For both. I mean for promotional most of the times.

MS. HOLQUIST: If you submit something, we send that data to DDMAC along with, you know - and we review the safety data. Typically, we go through our process,

and then we look at the safety data after we've gone through our process, because we look to see has the company found other names that we didn't find, and then we'll evaluate them, or we'll compare the analysis and we'll state if we agree or not. And if we don't agree with the analysis, we'll tell you why we don't agree.

DR. SALEM: Thank you.

MS. PAULS: Any comments from the panel?

DR. McGIRR: Yes. Maureen McGirr. Just a clarifying question and then a comment. So the way the current process has been described, it sounds like on a weekly basis, as soon as you get a new name, it's reviewed by DDMAC, and then the assessment is turned around fairly quickly, and then that consult is sent back to the review division and the sponsor is notified.

And it sounds fairly quick, and in my experience, it seems a little bit like a

lengthier process and that then seems to take a few months. And I can appreciate why it would between, you know, the resources constraints on DDMAC and then getting back to your division and writing a response, if necessary, back to the sponsor if there's a rejection.

And then I guess I'd like to understand when there is a rejection, is it a longer period of time? Does it have to go through some sort of additional reviews? You know, obviously, it has to be written up and then reviewed. Does it go through some review at the chief counsel's office that takes some time?

And then the reason I'm raising that is because if you add to this process a parallel process with the new pilot where you'd have to take up limited DDMAC resources with reviewing the data, I think it's a great idea to have data supporting it. I just get concerned that with the limited resources,

that you're going to get bogged down in reviewing the additional data.

And so where that makes me inclined to go is to what Una had suggested as an proposed alternative, which is not always to be, you know, burdening the agency with the data, but in circumstances where it's necessary maybe to have the data to support the package where there might be some disagreement.

MS. FRANK: I'd just like to say for the record, we are essentially a consulting group, so that we turn around our consults in about a week's time and then send them on so that the ultimate - you know, say if there's a time lag, we're just - we don't make the final call. The final call is currently from the review division whether to object to a name or not. And, of course, we always accept data. Now we do. And if you want to submit data, for example, for rebuttal, we're happy to review it.

MS. HOLQUIST: And just to get to some of your concerns about timeliness, that's a concern of ours, too. Currently, we're subject to evaluation of the name when the project manager in the review division decides to consult us. Sometimes that's immediately upon receipt of the name. Sometimes it's months later. So you may be under the impression that as soon as you submit your name, it's undergoing evaluation, and that's not always necessarily the case.

And under the paradigm that Dr. Dal Pan discussed yesterday under "safety first", we're hoping that these trade name submissions will come right into the door and be a direct assign and direct to our division, and that will cut down a lot of this lag time and that we will actually be able to - our office will be able to directly speak to the sponsors rather than having to work through a third party. And I think that'll cut down a lot on that lag time.

MS. PAULS: Question from the audience, please?

MS. BROWN: Sherry Brown from Bayer. And actually, Carol, you just responded to what I wanted to ask, because being a consult, the sponsor doesn't really have the opportunity to talk to DMETS directly or DDMAC directly. And I think if you could build that into the process or even, you know, have it taken care of it at the pre-IND meeting or pre-NDA meeting, that way - to have a direct dialogue would be very helpful.

MS. HOLQUIST: Yes. I think that's part of the proposal and that's part of building in the transparency of why we're making our decisions and whatnot, because we want to have that open dialogue, because I think no one can learn from it unless your hear why we're objecting.

MS. PAULS: Kathy?

DR. GANS-BRANGS: Yes. Kathy Gans-Brangs, AstraZeneca. So my quick question

then is there a plan for a manual of policies and procedures to help speed the process of the names going for review?

MS. HOLQUIST: Yes. Actually, that's even one of the requirements under the PDUFA IV goals is to create a map that will outline these new processes.

MS. PAULS: Any other questions, comments from the panel? Okay. I want to thank you all for humoring me and your flexibility in regard to stretching out the agenda. We are going to be a little bit flexible, and instead of coming back at 1:15, I'd like everybody to reconvene at 1 p.m., please, so we can pick up with Panel 4. Thank you.

(Whereupon, the above-entitled matter went off the record at 11:30 p.m. and resumed at 1:03 p.m.)

MS. HOLQUIST: Good afternoon and welcome back. My name is Carol Holquist, and I am the Director for the Division of

Medication Error Prevention in the Office of Surveillance and Epidemiology in CDER.

Over the last two days, we've heard a lot of discussion about what the best test practices for the evaluation of proprietary names might be. Now I'd like to shift gears here and talk a bit about how we might operationalize the pilot program in which much of the data that will be generated from the best test practices will be received and evaluated by the agency.

So first I'll focus on the proposed pilot logistics, talk briefly about some planned perspectives of how we might evaluate the name, then discuss how a regulatory decision might be made and then talk briefly about how the overall pilot might be evaluated.

As with any new process, the devil's always in the details, and I think we heard a little bit those little devils earlier today and yesterday. And actually, that's

exactly the type of discussion we need to have this afternoon. We really need to get to how can we really, truly operationalize this pilot.

So first, let's talk a little bit about the pilot logistics. This pilot is proposed to run for approximately two years with the expectation that submissions will begin to be received by the agency by the end of fiscal year `09. We need to be convinced that all pharmaceutical sponsors can adequately test their name before submission to the agency, so we're really going to need a representative sample of both large and small companies and evaluating all types of applications.

Because the submissions in this pilot program represent an increased workload for both DDMAC and for our Division, we're going to need to have some sort of voluntary enrollment -- I mean it is voluntary enrollment, but we're going to need to have

some sort of advanced registration, because we're not going to be able to receive all applications within a single month.

So with the review timelines and our resource constraints, we really can't take more than one to two submissions per month or a total of 25 to 50 over this two-year period. So we're really going to need to talk a lot today about how we might operationalize such a registration.

We anticipate applicants will have a number of questions before their submission, so we're asking that these be submitted in writing approximately 120 days prior to the date of submission. We'll answer these in writing and in certain circumstances be able to grant a face-to-face meeting. We recognize that alternative methods may be used, and if so, just as a courtesy, we'd like to be informed of these new methods. But given the review timelines and, again, the resource constraints, we likely won't be able to

provide any prior approval of these methods and that the evaluation of these methods would have to occur during the review cycle.

So what are we looking for companies to submit? We actually refer to this as a comprehensive submission in the concept paper. And basically, what this is is two sets of data. One which is the data that's traditionally required to do our normal review that we -- our current review that we have at CDER now which is basically we need to know the product information which is generally contained in the labels and labeling.

Then the other submission is the comprehensive data that the applicant will have conducted and which will include all their methodologies, their analysis of it, their data sources, and most importantly, the raw data.

As is with our current processes, we really want companies to think about a

primary and an alternate name, and just as we do now, we won't move to the review of the alternate name unless we find the primary name unacceptable.

So once we receive this comprehensive submission, the review clock will begin. If for some reason we determine that the data that's submitted is incomplete, we'll notify the sponsor and the review clock will be stopped, and a new clock will be restarted once we receive everything that we need in order to complete this review. The review timelines are exactly the same as what's laid our in the PDUFA goals for proprietary names, which is 180 days for INDs, 90 days for NDAs and BLAs. Although ANDAs aren't subject to any PDUFA goal dates, we try and evaluate them in a similar timeframe as the INDs, which is 180 days.

So once we receive this comprehensive submission, what we've proposed for the evaluation is what we refer to in the

concept is this parallel review. And basically, what we'll do is we'll take those two pieces of information that I just referred to before and have two separate teams evaluate these data. So once the comprehensive submission comes in, one team will evaluate the name just as we described yesterday. Commander Duffy described our current review processes. So this evaluation will occur just as it normally does, and this reviewer will come to their own conclusion.

And the other arm will be the data generated from the applicant. This will be reviewed. The safety evaluator will come to their conclusion as to whether or not the data supplied adequate information in order to render a decision on the overall acceptability of the name.

Once these reviews are completed, the reviews will be compared and we'll really be noting the differences in the data, our analysis and our findings. And the

acceptability of the name will really be based on the comprehensive data and not just on one arm versus the other.

The criteria for objecting to the name will be exactly what we use now which includes but is not limited to if the name includes a USAN stem, especially if it's one that's not appropriate for that product, if the name is somehow is misleading because of its ambiguity or maybe DDMAC objects to it, or it may be misleading for reasons under the regulation. Or perhaps the failure mode and effects analysis indicates that the failure will likely result in a medication error under the usual clinical practice settings. And through this pilot, we may find other unforseen reasons that we might find an objection.

So what will happen once a decision is rendered? This is exactly what we do now and we propose to follow the same process. So once a decision is rendered, the applicant's

going to be notified and the review clock stops. So if you're name's found acceptable, you'll be notified of that.

And if your name was originally evaluated in the IND, it'll be re-reviewed in the NDA stage, just as we do now, and that's basically to determine -- to make sure that none of the product characteristics have changed or any of the marketing information has changed in the product development.

Then we always evaluate a name 90 days prior to approval to ensure that nothing's come in in the interim that might be approved proved to that application. And because we can't reserve names or we haven't had the ability to reserve names, a name is never really approved until the application is approved.

If we find the name unacceptable, again, the sponsor will be notified in writing. However, we'll include our rationale as to why we're saying no. Then once you

receive that letter, we won't automatically move to review of the alternate name. We really want confirmation in writing from the sponsors that they really still think that name is viable for review, or you might decide at that time you want an alternate name. And once that data is submitted, a new review clock will begin. It's important to note that these review clocks are based on one name.

So at the end of Fiscal Year 11 or upon two years of accumulated data, we're going to try and assess what the adequacy and the limitations of the data that were submitted over this two-year period are. And it's going to be more of a qualitative comparison, and we're going to have to focus on what are differences between the FDA's review, the applicant's data. What did we find in each one of these steps. What did the sponsor find in each one of these steps. How did we come to these conclusions in our analysis and talk about a lot of this.

And I think this is a big discussion point for us today -- how can we best do this, and, you know, should this even be done by FDA. Should it be done by a contractor. These are all the things we want to hear from you all today.

And then once we have assessed all this, we would like to discuss the overall findings in another public meeting in approximately Fiscal Year 13. And, you know, from this meeting, we really hope to determine if the pilot review process better serves the public health needs to evaluate proprietary names.

So that's a very brief overview and I want to leave a lot of time for discussion, because I know this is going to be hopefully a very fruitful discussion this afternoon. Thanks. Does anybody have any clarifying questions?

MS. TOYER: Before we start on the clarifying questions, I think the panel

members have changed, so if we could start with Dr. Day, could you provide your name and affiliation, please?

DR. DAY: Ruth Day, Duke University.

MR. EMMETT: Andrew Emmet, BIO.

DR. LEE: Bob Lee, Lilly.

MS. IBARRA-PRATT: Elle Pratt, FDA.

MS. PAULS: Lana Pauls, FDA.

MS. TOYER: Denise Toyer, FDA.

DR. TAYLOR: Kellie Taylor, FDA.

DR. DAL PAN: Gerald Dal Pan, FDA.

MS. FRANK: Lesley Frank, FDA.

DR. KORN: David Korn, PhRMA.

DR. GANS-BRANGS: Kathy Gans-Brangs, AstraZeneca.

DR. NOURJAH: Parivash Nourjah, AHRQ.

DR. ZUCKERMAN: Ilene Zuckerman, University of Maryland.

DR. HARTMAN: Steven Hartman, Novartis.

MS. TOYER: And as Carol started to say, we'd like this particular portion of the discussion to really focus on clarifying questions from her presentation.

DR. NOURJAH: Could you go over when and what is submitted.

MS. TOYER: And jut a reminder, please state your name before starting. Thank you.

DR. NOURJAH: Parivash Nourjah.

MS. HOLQUIST: Carol Holquist. Basically, what we've asked for in the concept paper are two things. One is the data that we traditionally ask for for when do an analysis which is when a name is reviewed in an NDA, we typically ask for the labels and labeling, because that gives us all the information we need. It gives us the dosage form. It gives us all the product characteristics information, indications for use. We know the packaging configurations and all that, because we do the whole assessment of both the name

and the labels and labeling.

The other piece of the puzzle is all the testing that's been outlined in the concept paper for both the safety review and the promotional review. So we want to see the methods that were used, clear description of them. We want the data that is generated from those studies. We want the applicant's assessment of that data, but we really want the raw data so that we can make our own analysis of it as well.

DR. NOURJAH: But they have to send it to you at the time that you start your review?

MS. HOLQUIST: That's what we propose just so we would have one submission to keep track of.

DR. NOURJAH: So they finish their review of evaluation, they are given the report to you, then you start your review?

MS. HOLQUIST: Correct.

DR. NOURJAH: Okay.

DR. HARTMAN: If the sponsor's FMEA and conclusion is that the name si acceptable but the DMEP internal review concludes that the name is not acceptable, what standard would you use to decide the acceptability of the name?

MS. HOLQUIST: I think FMEA is not the only thing that we would make our overall determination on. As we said, it's that whole overall process. What we would also look at is we compare what was the makeup of your panel, were there failure modes that we detected that you didn't detect. It's that comparative review that we would have to assess and see were the differences enough for us to say well, we didn't thing it was adequately done or whatnot. And I think it will be the same for any of those test practices.

DR. HARTMAN: Well, why couldn't -- I'm sorry, that -- tell me if this is the right time for this question. Why can't the

identity of the failure modes, for example, be decided on, agreed upon early in the process so that there isn't any dispute as to what the protocol use is? And then if the protocol meets the FDA standards, and if it appears that the expert panel decision is rationale, seems to make sense, why not just accept the sponsor's submission?

MS. PAULS: Actually, that does sound like a, not an alternate proposal but some of the logistics. So can we get the rest of the clarifying? If you'll hold that point and we'll bring it back. Can we get the rest of the clarifying questions. Mr. Korn?

DR. KORN: David Korn with PhRMA. You put a slide that had a parallel review which was the traditional review and the pilot program arm. If the submission is to both the promotional review and the safety review at the same time, will there be parallel review within FDA which would be a different situation than the way it operates now as I

understood it from the earlier presentation with the flow of a proposed name?

MS. HOLQUIST: Well, we would give DDMAC the information at the same time we would receive it. So they would know all the product characteristics, but their plan is to evaluate, and Lesley, you can answer this, but is to do it in the traditional way as well as evaluating the other data.

MS. FRANK: That's correct.

DR. GANS-BRANGS: Kathy Gans-Brangs, AstraZeneca. A little bit earlier, the last comment, I asked if the last panel was about issuing of a map. I was wondering if that would be expected about the time the pilot program starts. And I'm asking the question -- my concern is would there be any holdup if a name goes in, it's submitted, between the center receiving it and it getting to the Division?

MS. HELBLING: The map isn't really going to cover the pilot process. It's just

going to cover what happens once a name is received, so if all goes well, that plan is supposed to be in place by October of this year. So we should be getting direct submissions at that time. Does that answer your question?

DR. GANS-BRANGS: So the concept paper speaks to the centers? It doesn't mention DMEP. So the dual goes to the appropriate center and then --

MS. HOLQUIST: Correct.

DR. GANS-BRANGS: -- we'll assume it gets to you quickly?

MS. HOLQUIST: You would submit it, your application, just as you would normally.

DR. DAL PAN: This is Gerald Dal Pan from FDA. Let me just let you know some of the complexities of a big place like FDA. So you submit your trade name as part of your NDA application, let's say, for example. And that comes in as an NDA application. There's nothing in that submission that particularly

notes that there's a trade name per se, and that limits the way that submission moves around either in a paper environment or an electronic environment.

In the IND world, we have special codes, that I'm sure many of you are familiar with, for new protocols, protocol revisions, toxicology studies. We're working now to try to get special codes for these trade name submissions so they can move around more easily and not be as dependent on project managers in a review division to forward them to us.

So those are the kinds of things -- those are very much infrastructure business process-type things, but those are the kinds of things we're working on. They don't happen overnight though. And of course, we'd have to let industry know how to send a submission so that it could be properly coded and routed when it comes in. But those are the kinds of things we're working on to make the very

mechanical elements of the process more efficient.

DR. GANS-BRANGS: Thank you. That's very helpful.

MS. TOYER: Any other clarifying questions? Dr. Day?

DR. DAY: Ruth Day. A lot of people over the last day and a half have asked what happens when there's disagreement between FDA and sponsor for a given name. I'd like to ask the opposite question. What if, after the end of the pilot study for two years there's lots of agreement, lots of agreement in the safety and in the promotional aspects? And there'll be exceptions of course Does that mean that in the future, FDA will decrease the work that it does and the sponsors will increase relative to now but perhaps put a cap on it given your experience and finding out what parts work really well and what parts aren't needed?

DR. DAL PAN: I mean if we can

develop processes that industry can use or industry develops processes that we can evaluate with confidence, I don't see any reason for both groups to do all this work. I think that's the whole point of the pilot is is this something that's feasible to do. I don't think FDA and PhRMA - Mr. Korn can correct me if I'm wrong -- would have put this in the goals letter if that weren't an ultimate goal of the program. So, you know, we don't do clinical pharmacology studies. We don't do chemistry stability testing. We don't do clinical trials. So what we're really testing here is is this something that industry can do, and at the end, we will see if this is something we can transfer over to industry. And then we would be a reviewer who would much more in the traditional FDA reviewer function. Carol, do you want to add to that?

MS. HOLQUIST: No. I think that's appropriate. I think what we're looking for

is to get companies to think through a lot of these things. I hear a lot from, especially PhRMA, that well, we do adequate testing. Well, you're one portion of the pharmaceutical industry. We don't see it across the board from all manufacturers, so we really have to be assured that everyone can adequately test a name before we could even think about shifting the burden.

And maybe that's what we learn from the pilot is that maybe only certain people can do this adequately and, you know, maybe it's not even feasible. I don't know what we'll -- you know, I can't even fathom what we're going to uncover during this whole pilot.

DR. DAY: If I could just -- pardon me. I just wanted to bring that forward, because I assumed that was the case but have that on the table, because there's worries about the other outcome. It might be that in the future if this works really well, but

there are some companies new to the whole process and haven't brought anything forward yet might prefer to have two options, either the traditional FDA review for name versus whatever methods fall out of the pilot project so that it could be sponsor-based or FDA-based. So do you envision that they're -- you know, you can't say now because it hasn't been done, but might that be something that could come out of this as well?

DR. DAL PAN: Well, I mean I think we'd probably have some sort of transition. I mean there's lots of new pharmaceutical companies or drug development companies, and they have to learn how to do pharmacology, toxicology. We don't do that for them, so there would probably some transition here.

MS. TOYER: I'd like to loop back around. I think Dr. Dal Pan indicated that PhRMA had put the pilot program on the table. Actually -- and I think Dr. Zuckerman asked what the actual objective is of the pilot, so

I'd like to here that from the PhRMA and the industry representatives to actually see what they feel the objective or the goal of this program is.

DR. LEE: It goes back to the question that was asked about reducing the work, making sure we don't repeat the same work, get some efficiency that way. But it's even a little more than reducing work.

I think certainly one of the goals of the pilot program is to reduce as much as we could subjectivity and try to have not just transparency but a greater -- lower the rejection rate by getting greater predictability to the extent that it was feasible, notwithstanding that there will always be information that the agency has that's up to date that may not be available to us.

But notwithstanding that, could we agree on methodologies that, if practiced, would result in confidence by both sides that

the trademark had been properly vetted and was as safe as one can make it with the known information available at the time?

And that was really, at least from the industry perspective the goal of this, and that's why there's so many questions around the parallel system and what happens if at the end of the day, you have a difference between an internal review by DMEP and then an external review and then you have a difference in the judgments of the two and why Steve, I think, was saying if it's going to come down to procedures within the FMEA process, can't we agree on those, can't we agree on what those processes ought to be.

The more we can get objectivity and reduce it down and agreement on processes, we would hope to increase predictability. That was our view of what the goal was.

MS. HOLQUIST: I think that was the goal of putting out the processes in the concept paper is that we could all agree to

what would be good test methods. However, I think like with anything that we review, just as has been the longstanding practice of the agency, we can put out best methods for conducting a clinical trial, but there will always be interpretations in that data, and there will always be differences of interpretations. So I don't think we can sit here today and say that if we put this methodology out there, you run your name all the way through it and you come out with an acceptable outcome that we could just agree with it without having our own evaluation of that data.

DR. HARTMAN: Well, what happens, though, if you're looking at the same data but you simply look at the data and say, we think this name is not acceptable because of name x out there, but our FMEA experts have concluded that that risk is minimal and otherwise the name -- and the name should be, in context, really ought to be accepted? It's simply a

question then of your judgment, you decide that your judgment is going to trump the sponsor's results? Is that what you're saying?

MS. TOYER: Before we answer that question, we're kind of transitioning into logistics. I just want to make sure noone else has clarifying questions on the presentation. It's fine to go that direction if no one else has clarifying questions.

DR. HARTMAN: The concern I have is that we have a standard --

MS. TOYER: Right.

DR. HARTMAN: It appears as if you have a standard.

MS. TOYER: I'm not cutting you off. I just want to make sure that there are no clarifying questions, because we are transitioning to logistics.

DR. GANS-BRANGS: Kathy Gans-Brangs. I do have one clarifying question. It's around the slide which shows the decision

rendered at the top and then the boxes on it. My question is is there an appeal process? That's not shown on the slide nor is it discussed, to my recollection, in the paper.

MS. HOLQUIST: Right. I think the same process is for appeal that are present now exactly will be here during the pilot as well. But it's also the objective of the pilot that we would hope to be able to have a bit more conversations with industry while we're doing these that when we have differences of opinion and differences of the data that we would be able to say this is why we have these differences of opinion, and then at the end of the day, if we still can't agree, then we'll have to take it to a higher level. But I would hope that there would be some lessons learned through this. And, you know, I guess my question to you is define what minimal risk is.

DR. HARTMAN: Well, I suppose one way I could slough off the question, I could

avoid answering it is to say that if I knew what the background rate was for medication errors, then if my test name had an error rate that was the same or less than the background rate, then the name ought to be accepted, because then the name doesn't increase the level of confusion. But we don't have that information, so that can't -- but I think that's a reasonable response.

I don't think the answer is zero. I think that there were other panelists -- I can't speak for them -- I don't want to -- can't quote them -- but I think there are other panelists who made it clear that if a mistake could happen, it would happen given enough opportunity and that there are different kinds of errors that can occur, some which are significant in the overall evaluation of a name safety and others which perhaps are not that significant.

But given that your -- it appears as if the FDA is taking the standard that any

potential for error is enough to kill a name and that the risk of harm from an error is not a significant factor and that every error is preventable by the choice of a correct name.

That puts, I think, the industry in a very difficult position when it makes a submission, because with those standards, it's very easy for the FDA to simply look at their own process and say, well, there's a name out here which we think, you know, could be a problem, and given our standards, we don't really care what the risk of harm is. That's a minor factor. It's an error and we really can't tolerate any error, because all errors are preventable. We don't accept the sponsor's submission.

And that, to me, presents a real problem, because we don't get the predictability that we want, and frankly, it's -- you don't even put -- with that kind of a process, you're not even putting trust in your own protocol.

DR. DAL PAN: You know, I don't think there's ever going to be a medicine, a name or any other characteristic of medicine that's going to be free from error all the time. I just can't -- it's like a drug that has no adverse event. It's not going to happen. But I really believe that this is an area where so much more research is needed that to expect us to say, you know, this is the cutoff, I think, is unreasonable. I just wouldn't know where to put it.

One of the things I would hope that comes out of this program is more dialogue between industry and FDA on the name on how the process works, how the different elements of the process work, and maybe how we can get some more data as to how these medicines and these names work out in the real world, because what we really want here is some process that will give us some reasonable predictability that bad things won't happen when this name is used.

And we use a process now that's multi-modal, that's somewhat subjective, that doesn't have a lot of background rates applied to it because those rates don't exist. So I think there's, you know, a long way to go before we can start putting absolute cutoffs. And we're still going to be using judgment here.

DR. HARTMAN: The only way, though, you know that you have a name assessment system that is producing names that are safe is after the names are out there and seeing what happens. Before that, pre-market, there isn't any way of creating -- there isn't any testing system that will assure us that the name is safe.

We have some understanding of what the drivers are. We understand that the use embedding certain kinds of information in a name, stems, dosage amounts, other things of that sort are really name error drivers, but beyond those kinds of drivers, our ability to

assess whether a name is safe or not has serious deficiencies.

What I think -- what I would suggest you ought to be doing is rather than testing the sponsor's submission against the DMEP process, which you're using as a gold standard, I think it makes more sense to look at the sponsor's submission and ask is this -- did it comply fully with the concept paper and does the result sound right in our expert judgment, as a group. In our expert judgment, does this result make sense? Did the cross all the i's and t's? Did they get all the modes right, and did they evaluate them correctly? And if your tacit knowledge and experience tells you that, yes, this looks right, you let the name go through. That's what I think makes sense.

DR. DAL PAN: Okay, first of all, there is no standard and the DMEP analysis isn't a gold standard either. We have to compare what the company does to something, so

we're comparing it to what we do. That just seems to make sense. But it's not that one or the other is a gold standard. And one of the things we'd like to do is see where these differences occur.

DR. HARTMAN: Why do you say you have to compare it to something?

DR. DAL PAN: Because it's a totally new process for us. We want to see -- you know, our staff is familiar with the standard process, and this seems, to me at least, to be just a very logical way to do this. If we had done this, what would we have come up with? And then what -- the value I think that is there, though, is to see how a company applies FMEA and gets a certain result and how we apply it, how a company searches for look-alike, sound-alike names and how we apply it.

We could potentially actually learn quite a lot from this ourselves. That's why we want to compare it. It'll give our staff a

way to look at something that they haven't seen before. Because these methods, you know, aren't perfect, that's why we're doing it this way.

DR. HARTMAN: You have a DMEP process which you don't know how well it works, and you're using that as the standard against which to measure a process that you want to be better.

DR. DAL PAN: Okay, let me repeat myself.

DR. HARTMAN: That doesn't make sense.

DR. DAL PAN: I just said it wasn't a standard. We're comparing a and b. We're not going to say the company fails if it doesn't meet ours. The company's may be better than ours, and we may be learning from that. So it is not a standard. Okay? We'll compare one to the other, but it's not a standard against which the company can only fail.

DR. HARTMAN: Give me an example --

MS. HOLQUIST: And also, we have evaluated names.

DR. HARTMAN: -- give me an example of where --

MS. HOLQUIST: Let me just -- can I just interrupt for a second? We have evaluated -- we have some knowledge that our system does work, because we have, in fact, identified a number of names that when they have gone out to industry, because we've been overruled by either the Division or gone up the chain, that they have ended up in error. So we have some sense that this process does work to some extent. And I think that's what we'll learn through the pilot is what pieces of this process, you know, best assess these names. Are certain pieces of it you always get noise from it, or does it provide good qualitative data? And I think that's another lesson we'll learn from it.

DR. HARTMAN: Okay. Last question

in this round. Give me an example of how if the sponsor submission said that the test name is -- this trade name x out in the market is not likely to cause confusion or a problem with the test name but so they consider that as a failure mode, they consider it, they analyze it, the FMEA panelists conclude that despite the name x out in the market, the test name is safe, you conduct the process, you look at x and you say, in our judgment, x is a problem. Under those circumstances, explain to me why you would reject your own DMEP conclusion and say that the sponsor's right, x is not a problem?

MS. TOYER: I think you're asking them -- you're asking the agency to predict something that they really haven't had the -- they don't have the answer to right now. And I think it doesn't -- it really parallels very similarly to an NDA review. When you submit your data, you're assumption is that the data that you submit supports the conclusion that

you have come to. The agency then evaluates that data and they may come up with a different conclusion. They issue that letter whether it's approvable or not approvable, what the case may be.

But in the interim, there's a lot of discussion about that data to come to some general consensus between industry and the agency about what was submitted and our analysis of that data. I don't think -- I think what the agency is trying to say is that that's going to correspond in this process also.

And not to really cut you off, but we have a lot more logistic questions. And since you had indicated that was the final component of that one, I'd like to really move along to some of the questions about the logistics when it comes to the particular companies.

And those are questions such as what companies will participate, how will we

select the companies, should companies have to submit names in all phases. For example, if you select one large pharma company, will that company have to submit an NDA and an IND. I'd like to throw some of those types of questions out to the panel and see if we can get some feedback.

MS. PAULS: Can I also please remind panelists to introduce themselves when they speak.

DR. KORN: I suppose I have a question in response to the question so bear with me. And that is do you envision an application process where you would actually make decisions about whether a company would be eligible? You had a question -- a point up about representative small and large companies. Do you envision an interactive or actually a gate keeping function on it?

MS. TOYER: I think we, depending -- because of the restraints with regards to resources, I think the agency is thinking that

there has to be some type of gate keeping responsibility. And with that in mind, we'd like to know how should we make those decisions about which companies should participate, because it appears from some of the earlier discussions that we do need a diverse population in order to be able to evaluate at the end, whatever that evaluation is, where we're going to go with this particular pilot. So how do we make those choices? How many generic vendors do we choose? How many reviews do we choose from large pharma companies, from small companies?

MR. EMMETT: Andrew Emmett with BIO. And again, I was very pleased that you took note of both making a representative sample of both large and small companies, and maybe one way of getting at that issue and figuring out what those targets are is to take a retrospective look back at the diversity of samples that you've received in the passed year or two years, three years and trying to

match those figures.

MS. TOYER: Bob?

DR. LEE: Bob Lee. I can't predict what my company will do, but in general, we are interested in filing our applications, our name applications earlier rather than later. So I would foresee participation being at the IND stage or somewhere between the end of phase two and the submission of an NDA. I would foresee a number of companies, a number of larger companies would be interested in a pilot program. We're still in the midst of deciding what that pilot program would look like. But such a program, I would envision that larger companies would be interested both between some filings between the IND and the NDA and some who would file at the NDA stage.

Filing at the NDA stage, you get some certainty, a little more certainty than maybe at the IND stage. But usually, we want to know earlier rather than later, at least a preliminary view of what the agency's looking

at.

DR. DAL PAN: This is Gerald Dal Pan. Can I ask you a question about that? If we are going to be able to accept say, you know, one or two submissions per month, does having it at the IND stage, which is much longer than the NDA review stage, give you a little more flexibility then about when you can send it in to accommodate to our timeline?

DR. LEE: If I understand it right, I think -- yes, I think that's right. You'd have -- between the time at the end of phase two and the NDA submission, there's quite a bit of time. And you have an opportunity to predict a little better, or you have some flexibility in when you can hit the 120-day application time and then follow-up with the name after that as opposed to trying to pin down the NDA submission date very closely. So I think it does give us a little more flexibility.

MS. TOYER: Just a follow-up to

that, not that I'm -- I'm playing devil's advocate as the moderator -- so is -- or what do you think about if the pilot only included, say preliminarily, IND applications, just devil's advocate?

DR. LEE: Well, I can only speak from my own viewpoint, my own opinion. I don't think that that would -- it does lengthen it to 180 days, getting an answer. But I don't think it should significantly impact the number of people who would otherwise apply.

DR. HARTMAN: I agree with Bob.

DR. DAY: Ruth Day. Not being in a company, never having been in a company, I'm sitting here thinking what is the advantage to a company of participating in the pilot program. What incentives are there? One I can think of is they can be part of the process of testing it and developing new ways that then might become a gold standard, something that's -- or a recommended approach.

Okay? So that's one thing -- being able to affect the future of where this goes.

Another thing might be some earlier feedback or something of the sort, but there's a certain amount of risks. I mean I don't think it's a bad thing if theirs is rejected, but there's going to be a spotlight on this program. And if it says Company X's name review was rejected under the pilot program, there's going to be more knowledge of that than if they just went through the usual.

So I'm not recommending that gift certificates be awarded, but can't the company representatives or the trade organizations give us more of an idea of why would a company want to participate other than being a good citizen?

DR. HARTMAN: Well, certainly predictability would be one, would be the primary reason I would think. Obviously, we have an interest, like everybody else, in having safe names out there. But it's not a

science. Maybe it's a social science, okay, but it's not a science. And we're a long way from being able to understand, to be able to predict whether a name is safe or not and whether or not this process will produce a name that's safer than what DMEP does or what the industry does on its own, frankly.

MS. STELLY: Bob?

DR. LEE: I think another way to say predictability is would be if this would lead to lower rejection rates. And that's -- and one of the things that we grapple with is that if there were objective standards, they would be easy to follow. It wouldn't matter if the agency repeated the tests, because we'd get the same result and we would know. The real issue comes down to where it gets down to subjective lines of inquiry.

And I think suffice it to say that under the section on limitations, I think one of the limitations will be if there -- one of the limitations we think or I think the

program has is this what is the proper standard on the error rate. And the idea -- let me just I think you get, when you start with the definition of a medication error being a preventable event and using that definition to then dictate what the error rate's going to be, namely, we're going to strive for zero, that's where -- that's the source of the issues.

Because even if we knew you were going to repeat the information if there was a different standard, a different tolerance -- and that sounds like it's suggesting that we're saying that patient safety is at risk. We're really talking about perhaps a fundamental difference about just how much sense it makes to try to say we can avoid all errors when you're using a process that isn't reliable. By reliable, I mean it isn't validated in any kind of objective sense.

And that's the crux of the matter, I think, is if you start with that kind of a

medication error rate, zero, and the idea that the standard is possibility rather than probability or something in between -- once you say possibility, it becomes very difficult to say that there's no possibility that a particular name can't be envisioned in some way to result in an error. And that's really, I think, where the fundamental problem will be in terms of trying to get consistency out of the pilot program.

MS. HOLQUIST: This is Carol Holquist. I'd like to just talk a minute about this zero error rate. I think where the discussion is is that for a number of years, ever since we've been looking at names, we have tried to find error rates, and it's been impossible to do without having some sort of direct observational methods in a number of different institutions. So therefore, we've never really tried to put any, you know, emphasis around that there would be any acceptable error rate.

And so the best thing that we could do is to say that we would have to try and prevent these things. And to try and prevent them is that when we go through using all these different test methods, and we show -- the tests methods end up showing that there is some plausibility that the name might be confused, and we're testing it in a very small room right now withe 120 volunteers.

I mean not even the name studies but even just doing our failure mode and effects, we realize that there is likely going to be error -- and then we might get a submission in from a sponsor that has a name study that's been conducted by an external firm who's maybe been able to do other test methods that we couldn't employ at the agency, and they're showing that there's some chances of confusion, we can't just say as a public health agency, well, that's okay.

We actually do look at what are the types of errors we see, and if wrong drug is

one of them and it's consistently what's being tested and the name that we think it's going to be confused with, and then the test methods that come out from other sources show that that name is also a problem, it's likely going to be a problem. And I think that's where we're coming from is that we, as a health agency, how can we say that, you know, your -- I'd like to hear, I guess, what your definition of risk is, because to us, you don't have to kill somebody for it to be a risk. You don't have to cause permanent disability for it to be a risk. There's a number of factors that you have to consider, you know --

DR. HARTMAN: Look, I don't --

MS. HOLQUIST: -- other than death and permanent disability.

DR. HARTMAN: I -- there isn't -- I don't have a mathematical -- there isn't a mathematical answer to what the level of risk is, in part, because you're talking about an

ethical judgment. You're talking about letting a drug out there. Every drug has some risk attached to it.

And you're talking about letting a drug out there that large people are going to have or people are going to be taking. So there's going to be some mistakes. There's going to be some harm. So it's an ethical decision. So it's not a mathematical decision as to what the level of risk is. That's the reason why this calls for the judgment of experts in the field and I recognize that and I'm willing to accept that. But the consequences of that, as a practical matter, are that once you set the concept paper and you decide that these group of experts are okay and they make the judgment, you accept their judgment.

MS. HOLQUIST: Well, I mean I guess, again, how can we say that we can accept their judgment without evaluating the data? I think it's just like any other

testing that's done by industry. And I think, I guess, I'd also like to know -- you keep going back to this risk-benefit thing, and I guess I just really need to hear what is really the benefit of the name?

DR. HARTMAN: Okay. You're not --

MS. HOLQUIST: A name is something that can be changed. I understand it takes a long time to get a name and go through all these processes, but length -- I guess I want to hear your opinion on that.

DR. HARTMAN: First, you're not -- what I understand is you're not evaluating the data. What you're doing is you're creating your own data. You have your own FMEA panel. They reach their conclusions, and right, so when you say you have the right to evaluate the data, of course you do. What I'm suggesting is you evaluate the sponsor's data, you see that it complies with the concept paper, and if it does and the results make sense in your professional judgment as

medication error experts, it's a rational, sensible judgment, it's you accept it. That's what I call evaluating the data.

MS. HOLQUIST: Okay.

DR. HARTMAN: I don't call evaluating the data running your own parallel DMEP process.

MS. HOLQUIST: Okay. Obviously, you have issues with the proposal of what we're here for, and what you have just described is exactly what we have proposed in the one arm of the study -- is that we would -- there's going to be a separate independent review of that data that comes in, and our expertise will be applied to that.

However, in order to educate the public and to educate a lot of the pharmaceutical firms, there may be things that we know about that you don't know about. And in order for us to come up through that, we have to sort of go through our own process, our own methodology, and say, okay, we looked

at it this way. Here's where we found some issues. And we might see patterns where pharmaceutical firms always fall down. Or we might see patterns where they do actually a better job. And I think that's the whole idea of this pilot is to find out where those differences lie so that we can all come to a similar understanding of how we will evaluate this.

MS. TOYER: I think also one of the things to keep in mind is that we're all making a lot of assumptions at the front end of the pilot without having that data in front of us. And so we seem to be semantically saying the same thing. You indicated that we're going to evaluate the data and make a judgment whether that data is sound, and that's exactly what Carol is saying -- whether that judgment is sound and meets the expert panel that we feel the agency has.

And so I think if we kind of get back to the point that I don't think we're

going to resolve this component of the logistical point. I think pharma has to make their submission on this point, and we're going to have to resolve what we do with the pilot after we get all that information in. But this conversation keeps coming back and back. And I don't think we're actually resolving it at this point, and we have a lot more to get on point. And then I'll let Bob --

DR. HARTMAN: just to clarify, I'm not speaking on behalf of PhRMA. I'm speaking on behalf of myself now.

MS. TOYER: We understand that. I'll let Bob comment on that, and then we're going to move on to another point.

DR. LEE: I just want to make one observation. When we sat, Steve and Kathy and I and others, in the negotiations in the summer of `06, one of the really exciting thoughts to us was an opportunity -- it was almost stated this way -- to have a give and

take and sit at the same table and have a discussion like the one we just had. And so I think you've fulfilled that hope of ours that we'd have that opportunity, and I think it's been -- thank you for giving us that opportunity. It's really been very appreciated.

MS. HOLQUIST: And I guess what I offer is what we -- we're here today -- is if you have an issue with what we've proposed to evaluate, we'd love to hear an alternative method which I haven't heard yet. So if we could kind of move to that sense of it and also some of the logistical things, like how are we going to pick companies for this? How can we register them. How can we be some sort of gate keeper, because feasibility wise, if we have to do all these reviews under the PDUFA timeline, and it is, you know, increased workload? We need to be able to, you know, only get two submissions a month in order to be able to evaluate this. So if we

can talk a little bit about that.

MS. TOYER: David and then Gerald, please?

DR. KORN: I have, I guess, it's a clarifying question, and I'm not trying to re-open the discussion on it, but the question is some of the discussion has been focusing like there's one method, and in your slides, you presented that there could be alternatives presented. And another piece of this could be your own experience as the time goes forward. And what is your vision of how dynamic the process would be given a Fiscal Year 13 public meeting again? And as people's scientific knowledge and test methods get validated as this progresses, how do you envision that working out?

MS. HOLQUIST: I think we want to open a collaborative process through this proprietary pilot program. And I think that's what we need to discuss today. How open can we be given the constraints that the agency is

typically under once a submission comes in about the proprietary nature of the submission in and of itself? So is there going to be an agreement between all companies who participate in this pilot that it's free game and every piece of information can be shared? Or can we only speak directly to the applicant holder who has that one submission?

I mean it's our view that it would be more productive for everyone if we could, whoever's going to participate in this pilot, that these are the people who are always at the table every time we're having these discussions so we can learn through these processes. And if there are new methods that stem from this, that, you know, we're open to accepting alternative methods, but we're going to need to evaluate them along the way.

MS. TOYER: I think one thing to take into consideration is that there was a discussion either earlier today or yesterday that dealt with changes in as we -- as

submissions come in and we see that things aren't working, how do we actually adjust the pilot at that particular time. If we find out that there's a component that's substantially coming in and it's not useful, how do we notify industry? How do we make those adjustments in the pilot? How do we evaluate the point at which those adjustments are made when we get to the final?

So those are other questions which I think kind of follows your point of how do you make any adjustments. How is it open enough when you're going along in the pilot and you find an alternative method that someone submits that's better than something that was originally posted in the pilot? How do we notify industry of that?

DR. DAL PAN: First, I'd like to say we're really interested in new and more valid ways of doing things, so at the end of this, if that kind of stuff has come out this, I'd be delighted. But I'd like to get back to

Dr. Day's question. She asked what's in it for companies to do this, and I think the answers we got were what's in it for the industry as a whole. But would each of you want to -- for those of you who are from companies -- want to be the first one to sign up for this? I mean are we going to get people to actually want to participate in this, because it is voluntary?

So I can imagine everybody wanting the results in two or three years and da better process in two or three years and more transparency. But when the rubber hits the road, are companies going to actually sign up for this, because if nothing else, the pilot cannot succeed if no companies sign up.

MS. TOYER: And before you answer that, can you add the discussion came out with the DDMAC portion. Do you see that as a benefit? Or do you see that as a hindrance? Or how will that component impact upon your signing up for that particular -- for the

pilot?

DR. HARTMAN: You know, it's hard to predict whether Novartis would sign up. We would obviously make some determination as to whether or not there was some -- what the benefit would be, whether there's a reasonable degree of predictability for example. And if there isn't, I might wait to see what the results are for the first five ro six results before I make the investment.

But I think it would be a significant investment. I'm concerned as to what it would be. And the promotional portion of it looks like the cost could be significant. If we're talking about 150, 300 respondents, no one knows yet. But we're talking about something that has statistical powers, so the numbers are going to be -- they're going to be certainly over 100 I would think. And depending on how many panels you need for ten people, it seems like that could be a cost. That could be a significant issue.

On the question of whether or not data should be public, I don't think that should be in the concept paper as a requirement, as a condition, because I think then you'll -- I think there are some pharma companies who will use that as a filter and say, that's out for me, I'm unwilling to do it. I do see there's an advantage to making it public, and maybe it could be done on a case-by-case basis. The sponsor will say at some point, yes, go ahead, we're willing to release the data. But I think that you may be limiting yourself unduly if that's the criteria to get in the door.

I don't know -- you know, you want a selection, but if all you can accept are one or two a month, at first, I would think you're not going to be too choosy, because you don't know what you're going to get. So you have to see. If the first couple of months, you get five or ten applicants, you might feel very good about your ability to select. But if

they start only coming in in dribs and drabs, any selection criteria you have may be irrelevant. You may simply want to take whoever comes in the door.

MS. TOYER: Dr. Zuckerman, before we hear from you, can we hear from the rest of the industry?

DR. GANS-BRANGS: Kathy Gans-Brangs. Again, I'm speaking more for myself than for my company at this point having read the paper and just going to one of your questions around would companies be able to submit both an IND and an NDA, timing is everything, and you know, as someone who worked in regulatory affairs fo a very long time, you wouldn't want to delay a submission to get into a pilot program. So that would be, you know, the one thing I would like to comment on at this time. Thank you.

MS. TOYER: Emmett?

MR. EMMETT: Andrew Emmett with BIO. And of course, each individual company

is going to have to weigh the benefits of participating in the pilot program. But I think to really encourage robust and diverse participation, we have to be very, very clear of the expectations for that company of what's going to be in each individual's submission and be as clear and concise as possible on the testing requirements so there's no uncertainty on the part of the companies about exactly what they're getting into.

Also, I believe, you know, many companies are already conducting this type of testing independently and through vendors. And to the extent possible the requirements can be harmonized with what companies are already doing and ensure that it's not any additional burden on top of their current activities will really help foster participation.

DR. LEE: I think Lilly starts from the starting point that it wants to participate in the pilot program. I think it

would find the promotional piece on balance probably more of a deterrent than not, so it probably would rather not see the promotional piece in there. And whether or not there would actually be participation, obviously, it has to wait until we see what the final concept paper looks like. And we haven't fully analyzed from a statistical and survey point of view some of the prescription simulation portion which is probably the one that's most bothersome to me.

And some of the other data requirements do raise issues that Exhibit have to wrestle with in terms of privilege. There are aspects of some of the data submissions that we might not even release in our own trademark search for legal reasons, privilege reasons. So some of those have to be worked through and will probably be in responses to the docket.

And it, really, at the end of the day, has to be on balance, something that

makes sense in our own perspective as to what is a reasonable approach toward gathering information for name safety. So it's hard to say until we see the final concept paper after all the comments are in.

MS. TOYER: David, did you have any comments and then Dr. Zuckerman.

DR. KORN: As Andrew said, it's really a matter for the individual companies.

MS. TOYER: Thank you for being patient.

DR. ZUCKERMAN: Okay. Ilene Zuckerman, University of Maryland. I would like to suggest an alternative methodology based upon the discussion that I've heard. I'll tell you what it is and then I'll tell you why and we can talk about it.

The alternative methodology would be to implement the pilot in phases where in the first phase, the decision for the recommendation for approval or disapproval of the name would not be based upon the new

methodology. It would still be based upon the current methodology only.

And my rationale for that is that it sounds like, from the discussion that I've heard, that you currently have a system in place, and nobody is really -- I didn't hear any major concerns about that system from the industry. You know, that that process, from their perspective, seems to work. They don't have any major concerns with it, so given that and that the concern is well, what if -- you know, now we have this dual parallel system, dual parallel process. What if one process says yes and one process says no. How's that going to be resolved? And then am I at risk because I'm volunteering to be in this new program? And this more robust newer process or supposedly, hopefully more robust newer process might actually put my name at risk for not being approved. So why would I participate in this program?

So as in any new process, we don't

know if the new process is better or worse or consistent with the current process. So I had listed out some objective because I hadn't hear any before. One of the objectives of the pilot should be to test the feasibility of the applicant's ability to carry out the review on their own with the methodology that has been outlined.

And so the first phase would involve going through that process, getting feedback from the industry about the process, looking at their methodology and evaluating it from a feasibility perspective and from an acceptability perspective so you could have more information on all these issues about cost and time and logistics and then move on to the next phase.

MS. TOYER: Can we get some discussion on Dr. Zuckerman's proposal? Dr. Day?

DR. DAY: I think there are concerns that industry has. One is the high

rejection rate. I think we heard yesterday it could be 30 to 40 percent. And so anything that might change to reduce that would be of benefit, and one of the ways to do that is to have, you know, new methods that are more transparent and so forth.

And then the other issue is about transparency. So whether it would eventually be the FDA using these methods or the companies, just a more transparent way and a way to assure that all the t's have been crossed and i's dotted along the way to reduce the probability of the rejection rate would be a positive outcome. And I think there are other concerns that industry has. And again, I'm not from there, so I can't really speak to it, but I think more of those came up yesterday.

But it is true that there weren't a lot of specific complaints, but let me sort of refocus this. I think one of the stumbling blocks is the promotional part, and I

personally think it's simpler and easier to do. I would recommend a simpler approach to doing it than was recommended in the concept paper. But I really think that can be done quickly, cheaply, and I don't think it's that big a deal to do.

I think there is more to do on the safety side for the testing, but I would like to go back to Dr. Frank. Someone asked this morning what percentage of names have been rejected on the DDMAC side, and the data weren't available today. But a little historical review of that in the last five years, would that be possible to do?

MS. FRANK: Not at this time, no. Sorry.

DR. ZUCKERMAN: Not at this time today, I know but --

MS. FRANK: Well, the process actually has morphed over the years and --

DR. ZUCKERMAN: I see.

MS. FRANK: -- to where we are now

--

DR. ZUCKERMAN: Right.

MS. FRANK: -- both in the safety and with respect to promotion. So, you know, those variables also there, so that sort of would skew the data I think.

DR. ZUCKERMAN: I see. I guess I remember Dr. Holquist saying something like -- or someone -- here are the processes, and then with a parallel review by DDMAC, if they say no, then it stops. And so I though there was --

MS. HOLQUIST: Right. Currently, our old tracking system never could capture that type of data, so we have a new tracking system in our office where we're trying to capture if DDMAC said no to a name it's closed out. And so we'll have a way to, probably in another year, go back and see how many of the no's were actually DDMAC rejections. We won't know, probably, why they were, you know, what you're referring to, but we'll at least have

some more numbers.

DR. NOURJAH: After listening to the discussion and my concern about not having this methodology well studied, and we don't know -- I think we feel that we don't know how valid they are. It is too early to start a program. I like the fact you call it pilot program. It's really pilot meaning we are going to learn from it. It's not something after two years, we are going to make a final decision. It's just we are beginning to learn. So the way I see it is that, and from yesterday, I saw it like that just because the methodology is not tested yet, it's not scientifically based, it's not objective yet, it's subjective.

And I, honestly, at this point where we are, think FDA should be considered as experts, because they work many, many years in this area. Therefore, I put lots of weight on their conclusion. And perhaps I would want to learn more from them, just the opposite,

unless the industry comes with or academia come with more adequate valid methods.

And concept paper to me at this stage is so preliminary. We should accept that, and we shouldn't say if, you know, we follow the concept paper, we did every aspect of it, and we don't see any problem with it, therefore, FDA, you should accept it just because we are too far away from final. And we should accept that.

And I think we should not even make decision or what the company conclusion is at this moment or the next two years based on their studies. You should do whatever you were doing so far. You should go follow your conclusion based on traditional methods, because the way I'm hearing it, you want to engage the companies. So if this is the goal, make it voluntary. They can come at any time they want. They can submit to you the conclusion at any time, because it's for their benefit the more we learn about it. They can

do the work so the predictability goes up, the process of approval goes high. So this is the benefit they get at the end.

But we all have to know this is just the beginning. That's my comment.

MS. TOYER: Thank you. It sounds like your comments are mirroring Dr. Zuckerman's. We were scheduled to take a break at 2:30. I think we're going to break now. It is 2:20 by my watch. Why don't we try to be back in approximately ten minutes at 2:30, and we'll get started on this next part. Thank you.

MS. PAULS: And just before the break, I just want to let you know several people have approached me in regard to cabs out of the Metro area. The hotel has arranged for a bank of cabs to be available around 4 or 4:15 today to go to various places.

(Whereupon, the above-entitled matter went off the record at 2:20 p.m. and resumed at 2:36 p.m.)

MS. TOYER: All right, I think we're ready to get started. We're still in the section of logistics of the pilot. I think we've gone through a lot of that. Also, we're in the component of -- I think one of the things that we might want to bring back up that was a question, PhRMA earlier in the day dealt with the potential for meeting prior to the submission of the pilot and having a discussion about the failure modes. That was a question that I think I tabled from an earlier -- from when we talking about something earlier, so I'll put that back out as a discussion point from industry if would like to. I'm not sure who brought that up. If you'd like to provide some further discussion on that?

DR. HARTMAN: I raised the point and it was in connection with failure modes, but the point isn't limited to that. The question is whether we could have the protocol that the sponsor plans to use agreed upon by

the agency so that it would improve the likelihood that the sponsor submission would be accepted.

MS. TOYER: Just a point of clarification, are you paralleling this discussion as an in a special protocol, as in the current existing population of a special protocol? Or are you saying more so to the point that we try to get agreement on the major points and then the data becomes a review issue?

DR. HARTMAN: The latter.

DR. TAYLOR: I mean the agreement on the major points, we've laid out in the concept paper what the FMEA process should entail, so that sort of is agreed upon. And then the deviations from that, we've ask that, as a courtesy, it be submitted to the agency, and we would try to give feedback and commentary on that but bearing in mind that the resource limitations and time constraints implemented by the PDUFA guidelines would have

some implications as to whether or not we could do a formal "approval" of the protocol.

DR. HARTMAN: Well, suppose with the submission, the FMEA would describe already what the failure modes were, and likewise, the various other components would go into a little bit more detail, would the agency then be in a position to evaluate that and say, yes, we agree with those failure modes, we agree with this protocol we agree with the way you're going to be doing the name simulation studies and et cetera?

DR. TAYLOR: I think it's something that we could -- I mean, to me, that sounds almost like a rolling submission, and from a workload standpoint, that would be challenging.

MS. HOLQUIST: Yes. I think what we've asked is that we've laid out some methodology in this concept paper. We've asked for feedback on whether or not these are feasible, if they're agreed upon. We heard

some discussion about maybe some other test methods that we might employ early on before we go to a lot of these methods. We've also put in the concept paper what the expectation from the analysis would be is that we want the raw data, everything that you used, with respect to the failure modes, how you have chosen the individuals that make up the panel of experts.

What we do want to know is what the failures that they found were, how they walked through this thing. We want to see all the methodology. We want to see all the raw data so that we could, in turn, look at what has been submitted and make a determination based on our expertise was the data adequately done, were there limitations to it, and if so, what are they. And that's how someone who's evaluating that data would look upon it and come to a conclusion.

DR. HARTMAN: Just to clarify -- what I'm looking -- what I'm exploring is a

submission that is detailed so that it might provide the names of who are going to be the FMEA reviewers so that if you have any questions as to their qualifications, that comes up front. That doesn't become a point for rejection, so that understand what the failure modes are, so that isn't any longer a matter for debate or for rejection, and likewise, the other points in the submission.

But the idea is to do it in a way in which any -- that your rejection of a name which the sponsor's results say the name is safe isn't one of judgment but it's fact-based rejections -- we're rejecting the sponsor's submission, not because in our judgment the FMEA panel made a mistake, and in our judgment, we would come to a different decision on the same facts, but rather our rejection is based on a fact -- you didn't know about a drug or you didn't include a drug in your analysis which we think is a problem, there's something in the pipeline that you

weren't aware of, there's some other fact that you got wrong. But absent of fact-based rejection, okay, the sponsor's submission would be accepted.

MS. HOLQUIST: I think that's exactly what we've proposed, that we're going to look at this data, we're going to look at the adequacy of the data, and we're going to look at what were the limitations of that data. So for instance, if in your failure mode and effects analysis you went through the whole failure modes, you may have listed about ten failures. Well, we may have identified additional failures that weren't identified in that that we think are just as important or may actually end up in the wrong drug being administered. Those are exactly the types of things that we're going to look at when we look at this data.

We can't just take the data and rubber stamp it and say you followed the analysis exactly the way it's laid out and

therefore we're good to go. We have to look at each one of these phases in the test practices, look at how it was designed, look at how it was carried out, look at what the results of that, you know, what came from each one of these test methods, and look at them on a whole. And when we find these differences or these fact-based things that you keep referring to, we will have those discussions with you and say, here's where we think the analysis -- or your analysis is different than ours and talk about it and hope to learn from that so that we can create these better practices so that we'll have less and less of that as time goes on.

I don't think we're going to go out the gate and say, we're good to go, everybody can follow this, and every method that we've proposed in this paper is 100 percent what we're going to see at the end of the two years.

MS. TOYER: Before you start,

Steve, let me ask a point of clarification. I think what you're saying is that you're asking for this pre-submission of the proprietary name, these agreements. Is that correct?

DR. HARTMAN: Yes.

MS. TOYER: Okay. I think the only problem with that is, in the PDUFA world that we're working with, what you're kind of asking us to do is to do the review work before we get the submission. And I think that may become -- that would really be a resource issue, as Kellie was touching upon, that we probably -- we, number one, have to do the pilot reviews under the PDUFA requirements. That's what we've been instructed, that we can't assign a different review clock to those reviews. And so with that said, you're asking us to take upon, say, a third review of something not on the clock, but we're doing the work. I don't know if that clarifies.

DR. HARTMAN: Yes, it does. Thank you.

DR. GANS-BRANGS: Yes. Hi, Denise. Kathy Gans-Brangs. Just a follow-up question on that. You brought up the special protocol assessment, so would that, in fact, be something that the agency would consider incorporating along those lines in this?

MS. TOYER: I think that would be a difficult task, because the special protocol assessment is a 30-day clock, and I think it would be almost impossible for the Division to take that upon, and to give you a read on that protocol within 30 days, and have to also manage the new PDUFA clock. I don't know, Carol, if you have a different comment?

DR. DAL PAN: This is Gerald Dal Pan. No, I mean the special protocol assessment criteria are set forth in the PDUFA goals letters, and we just don't have the staffing to take that on at this point.

DR. HARTMAN: Just one thought I throw out. For certain types of drugs, certain categories of drugs, the failure modes

are probably rather standard, and they will travel through basically the same hospital paths. They travel through the same retail paths. They aren't that -- some drugs will be very different and unique, but there probably are, I think, a lot of drugs that, as they travel through from prescriber to administration, travel through the same nodes. So that's just a thought, and at some point, it may be possible to create templates as what the failure mode analysis should look like as far as where the nodes are, and things of that sort.

DR. TAYLOR: Just to be clear, the failure modes are based on the orthographic and phonetic characteristics of each name, so in order to identify the failure modes with each name, I don't think you could, in fact, come up with a pre-set list. For certain types of nomenclature with suffixes, dual trade names and things like that, there would certainly be particular failure modes that

would be common to that type of nomenclature that is being proposed. But I don't think you could come up with a standard list of failure modes.

DR. HARTMAN: What I meant was that the nodes, where the error can occur as the drug travels from prescriber to administrator, since a lot of drugs travel through the same commercial path --

DR. TAYLOR: The nodes certainly -- I mean, at any point in communication --

DR. HARTMAN: That is what I'm referring to as being standardized in some cases, because the drugs travel along certain pathways. They'll go from prescriber, be handed to -- one path might be prescriber, patient, pharmacist, patient. That's one path. And for a lot of drugs, retail drugs, there will be a limited number, half a dozen, eight, three, and so that, the way the drugs travel through the chain, and where the errors can occur, those nodes, I think, may be

standardized, but that's just a thought.

MS. TOYER: We should probably try to transition to the evaluation of the pilot overall. I think we've had some very good input, specifically from Dr. Zuckerman, and Dr. Nourjah with regards to potentially running the pilot as a stand-alone. I think we've had good feedback from industry with regards to what your potential participation would be, and what the possible pitfalls and benefits would be. And we look forward to getting a lot of that feedback in the document.

As we transition, I think we had on the slides some information about overall evaluation, and I'd like to transition to that direction at this particular time, recognizing that the pilot may undergo some changes as far as -- based on the opinions that we've received. So if anyone has any points about how we should -- should the evaluation be conducted by a third party, should the results

be brought back to this group, or should there be some other type of public disclosure about the results of the study.

I think there were questions about what do we deem as a success or failure. What are some of the specific measures that we're looking for. I'll open that up to discussion.

DR. ZUCKERMAN: Ilene Zuckerman, University of Maryland. I hate to keep repeating the same thing, but the issues of evaluation would be dependent upon what are the specific aims of the pilot. If the specific aims of the pilot include testing the feasibility of the process of the industry to be able to carry out these procedures, then, you know, that's maybe somewhat more of a qualitative evaluation.

If the evaluation is to -- if the purpose of the pilot is to develop standardized methods for name testing that are, as it says in the slide, better than - it doesn't say better than what - but better than

the current evaluation, that would mean a different approach. So again, I just get back to, you know, can we list out what the aims are.

DR. DAL PAN: Perhaps it would be helpful if I actually read what the goals letter of PDUFA IV said that sets up this pilot. So it says, "b" -- presumably there's something "a" before that -- pilot program -- "During PDUFA IV, FDA will develop and implement a pilot program to enable pharmaceutical firms participating in the pilot to evaluate proposed proprietary names, and submit the data generated from those evaluations to the FDA for review."

And then there's some sub items here. "One, FDA will hold a public tactical meeting to discuss the elements necessary to create a concept paper describing the logistics of the pilot program, the contents of a proprietary name review submission, and the criteria to be used by FDA to review

submissions under a pilot program." That's this meeting today.

"Subsequently, by the end of FY `08, which is September 30th, FDA will publish the concept paper. Two, by the end of FY `09, FDA will begin enrollment into the pilot program, and three, by the end of FY `11, or subsequent to accruing two years of experience with pilot submissions, FDA will evaluate the pilot program."

So the way I read it, it didn't give the kind of precision that I think you're justifiably looking for. And so I think one of our goals is to see the feasibility of companies submitting this information, and FDA reviewing it in a very qualitative way. I think some outcomes of this could be increased dialogue between FDA and at least individual companies on this process, learning from each other on this process. And one outcome of that could be more industry-wide dialogue with FDA on improving this process.

But again, these are very qualitative things, and my own personal view is that those are the kinds of goals I thought this program would have, and would have sort of qualitative evaluations in that way.

DR. ZUCKERMAN: Ilene Zuckerman, University of Maryland. So what I heard you say - and that was very helpful - and so what I heard you say was the goal of this was to enable firms to be able to evaluate and submit their information. So that, to me, suggests that the pharmaceutical companies do no worse than what's currently going on, so that, you know, part of the evaluation, to see if they are able to do this is, do those decisions match the current methodology, the current procedure. And so, you know, that could be one component of the evaluation, just the concordance between the two.

And I just want to stress again that, since this is a pilot, any new procedure, any new intervention, potentially

has unintended consequences, and so that the new intervention, the new process, during the pilot phase, should not be used in the decision-making process of the determination of the name approval so that, during the pilot, the current methodology, the current procedure, should be used to make those decisions.

And during the pilot, you evaluate the feasibility of the ability of the pharmaceutical firms to do this. And then at the end of the pilot, you evaluate the information to determine if you met the aim so that, in essence, you can do the evaluation, you can do it ongoing, you can look at it ongoing, but it's basically a retrospective evaluation.

MS. TOYER: Any other comments on that point? Dr. Day?

DR. DAY: Ruth Day. I do understand Dr. Zuckerman's comment, and agree with it in part, but I think that another goal

has to be so we could separate out the decision making. Okay? If we just talk about this, the decision making about the drug names that come forward from the companies who participate in the pilot program, fine. If you all agree, the decision-making will just go on in the usual way, and not based on the pilot. That would be one way to do it.

But my view of this whole exercise is to see how, not only current methods are working, but new methods that, (a), are more transparent, and (b), are quantitative in nature, and (c), are replicable across different units, companies, and over time, and so forth, and have statistical testing as part of it, and can even be used to test hypotheses. And to me -- so if we can just separate out what's going to happen to these wonderful volunteers who'd agreed to be in it, they could elect, or somehow it could just be decided that it won't be based on this new thing.

But I just see this as a wonderful adventure to learn how to do this, and to verify what's already going on that's good, and to increase the range of tools that can be used to do this. So in the future, who knows what happens, maybe there would be an array of tools, and after the pilot is over, then companies could decide, we're going to do tools A, B and X for safety, and P, Q and N for promotion, and so on, but they'll then be tools where we'll know the value.

So one of the outcomes could be is this particular tool did not tell us enough, or had problems, let's not recommend it in the future. These other tools worked all the time, or they worked all the time when, you know, there was a certain kind of drug involved, but not for others, and so I see a potential outcome of this is having a better tool kit.

MS. TOYER: Parivash.

DR. NOURJAH: I like the idea of

Dr. Day to use it for that purpose, too, during the pilot study, which is, you know, you use your traditional method for approval. You can also compartmentalize your evaluation, or reviewing in two parts, because you have hypothesis testing that you want to generate as many as potential names that -- because we want to really improve the sensitivity as much as we want to reduce -- to have high specificity and high sensitivity, but we'd rather to be sensitive to capture potential names.

So one compartment is, what tools really improve that, and you can compare it with whatever tools you have, the new technique comes, you can compare it with your old tools.

And the last one is to FMEA methodology, again, maybe some companies come with a new, objective way to do it, but if they can -- you can see what methods they add, or adequate method they add -- but you can ask

a third party to come and dispute any discrepancy between you and the company, because I am hearing that FMEA may -- some companies may not agree with your judgment. You can bring another group, maybe on that end, to dispute the problem, and you learn from that dispute what's going on, and you add to the system, and improve the system for both parties, for FDA as well as the company.

MS. TOYER: Can I ask a point of clarification? So in your model, there would be essentially two compartments that an applicant could choose to participate in, or maybe it's the whole one. I'm not sure. The first one would be the hypothesis-generating component, which would follow very similarly the information that we've presented. The second one would be the FMEA, but the decision-making in your particular view, different from Dr. Zuckerman's, would be that, if there was a difference at the end of the two parallel decision-making, you could use a

third party to help in resolving that, because the only change would be, if your component, if the FMEA part said that the name was okay, and we said, no.

DR. NOURJAH: Right. This is the way I'd go is that, first of all, this is a pilot study. I'd go with the traditional method to decide for the name, but I am going to be open for new methodologies to come during that pilot study, and I compartmentalize my evaluation in two parts, because one part is hypothesis testing to generate name. This is my first procedure. The second one is a screening, and determining if the name should be -- is a risky name. So I evaluate two different methodologies. I mean, as they come, they can say they want to do the second aspect or the first aspect during that pilot study. You look at the methodology for those two parts.

And for the final decision overall -- you see, maybe I am not clear about the

last portion. What I'm talking about -- the FMEA is a very subjective issue. How to resolve it -- this is one alternative I'm providing. If you have a problem with the company on deciding, I would recommend a third party come to resolve this dispute.

DR. DAL PAN: Okay. Well, thank you for these comments. I think they're very helpful. I think there's a number of things that we'll have to consider as we listen to your comments. One is the idea of approving it based on the traditional method, and using the company submission really to evaluate the pilot and nothing else.

I mean we have to, as a regulatory agency, consider the implications of using company-generated data on some aspects of its product safety that we don't use in a decision. And that's not typically the way a regulator thinks. So we'd have to at least think about what the implications of that would be, and I think there are times we do

bring differences on complex decisions before third parties. Those are called, generally, advisory committees. So that's something we could do.

Often, when we disagree with the company, we just sit down and hash it out, and each side says it's own point. Clearly dialogue, though, I think is going to be really important in understanding how each of these tools is applied, and used, and how the results are interpreted.

MS. TOYER: Any other comments on the evaluation pilot overall?

DR. HARTMAN: Just - maybe I'm stating the obvious, but I think - is there agreement that we're ultimately looking for is a name assessment tool, or a set of tools, a variety of tools, that the FDA feels confident that they can trust the sponsor with the results of what a sponsor's name evaluation result would be if they were to use one of those tools? Is that -- I'm assuming that's

what we're -- that is sort of the general goal, what you'd want to do at the end of the pilot.

DR. DAL PAN: I would say we wanted the best possible toolbox, to use that term, and to know that it can be applied reliably, and that we would have a standard way of looking at submissions that companies send in, just the way we do for clinical trials, pharmacology studies, toxicology studies. There are sort of standard ways of doing these, and, you know, the agency has decades of experience with that. And like all these submissions, we review the data. We review how the companies interpret the findings. We review how they conducted the studies, and then we make decisions on them.

DR. HARTMAN: Well, maybe then we disagree, because you're -- what you're looking for is broader than what I think you should be looking for. I think you should be looking for a name, or a set of name

assessment tools that the sponsor can use, and that you will accept the results of, that if it complies, if the sponsor complies with the protocols, and you -- as I said before, and you see that the sponsor's complied, and the results make sense, you don't see anything wrong with it, than you accept it. And that isn't what I hear from you. It sounds like that you're still willing to contemplate continuing a pilot, in effect, do your own DMEP internally, compare it to what the sponsor does, and then arrive at a conclusion.

DR. DAL PAN: No. I mean, I don't envision that, in the long-term, we will forever have this parallel process, because that doesn't make a lot of sense. But what you said - I forget your exact words - but we would see that it makes sense and, you know, see that it's a reasonable conclusion. That's what I meant by reviewing the data.

I mean, we do that with every single NDA and IND that comes in. We review

the data. So if a company says, we've looked at all this data in 200 phone books worth of data, and we believe our product is safe and effective, well, we look at that data, too, and we come up with different conclusions. And we will, I think, always reserve the right to come up with a different conclusion. We analyze a lot of data extensively in some cases - not in all - and, you know, we will apply that general framework to what we do with Med-ERRS. As Carol says, it won't be a rubber stamp.

MS. TOYER: And with that, I think we should -- I'll turn it over to Lana for the open session. I want to thank the panelists for a lively discussion. And Lana?

MS. PAULS: Thank you, Denise. We have three registered speakers for the open public session. They're all familiar faces, because all three of them addressed panels one and two yesterday. In the interest of fairness, I thought I would go in the opposite

order, though. So the first person to address the panel is Susan Prouix, the President of Med-ERRS. Susan?

DR. PROUIX: I'm not sure I want to go first. I was afraid yesterday about the non-prescription thing. This holds nothing compared to yesterday.

I'm just going to say -- I'm going to just make a few thoughts again, and a lot has been tossed around since I wrote my thoughts, and we have so much more to think about, and we will be submitting something on the docket before July 6th. But I'll just throw a couple of ideas out there, and I know it's the end of Friday, and everyone's head's starting to hurt, so I'll try to keep it brief.

Again, agreements, disagreements and some questions is how I sort of handled it yesterday, and I hope to do that again. So we agree that the FDA review should be done in parallel with two FDA reviewers if you're

going to do it in that way. However, one's looking at their own data, and one's looking at the methodology and the data. And I guess a few questions about that is, are you going to stop a review if you don't like the methodology up front, and not move forward, not even looking at what the results of that methodology is by the -- in the comprehensive review?

What I'm suggesting is perhaps that one FDA person look at the methodology and say, yes, and then a second person look at the actual data, so that they're not looking at two parts of it, and that the two data reviewers can then compare. Just a suggestion.

This has gone back and forth a million times. What about the discrepancies between the two safety evaluators, and how will that decision be made. When is that going to be shared with the sponsors, and we're hoping, some of us -- there are some of

us experts, we believe, out there, and who do that, we think, as well as the FDA. We have the same type of background. We'd like that information shared with our clients, who can then share it with us. When would that be happening?

We'd like to learn as quickly as possible about those results so that, if changes do need to be made -- you know, we're talking about 2013, so we'll see you all in five years again. Hopefully, we'd like to do some feedback before then, and we hope that the vendors will be able to be involved with some of those discussions, as well. If the goal is increasing transparency, then we'll obviously need some feedback along the way, and it goes back to what Marjorie Phillips said yesterday about rapid cycle improvement.

There was something in the document about, if the first choice name is rejected, for the second choice names, the FDA may not conduct a comprehensive review between their

own process and the industry's new process. We believe that the same methodology should be used for the second name. There you're going with apples and oranges again, and why would you set a different standard for the second choice?

And I know it may be due to resources, but you wouldn't be able to include that second name in the data results for your pilot. So our suggestion would be that you should follow the same process for the second. If the first name is rejected, you're going to follow the same process for the second name.

Another just basic question: are the companies signing up per submission, or per company? If they're not signed up, are you going to be following just your regular way with them? I imagine that's the case. If they have a deviation from the process, if they decide to send in an alternative method, does that mean they're still in the pilot?

Does it mean they're not in the pilot? And how are you going to evaluate that data and the alternative method as part of the data set for the pilot? I'm not sure, again, if it's applies and oranges, and I'm not a statistician, but again, things to think about.

It sort of seems to me that using the pilot, or being involved in the pilot, and I'm not a client, but they have more chance of no, because they're never going to submit a document to you where their name is not acceptable. So they're going to submit a name that they believe has followed the process, and that has an acceptable outcome. So they can get a no based on what you're doing in your process, or they can get a no based on, you don't like their methodology in the new process. Or they can get a no based on the outcome -- that you look at the new review, and you don't like the outcome of their methodology. So it doesn't seem like a very -

- it's like a lose-lose situation, almost. It seems like they have more opportunities for rejection, as opposed to acceptance.

For incomplete submissions, how long will it take for the FDA to notify the applicant, and how will it be determined that it's an incomplete process? I guess you'll have to specify that.

We haven't talked about -- you know, I know the clients sitting at this table often submit methodology now, and we haven't really talked about that. That's sort of been forgotten. There are those of us, quote, vendors in the audience, who do now do name safety testing processes for PhRMA, small companies, big companies, and that really hasn't gone into the mix at this point.

I have a couple of questions based on that. First of all, when they're submitting their old way, the traditional way, some companies up front submit documents such as those that Med-ERRS produces, or some of

our competitors. Would you expect them to submit that, or are you talking about the bare bones submission when you talk about the old way now? And that's actually going to add another level of complexity to the mix.

And then the other issue is, if they did, you'd obviously never see anything between the old way and the new way that was different. You'd always have the same outcomes.

I just think it's going to be difficult to determine, you know, is your way the best, is Med-ERRS the best, is Jerry's way the best? You're not even looking at those, really. It's really hard to determine error rate, which is one of the things people keep tossing around. We think that's a really scary term. It's too rare an occurrence. I talked about yesterday if we're going, for the name simulation studies, setting up error-prone situations. I'm just not sure how you're going to determine which way is safer

in any quantitative fashion, because error rates are so rare. It's just very difficult. It's what we said, or it's what you said. It's sort of a he-she said.

The process is still going to be based on opinions. It's still going to be qualitative in many ways, which is highly subjective, and we understand that is a strong limitation right now.

Our ultimate goal in all of us is to reduce confusion between products which could lead to medication errors. And we're not sure how that's going to occur comparing these two processes.

And what happens in between the time of 2011 and 2013? How are submissions going to be done? Are we going back to the old way? Is there going to be a new way developed? Or maybe we just need to see what happens in the next couple years. And also, does FDA have any plans to change their own methodology between now and the pilot?

I just have a couple more thoughts. I'm going to just reiterate, and I think Dr. Day said that, and I mentioned that yesterday, that I think it's going to be really important to determine which portions, or which steps in the methodology are important, which ones are valid, so to speak. I'm not sure I should be using the word valid, but which ones are working, which ones are helping determine a best outcome, and try to eliminate some of those along the way, because again, time, resource, manpower, and money. If we can throw some of those out along the way because we find that they're either redundant or not useful, I think that would be significant.

And I believe that increasing transparency is going to be very helpful. I think it would be helpful if the FDA could let the sponsors know where they are in the process -- we're at the DDMAC stage, we're at the stage of looking at your methodology, et cetera.

And then finally, my last statement is, if the companies will never have all the data available, which is what -- Carol, you said that -- they're never going to have all the data, so how are they ever going to be able to come up with the right answer? So my feeling is that, as Steve was saying, and I kind of believe the same thing, and that's what I thought this whole meeting was going to ultimately be about, was that the companies eventually would be submitting data that was meeting certain baseline criteria that the FDA would then find acceptable, but they'll never have all the data, according to you, because they're not going to have post-marketing error information that's private to you, and they won't have the pre-approval list.

So my feeling is that, basically, we're going to be providing data to the FDA to evaluate, and that I'm now sure how much thinking you really need us to do anymore. It's more like, we're just providing as much

data to you as possible so that you can make the final decision.

It's just something to leave you with. Thank you. I'll be happy to take any questions.

MS. PAULS: Okay. We have time for maybe one or two comments. Go ahead.

MS. HOLQUIST: Carol Holquist. I'd like to just respond to the fact that you're not going to have all the data. I can tell you, over the last ten years, how many names that were rejected because something was in the pipeline. We've probably had maybe two or three of those, so I think the fact that everybody's worried that they're not going to know all the names is really somewhat inflated.

And with respect to the post-marketing data, we've actually put in the concept paper ways in which companies can acquire this data. I think it's, you're going to have to build up some expertise into the

analysis of that, and what it means, and I think that's where a lot of the interpretation of the data comes into play. And, you know, as Gerald said, we're always going to have -- we may always have differences of opinion, and it's our hope that we can articulate those, and have rich discussions, and learn from them.

DR. PROUIX: It's good to hear that there's only been a couple, and that's encouraging. Thanks.

MS. PAULS: Okay. If there's no other questions for -- I'm sorry. Bob?

DR. LEE: Bob Lee. I wonder if the FDA has any immediate reaction to Sue's comments about, if we use Jerry's approach, or Sue's approach in terms of doing name evaluation, and were to submit that as part of the regular DMEP's review at the same time that we submitted a -- through the pipeline, meaning the -- meaning whatever -- I mean through the pilot program, whatever the pilot

program study was, you'd sort of get a comparison of a DMEP's enhanced review with material that was provided by -- in the more normal fashion, versus a pipeline study that has all the data that's outlined in the concept paper.

MS. HOLQUIST: I mean, I think we would handle it as we do now, which is we evaluate that data in addition to our own analysis. I think what happens, though, is how we receive that data. We don't always get the raw data. We often just get a summary statement of what was found, and so you really don't get any insight into the methodology that was used, what some of the results were. And if you're going to do that, I would actually try and encourage companies to be more transparent about their processes so that we could do more of a better assessment of them.

MS. PAULS: Thank you, Sue. We're going to move onto the next speaker, and that

is John Breen, the Research Director of Interbrand Wood Healthcare. John?

MR. BREEN: Well, first off, I apologize, because I did not realize I was speaking this afternoon, but I will offer a couple of points just based upon what was said today. I think, ultimately, the point that's come through today is that a dialogue between the agency, sponsors, et cetera is critical. And I think some of the points that have been made in terms of setting some basic parameters for study design is a very good point. To get some sort of preliminary checkpoint along the way about what is being proposed to be done would be very helpful, because it will provide some additional assurances for the companies conducting the work.

The only other point I would like to make is, and Sue made it, as well, is that, you know, there are companies such as our own that are conducting this work on a, you know, regular, even daily basis. And I had made

some comments yesterday that we would be happy to provide, you know, best practices for different components of the process. And we would definitely like to have a voice in that discussion and, you know, offer again our opinions around those things.

So again, I thank you for the opportunity to speak, and if there are any questions for me, I'd be happen to answer them.

MS. PAULS: No questions? Thank you, John.

MR. BREEN: Thank you all very much.

MS. PAULS: We have a third registered speaker, and then we have one person that approached me at the break: Jerry, of the Drug Safety Institute.

MR. PHILLIPS: Okay. Good afternoon. I am Jerry Phillips, and thanks for having me here this afternoon. I just wanted to make one comment before I started to

get into the evaluation of the pilot program that was addressed earlier about delays of submissions, whether people are flexible enough to have delays. There is a risk of delaying from the time the research is done. When we do research as a vendor, we always encourage our clients to submit that as soon as possible, because the risk of approved names after the research is done is absent from that. So the longer you wait after research is completed, obviously, there's going to be things that are missing in that risk analysis.

I'm going to talk about maybe three different ways in which you could evaluate the proposal. And I'm not sure which one's the best way, but I'll just give you some ways to think about it. As you know, DSI is a vendor. We do market research and safety research, and we submit data to the FDA. And after this final draft concept paper, we will be incorporating the methodology, and your

suggestions into that methodology, and all the clients that come to us will have that evaluation in their -- in the FDA reports that come to you. So, as it was mentioned earlier, you are going to receive the same data submission packages outside the pilot program than you will have in the pilot program. Not that that's a big issue, but just something to think about.

Because we've been doing this for a number of years, I think you should be familiar with the methodology. Having the guidance document, we'll try to standardize that, which is a good thing. And as I mentioned, we will do that.

I suggest that maybe you modify your way that you're going to evaluate your proposal. I recognize that there are differences of opinion that can occur between two safety evaluators, or two people looking at data. I think one of the key concepts for me is that, what we want to try to do is to have

the right data being submitted by the applicant. The differences of opinion is somewhat considered variability between the opinions of two reviewers. Even if you were looking within FDA, if you had one reviewer and the second reviewer, if the data is the same, but the opinion is different, well, that's not the fault of the applicant holder, but that's a difference of opinion in the reviewers.

And I think what we're trying to do is try to get standardized so that we can get the correct data to you for your analysis.

I also have a concern about the burden that running a parallel process will have on current resources that might delay proprietary reviews within the agency. And running that parallel process may be quite complex. So this is where I will offer a couple of different scenarios.

One scenario is, under the pilot program, you're going to run two different tracks so that, when it comes in, you're going

to simultaneously review under your current process, and one under the pilot process. You could think about a cohort study, a smaller group.

Instead of doing it one-on-one, you could do a smaller number in the -- a smaller number sample size than doing it one-on-one. I'm not sure if I'm making that clear, but if you're going to do 50 in the pilot program, you could think about only looking at 10 or 20 in the cohort study of seeing what the differences are, instead of doing it 50 times. That's just another alternative approach.

I'd also think about, as you're looking at the results that come in from the cohort study to the pilot program, that you're looking at the data, whether the applicant has missed certain key elements of the data instead of the opinion, like I mentioned before.

Another way to do it -- another alternative that I was thinking of is that when the -- instead of having the pilot program

where you have registered applicants, et cetera, since you have current data being submitted voluntarily by manufacturers, those that are in the PDUFA process, you could elect, as the FDA, to determine how you want to look at that data.

So if the data meets the guidance document under the pilot program, you could elect to say, I'm going to take that data and review it solely on its basis, or I'm going to elect to put it into my normal process where I rely upon my data, and I look upon the ancillary data as a supplemental piece. That way, you could control your workload, and you could evaluate it accordingly to your workload, and compare the results.

And the third way that you could think about doing this is, during the pilot program where you have registered like you have it set up, you have, instead of doing the parallel process, you could have manufacturers come into the pilot program, and they would

either be sent into the regular process of review, or in the pilot process. That way, you're not running up a simultaneous review; you're not wasting your resources by doing another review process. There are disadvantages to that as far as comparability, but it would save resources.

I think the primary endpoint, or the objective of the pilot, might be thought about reducing medication errors. I think that is the overall goal of the DMETS program, or the DMEP program, and the agency's objective is to reduce sound-alike/look-alike confusion in promotional things. So what I say is that you could measure -- you could use the pilot to measure whether you're having any impact, negative or positive, on the rates of known confusion pairs, and I have a suggestion on how you could do that.

I think it would be instructive to look at the number of name confusion pairs prior to the beginning of DMETS in 1992 or

2000, and look at, for a period of time, the names that have been cited as medication errors under the labeling and nomenclature committee, the old process. And then, you could also look at the period of time since DMETS up until the pilot to see if the name pairs have increased or decreased. We hope that they have not increased, and we assume that the process has decreased the number of name confusion pairs.

And then, during the pilot, you could also evaluate those names that have got approved under the pilot to see if you had a greater rate, or those names were evaluated in the same way. So that's another way in which you could measure the effectiveness of the program.

There might be other objectives, such as looking at the review times as a measure of the pilot. Does the pilot help the FDA review names quicker, and thus reduce the backlog of name reviews, might be an endpoint. Or does the pilot program lead to higher

approval rates, or lower rejection rates? And this could be measured by comparing the rejection rates of both the pilot reviews, and those off the pilot during the same time.

I also would, as an additional point, suggest that the primary and the alternate name be reviewed, just like it does in the normal process, so that you don't stop the review process, and then go ask the applicant. The applicant has already made a decision that the primary and the secondary names are acceptable, and that you consider that, and not stop the review, because part of the incentive of putting in the second name is to try to save time as far as the review time at FDA.

And my last point would be that we would encourage meetings between the vendors and FDA so that we can work on issues related to methodology. Since we are doing this for a large number of applicants, that may be a more effective means of implementing change within

methodology, since a lot of clients do utilize the vendors for this sort of work. Thank you very much. I'd be glad to take any questions.

MS. PAULS: Any questions for Mr. Phillips? Yes, Gerald?

DR. DAL PAN: Actually, I have questions to industry members here based on something that Jerry said, and I think the other speaker, as well, about having both names, the primary and the secondary, be evaluated under the pilot program. You know, the second name would be evaluated if the first name is rejected. That would involve industry conducting and submitting the full package for both the primary and secondary. And this is going to be an important operational point, so I was wondering if some of the industry members would comment on that aspect of it, because it is an important point. Would the pilot program be something you might want to do if you just did the first name, or would it be equally acceptable to participate if you had to do both

names that way? It's important for us to hear that, because that was one of the things we had in mind when we said that?

DR. LEE: I'd like a little more flexibility. You have some flexibility in it now. You're not certain your second name would be reviewed, even if you had a full package available, under the way you've described it here. I think I like that flexibility at this point, because I don't know what the experience with the pilot program is going to look like.

DR. HARTMAN: We tend to test names in groups of ten or more, and so we would have all the data already for all ten names. So the first -- and our first and second name, most of the time, would be among the ten, so it's there. So it doesn't really make that much of a difference. That said, there's nothing wrong with flexibility. But it's not much of an issue, I think, for many large companies, at least not for Novartis.

MS. PAULS: Carol?

DR. GANS-BRANGS: Kathy Gans-Brangs. Flexibility is a good thing at this point.

DR. DAL PAN: And, you know, our considerations were internal workload, as well, but I did want to get the industry side of that. How about some of the smaller companies you may represent with BIO, or with PhRMA, smaller companies?

MR. EMMETT: Well, I think there's certainly a consideration of resource allocation, both on the company side, and on the FDA side, that should be taken into account. And I would certainly support having flexibility.

MS. PAULS: Carol? I'm sorry. David?

DR. KORN: I also think that the flexibility is there, and the question could be separated whether people had an obligation to submit it together. And I think that that would be very different than a situation in

which there is a rejection, and you have an option to come forward.

MS. HOLQUIST: This is Carol Holquist. I just want to clarify something Jerry said. Jerry, the process that we proposed in here about not going to the alternating is actually our current process, because we're finding that a number will move to the second name, and then a lot of companies will want to withdraw it halfway through the name review, so it's actually a waste of our resources. Or the alternative name that's actually submitted is almost identical to the name that we turn down, and in evaluating it, we'd likely come to the same conclusion because of the reasons why we're objecting to it. So that's why we're actually trying to ask industry up front is this -- based on our disapproval, do you still want to go forth with this?

MR. PHILLIPS: Okay, thanks.

MS. TOYER: And also to add to

that, the PDUFA requirements allow us 90 days for each name.

MS. PAULS: Okay, thank you.

MS. TOYER: Just one point of clarification. You mentioned guidance. Were you talking about the pilot program when you used that term?

MR. PHILLIPS: Yes, right.

MS. TOYER: Okay. All right.

MR. PHILLIPS: Yes.

DR. TAYLOR: Jerry, one more point of clarification. With regards to the look alike-sound alike name pairs, where would you suggest that we look for this list, and secondarily, how would we normalize for changes that we know have occurred with reporting incidences over time since the IOM reports, and the subsequent final IOM reports, and how would that play into evaluation?

MR. PHILLIPS: The way I would do that is do it by searching for approval, so I would look for the approval names during that

time period, and then I would search that list of approved names against the USP MedMarks list, where there are known medication error reports with proprietary names, and then just calculate your -- the number --

DR. TAYLOR: USP MedMarks is primarily hospital data -- I mean primarily established names data.

MR. PHILLIPS: It combines both -- someone can correct me if I'm wrong -- but it combines both the hospital data in the latest report along with the ambulatory care, the ISMP, the voluntary reporting systems data.

DR. TAYLOR: I think that they're not always actual errors either. Correct me if I'm wrong.

MR. PHILLIPS: The new report that has come out has actually classified the category of the errors associated with the name pairs now, so that you can actually see those that have actual errors.

DR. TAYLOR: I still -- I mean, for

the record, I just think that there's going to be real limitations in being able to pull across from multiple databases, and people report a lot of different areas, and there's no one central repository for these look-alike/sound-alike names. I'm just wondering how we would ever compare across products, and across reporting systems, and across time?

MR. PHILLIPS: Yes. Across time is going to be difficult, because the MedMarks data isn't -- well, I don't think the data is available per year so that you couldn't look at it. Of course, you could do error searches, which would be time-consuming, but you could look for reports within your own database.

DR. TAYLOR: All right. Thank you for your comments.

MR. PHILLIPS: Thanks.

MS. PAULS: Thank you. Mr. Rosebush from Epstein Becker and Green, if you'd like to address the panel, please?

DR. ROSEBUSH: Thank you for your

time. I'll try to make it quick, being that I'm the last speaker and all. But my name is Dr. Lee Rosebush. I'm with Epstein Becker and Green law firm. I'm actually a Pharm.D. and a J.D., so I'm going of trying to mesh everything here together.

Actually, I have two points. I guess the first one was a lot of today seemed like everybody was trying to push toward the scientific point, or scientific evidence. And I guess if you're going to try and use the scientific evidence approach, which is fine, and we're still going to have the subjective judgment question at the end, do we really still need as much scientific data as everybody is talking about? Because, really, everything you're going to fall back on your subjective judgment. That's what we've been doing for long periods of time.

And the second question, again, along the same lines would be - I know yesterday I talked a little bit about Phase IV

studies - but if you're going to do the pilot, a way of maybe possibly coinciding with everybody's ideas and agreements would be, if you're going to have the sponsors do FMEA data and such, and go ahead and have them still turn all that data over to the FDA, couldn't you then, in turn, enforce, such as a Phase IV or some sort of equivalent post-marketing surveillance, and have them go ahead and change their name, if need be, after two years, but let them use the name that they have gone ahead and used with their FMEA data? The reason being is that, if they choose a name, everything would fall back on them, including the liability and the cost of changing names and what not. This way, they get their idea of using their name, and the FDA would get their idea, as well, for safety. Is there any questions?

MS. PAULS: Are there any comments from the panel on Dr. Rosebush's ideas?

DR. TAYLOR: Just a comment on the

name change scenario. We know, from post-marketing experience, that that is very difficult to accomplish, and we have names that have been changed that are still in use today, and still a source of error. And in some cases, that source of error actually is magnified after the name has changed, because prescribers are so reluctant to let go of that brand name. So it is something to consider also when looking at that proposal.

MS. HOLQUIST: And also, we found over time, when did this sort of Phase IV commitment early on is that two years of data isn't really enough, because oftentimes, it hasn't even really penetrated the market well enough at that point in time.

DR. ROSEBUSH: The other -- to comment on those -- is it all right if I comment? As a practicing pharmacist - I've actually practiced both and practicing law - as a practicing pharmacist, you could argue that the liability charge, and the cost of them

having to go through their name, and the reputation damage, would counterbalance the cost and everything that would be associated with that. There are a few chances of error, which you could argue that the amount of agony that a physician would have to go through and a pharmacist has to go through of learning the new name would pretty much put that reputation out of wack.

DR. TAYLOR: Yes. Could you clarify that? I'm trying to -- are you saying that the liability would fall onto the pharmaceutical manufacturer, and thereby the process of --

DR. ROSEBUSH: You could argue that, but you could also argue the cost of labeling changes, the cost of new marketing, the cost of everything else that's associated with that, as well. So it's going to make them -- force them to do better surveillance at the beginning. And therefore, they're going to make sure that the FMEA data they're

approaching and they're using is better at the beginning.

DR. TAYLOR: It's still surveillance. It's the limitations of surveillance. I think that you would still run up against the same problems, even when we have experience with post-marketing commitments and things like that. I think you're still going to run into the same issues.

MS. HOLQUIST: Yes. I mean, just to give you an example, some of these name changes that have occurred, you know, we may have only had 30 reports total submitted. So I mean, what's going to be your criteria to use to say that, okay, this isn't safe, either? I mean, it really depends on the outcome. You know? You might have -- you know, we've had some where we've had less than that, but it's been death as the outcome.

DR. ROSEBUSH: Right --

DR. TAYLOR: So do we want to put that risk on the public health? Again, I get

back to what is the benefit of the name when you have the extreme on the other side?

DR. ROSEBUSH: But you could argue that we use the exact same logic, and the same testing as we use now. I mean, we have drugs that we know of, as a pharmacist, that when you put them up against each other, there's a huge chance of error. It's things that start with the same three letters, or things that have the same dosage strength at the end. So if you're having a risk that's out there now, is there really a difference between what's out there now and what that would be?

MS. HOLQUIST: I think that's our goal is to try and minimize that risk, because we're trying to get better test methods to identify those early on so they don't reach the market.

DR. ROSEBUSH: Okay.

MS. TOYER: And just a final statement on that. I question whether, in the current arena of PDUFA, and post-marketing

commitments, and REMS, if we could even institute that as a Phase IV commitment.

DR. ROSEBUSH: All right. Thank you for your time.

MS. PAULS: Thank you. I just have a couple of logistical comments, and then I'll shift this over to Dr. Del Pan for some closing comments. I just want to re-encourage everybody to submit their comments to the docket. There is information on where to go to submit comments to the docket out on the front table. The docket will close on Monday, July 7th, and in addition to that, I've also had several people in regard to the cabs -- there are the cabs out there, but many of you that are unfamiliar with the Metro area, the Metro, the redline that will take you directly to National, is only two blocks away. So that was very simple. Dr. Dal Pan?

DR. DAL PAN: Okay. Point of clarification from someone who lives on the redline, you actually have to change to another

line to get to National Airport.

(Laughter.)

DR. DAL PAN: But there are plenty of maps there. You even have choices as to how to get there.

Well, I'd like to thank all the panelists from the last two days for engaging in this conversation. I think it's been a rich conversation, lots of debate, lots of stuff for us to think about.

And I'd like to also thank all my FDA colleagues from CDER and CBER who were involved in this, as well. I think we learned a lot. There's lots for us to think about, lots for us to do when we go back and finalize the concept paper.

As Lana said, I urge any of you who have points you want to make to submit them to the docket. I think that's really very important, and I look forward to the pilot starting. I hope we get companies to enroll in it, and I really look forward to the dialogue

we're going to be having over the next few years about how we can best approach the issue of testing proprietary names for medicine. So, thank you all very much.

(Applause.)

(Whereupon, at 3:45 p.m., the foregoing matter was adjourned.)