One of the places where we specifically got feedback, back in December of 2005, was in a public hearing, where we asked the public to tell us what they thought about our current risk communication strategies surrounding drug safety information. Now this afternoon, you're going to hear a little bit more about how we're responding to some of the recommendations, but these are some of the recommendations we got.

What we heard from that is, we should be engaging healthcare providers more. We should be improving internet access for patient information. We need to consider better the balance between benefits and risks in terms of the communications that we disseminate. We need to standardize the multitude of communication tools that are currently out there for the public, for the general public, and for healthcare providers. And we need to address the needs of those with low health literacy, and poor English

skills. We already are addressing some of these. I can assure you of that. And, as I said, you'll hear a little bit more about that later on today.

That report, which was about drug safety, in general, also made two recommendations specific to communication. One of the recommendations was that CDER, which is the Center for Drug Evaluation and Research, should develop a cohesive risk-communication plan. And I believe Paul Seligman will be talking to you about what CDER is doing in relation to that recommendation later on today.

The second recommendation was that Congress should establish an FDA Advisory Committee, a Committee to advise us on communication with patients and consumers, and that's where we get to you all, because we thought that that was a great idea, and it was out there, it was like, yes, let's jump on this, because we absolutely agree.

And we also felt that, well, nice for Congress to do it, but there are administrative procedures that you can conduct that would allow us to do it faster, so the IOM report came out in, I think, September of 2006, and by, I think officially it was signed, the charter was signed in May of 2007, but in June, we announced the establishment of the Committee, which we have the inaugural meeting of today, and this is basically what your functions are in the charter. And I will -- if you guys don't have a copy of that, we'll make sure that we'll get you one.

Specifically, the Committee is designed to advise us on strategies and programs to communicate about the risks and benefits of the products that we regulate with the public, so as to facilitate optimal use. It's there to help us to review and evaluate the research that's relevant to this, and to facilitate interactively sharing risk and benefit information with the public, again, to

help people to make informed independent judgments about use of the products that we regulate.

Referring back to -- and what this particular function is meant to emphasize the two-way aspect of risk communication. I was just going to refer back to John Paling's observation that communication is about what audiences want, and I would say, also, it's about what the audiences need. But certainly, in order to find that out, you need to have a two-way conversation.

The composition of this Committee, which I think you can kind of tell by the variety of people who are on it, was deliberately designed to be different, not just for the sake of being different from other committees. It is unique. It's unique because your function is unique, your purpose is unique, and it reflects that.

We thought that it was extremely important that, in addition to having the

technical expertise to give us the advice that we need concerning risk communication, the people who understand the research, the basic applied, the applied basic, and who can communicate that with us, that it was also important, extremely important, to get the experiential insight, the real-world experience of the people with whom we communicate, with the consumers, with the patients, with the healthcare providers, and the healthcare communicators. And, as a result, we have a much larger proportion on this Committee than any other in FDA of people who essentially bring that perspective to the Committee, and will bring that perspective, presumably, to the deliberations of the Committee.

The other way that this Committee is very different from others is because of the scope, the coverage of the multiple products that we regulate. Other committees have industry representatives. We cover

foods, and drugs, and biologics, and devices, and cosmetics, and radiation-emitting products. And it's hard for us to imagine how one person could potentially representative the perspectives of all those committees. So what we did, instead, was say, well, we will borrow representatives from the other standing FDA committees as a function of what the agenda items are, and use those representatives, as appropriate, for our discussions, because we just couldn't see having one, so that's the other way it's kind of different.

This is the focus, basically, that we're talking about, that this Advisory Committee is charged with. We're talking about looking at general practices, and processes that FDA uses in terms of, we need to -- in terms of addressing the overall needs of the different audiences with whom we communicate. And we're talking about issues that are relevant to large product categories.

Unlike most of the other FDA - well, all of the other FDA technical committees - we are not focused on specific products. We're not focused even on specific product classes, and by classes, I'm using the kind of the smaller therapeutic class meaning of that term. We are focusing on the larger classes, if you're thinking, for instance, drugs, devices, foods, so we will do that.

So this is what we're looking at in terms of the long view. I found this. I'm pretty sure it's clip-art, and it's available to everyone, so I'm not hopefully using anyone's photo that is not being acknowledged. We're looking at the road ahead, with, hopefully, the rainbow at the end. You notice the rainbow is kind of off to the side of the road, so maybe it curves a little bit along the way, but we're going to follow that.

More immediately, today we're going to C- this road is an open one, and in some ways, that's a misnomer, that's kind of not

really a good reflection of FDA's situation. What we should have is kind of guardrails up on the side, because the truth of the matter is, is that our road is not an open road. It is a road that is defined by our regulatory and our legal authorities, and so those guardrails are some of the things that you're going to be hearing more about later today.

We're going to be talking - well, not we - Bill McConagha will be talking about that, Jarilyn DuPont will be talking a little bit about the implications of the FDA Amendments Act for this Committee, because, in fact, you were thought of in that -- what I neglected to say is that, after we established the Committee administratively, Congress also decided that the Committee was important enough that it should be established by mandate. And the FDA Amendments Act, in fact, also established the Committee, and made this a permanent Committee that does not need to be chartered every two years.

FDA Amendments Act also has some specific provisions in there indicating that FDA needs to consult with you on certain topics, and that's what Jarilyn is going to talk about later on.

In the afternoon, we're going to have an open public hearing, which will be followed by some people talking about some key FDA risk communication activities, and then we will -- you will talk about some possible scenarios that we might have to face in our everyday activities.

Tomorrow's focus is on a template, a draft template that has been developed for press releases on recalls of FDA-regulated products. In the morning, you'll hear background, and there'll be an open public hearing, and then you'll start the discussion, which will end in the afternoon, so that kind of gives you the short view of the next things up on the agenda. And that is it for me.

DR. FISCHOFF: Thank you, Nancy.

Would you like a question or two?

DR. OSTROVE: If you would like to, yes.

DR. FISCHOFF: Do we have a question or two?

DR. OSTROVE: I know I wasn't that clear, so come on.

DR. FISCHOFF: Or you were totally clear. Well, thank you, Nancy. And we have you here, so we'll get you. We were fortunate to have some extra time with the Commissioner, so we're running late, but sensibly late. If it's all right, why don't we take our break now, and then we'll have all of the guardrails. We'll start with our guardrails after the break, with the legal constraints, so thank you, everyone. Come back in 15 minutes, punctually.

(Whereupon, the proceedings in the above-entitled matter went off the record at 10:12 a.m., and resumed at 10:27 a.m.)

DR. FISCHOFF: Our first speaker

will be William McConagha, did I get that right, I hope?

MR. McCONAGHA: Yes, close.

DR. FISCHOFF: Close. Okay. Telling us about the legal authorities and protections relevant to risk communication. Thank you.

MR. McCONAGHA: Great, thank you. Good morning, all.

I just want to begin, as others have, just to take the opportunity to thank you all for being here very sincerely. As one at FDA who deals intimately with the oversight of the Advisory Committee program, and also has worked for a long time on risk communication, I am personally very grateful that all of you are here, and that you're sharing your time and your talents with the Agency in helping us to move forward and try to achieve our public health mission, so many thanks.

I have the next 30 minutes or so to

talk to you all a little bit about the speech that FDA regulates. And I think those that organized this first day of the meeting felt that as you thought about risk communication, it would be useful for you to have some background, some context in which to think about the way that the Agency generally regulates speech. And so, with that in mind, the idea here is to give you a little bit of a background, a little bit of a broader context in which to think about the issues that you'll be working on and confronting in the days, the months, and the years to come.

The idea of speech that FDA regulates, the concept is a complicated one, and we could spend an entire day, two days talking about it in great detail. And, obviously, time is limited, so what I'm going to do is talk in fairly general terms. But what I'd like to do is achieve basically two goals when we're done here. The first is just to give you kind of a broad overview of the

types of speech that the Agency regulates. And then, also importantly, to discuss the limits of FDA's jurisdiction over that speech, which is an important part of the message we're trying to convey.

There are many who operate under the misconception that the Agency has kind of unfettered authority and discretion to unilaterally dictate to the world what labels should look like, and what kind of speech is appropriate and not appropriate in commercial discourse, and it is not the case. It's vastly complicated, and what the Agency does always has to be understood within the context of the Free Speech protections under the First Amendment of the United States Constitution.

Now, as you know, FDA has a broad regulatory portfolio. We regulate drugs, biologics, medical devices, foods, which include dietary supplements, cosmetics. And I think it's important, what's often said is that for every dollar that the American

consumer spends, 25 cents of it goes to products that the FDA regulates, and so you can appreciate that it's enormous jurisdiction, and the types of speech involved in the promotion, sale, development of those products that the FDA regulates create a broad number of regulatory issues that the Agency wrestles with.

Now, as Nancy said, the Agency's mission is a profound one, and it's basically to protect and promote the public health. And to be sure, the Agency's regulatory jurisdiction, interest, authority pertains to the products it regulates in and of themselves; that is to say, we are clearly interested in the physical integrity of products. Are foods contaminated? Are drugs sub-potent? Have devices been properly manufactured so they meet their specifications?

Certainly, there's no question that the Agency devotes much of its regulatory

energy and oversight to dealing with the integrity, the physical integrity of the products it regulates, but it is also involved in regulating the speech associated with many of those articles, including speech that appears on labels, in advertising, in the print media. And that's what we're going to talk about in more detail this morning.

Now, certainly, the Agency's interest here is fairly broad. And to help frame the discussion moving forward, I just thought I'd give you one example, and we'll use a prescription drug as an example, to give you an idea of how the Agency's interest in speech and its jurisdiction there really affects a product in all phases of the life cycle.

As we'll talk about in a moment, at the very outset, commercial speech bears on whether or not the Agency has jurisdiction to regulate a product as a drug, or a prescription drug in the first place. And

then at the end of that life cycle, or at the kind of other end of the spectrum we see that even well after a prescription drug may have been approved by the FDA as safe and effective for a specific intended use, that the Agency has all sorts of regulatory interests and concerns with the way that product is promoted, the way that product is advertised, the way that product is sold throughout the United States, even well after it's been used for years, and years, and years.

Now, to discuss, it's hard to generalize about kind of all sorts of speech and put them into kind of individual categories or buckets, and it's an imprecise science. But what I'm going to attempt to do this morning is talk about kind of broad categories of speech, just at least to help you guys frame your thinking about the sorts of areas in which the Agency is concerned, about the sorts of things that are said about the products it regulates, and, hopefully,

will, again, give you some context as you move forward with your own thoughts about risk communication.

The first type of speech that I want to touch base on is this notion of intended use. Under the Federal Food, Drug, and Cosmetic Act, whether FDA has jurisdiction to regulate a product as a drug, a cosmetic, a dietary supplement, or device depends on the intended use of the article. And sometimes this is kind of a counter-intuitive notion. People, think oh, a drug is a drug because of the chemical in the drug.

In fact, the way the law works is that we look to the intended use of the product to determine whether or not that product meets the regulatory definition of a drug. And the example that I offer for you in the slides here is that if a product, an article is intended for use in the cure, treatment, mitigation, prevention of a disease, then it's a drug. And, so, the idea

is, if I were to hold up a glass of water and drink it and say nothing about it, all things being equal, we'd recognize that's a glass of water, and that's fine. But if I approached one of you and said this glass of water will cure cancer, that changes the regulatory status of that drug, at least in so far as FDA is concerned.

Once you are making representations about the fact that that glass of water can cure, or treat, or mitigate a disease, it becomes a drug within the meaning of the Federal Food, Drug, and Cosmetic Act. And so what that means at the outset is the Agency is looking at commercial speech, representations made about an article to confer its jurisdiction over that article in the first place.

Now, the next type of speech I want to talk about here is FDA's regulatory interest in the label. The Food, Drug, and Cosmetic Act defines a label as the display of

written printed or graphic material upon the immediate container of any product. And I think this is a fairly self-evident definition, I think we all basically know when we're talking about labels.

I think it's important to understand for your purposes that the Agency's kind of regulatory interest and authority over the language on labels varies, to some degree, depending on the type of article at issue.

As Nancy mentioned, there are many articles, like prescription drugs, certain devices, some over-the-counter drugs, biological products that the Agency pre-approves. And when the Agency pre-approves a product, it also reviews the labeling that is submitted as part of the pre-approval application. And so, in that case, the Agency, in reviewing and approving the labeling, will have some kind of regulatory interest or say on virtually all of the substantive content on that label. And that's

often referred to as FDA-approved labeling, very catchy phrase, I know.

There are other products, of course, that the FDA regulates, but it doesn't pre-approve. Examples would be foods, cosmetics. Even in those instances, the Agency has a regulatory interest in some of the language on the label. A perfect example would be in the case of an OTC drug that the Agency hasn't pre-approved, but, nevertheless, regulates as a drug. The Agency requires, in certain instances, that certain warnings appear on the label, so that when we all go to a pharmacy and pull a drug off the shelf, and we look at the Drug Facts label, we'll see that there's a warning section there in that drug facts format. Those warnings are prescribed by the Agency. They're required by law to appear on the label.

Now, in some instances, at least with respect to dietary supplements, the law requires that if a sponsor or a seller is

making certain claims about that dietary supplement with respect to the way it affects the structure or function of the body, the label actually has to contain a disclaimer, and this is a disclaimer, it's a standardized disclaimer that appears in the law that clarifies that the claims being made for the relationship between the dietary supplement and the structure function claim being made have not been pre-approved or evaluated by the FDA.

One key thing that holds all of this together, and is true of all the labeling that the Agency regulates, whether it be labeling that we pre-approve, or labeling on products, and labels on products that are for articles we regulate, but don't pre-approve, is that the law prohibits any kind of false or misleading language or presentation to be on the label. And so, the Agency has a regulatory interest in making sure that the labels are truthful, and not misleading, and

that they don't deceive consumers.

Now, I just spoke to you a little bit about labels, and I sloppily used the term "labeling" there a couple of times. They are actually distinct concepts, as far as the law is concerned. The label, as I've just described to you, is the, kind of the written printed graphic material on the immediate container surrounding a product or article.

"Labeling" is defined in the Act as a slightly broader concept. It includes the label, but it also includes the materials that accompany the label. And this could be anything from a package insert, to the professional labeling for a prescription drug, to a pamphlet that is distributed in conjunction with the sale of a product. And, of course, the Agency has an interest in what's said on that label, as well, and on the labeling to the extent that it speaks to the product at issue.

As with labels, the Agency's kind

of concern, regulatory authority here is generally kind of two-fold. On the one hand, the Agency requires that certain words appear in the labeling. For example, with prescription drugs, there is a requirement that the labeling in some form contain adequate directions for use. It could be on the label, or in the labeling, but it's got to accompany that drug.

By the same token, FDA also restricts or prohibits labeling from containing certain information. And this, I didn't speak to this a moment ago, with respect to labels, but this is the case. The most obvious example here is, if the Agency pre-approves a drug, or a device, or a biological product for a specific indication, the Agency prohibits the labeling of that product from basically claiming that the products works for indications for which it has not been shown to be safe and effective. And so, in that respect, both labels and

labeling also deal with the restriction of speech, and the Agency's interest in making sure that what it's approved, especially for products that it pre-approves, is accurately reflected on the label, and not misrepresented.

The next kind of type or area of speech that I want to talk about is advertising. Now, most of the discussion in the world of advertising around FDA products relates to drugs. And as Nancy mentioned, there's actually a regulatory distinction in terms of who has primary jurisdiction over different types of advertising for different FDA-related products.

In the case of drugs, the Federal Trade Commission regulates the advertising for over-the-counter drugs. FDA has primary jurisdiction for the advertising related to prescription drugs.

The rules that FDA applies and looks to in the regulation of prescription

drug advertising vary a little bit, depending on whether or not the advertisement is in print media, meaning in a magazine ad, or in a newspaper, or whether or not it's a broadcast ad, meaning something on TV or the radio, et cetera. But there are two kind of basic themes, I think, that we can cull from this that are worth sharing with you this morning.

The first is that the Agency requires, and I should say the law requires. Let me just be clear about one thing, a little disclaimer as we proceed, these slides reflect, for purposes of simplicity, kind of saying FDA requires, and I've mentioned a couple of times FDA requires, what I really am saying there is FDA requires is a shorthand for saying that the Food, Drug, and Cosmetic Act, or its implementing regulations require. I want to be clear that what I'm talking about are rules that are grounded in the law.

But, to be clear here, the law, and in this case the regulations that the Agency

has promulgated and implemented in furtherance, in executing the law, deal with two basic themes with respect to the prescription drug advertising; and that is, that the side-effects need to be disclosed; that while it's entirely appropriate and protected by the First Amendment that sponsors and companies talk about what their products are approved to do as prescription drugs, that at least there be some balance there, that consumers be alerted to the side-effects, and that's why in a TV ad, we see for a drug, there will often be violin music or light picking on an acoustic guitar, and somebody moving through all of the common side-effects, or significant side-effects that relate to a prescription drug product, so the side-effects is an important part of this.

The other important part of this is there not be kind of unapproved claims. And to that end, this is the kind of the bottom line of the slide here, the idea is that the

Agency, and through this regulation, prohibits advertising from making claims that a product is more effective, more useful in a broader range of conditions, or more useful in a broader range of patients - basically, meaning that it has a use that has not been approved - unless that use has been demonstrated by substantial evidence, or substantial clinical experience.

Now, this is a complicated area. I'm not going to get into whether or not substantial evidence, and substantial clinical experience necessarily equates to FDA pre-approval. What I do want to kind of clarify for everybody is the idea that the Agency has a regulatory interest in making sure that unsubstantiated claims for drugs are not offered in the advertising, or the promotional literature for those drugs.

Now, of course, there are other types of speech that people engage in all the time to promote the products they sell, and

not all of them easily fit into a legal definition of advertising, or labels, or labeling. There's all sorts of kind of oral or verbal exchange, all sorts of kind of conversations that take place. As all of you know, there are drug reps, or detailers, representatives who, on behalf of companies, will visit doctors, offers samples, try and promote the drugs that those manufacturers sell. There are all sorts of symposia in which there's scientific exchange of information. Sometimes it's purely scientific, sometimes it's manufacturer-sponsored. There's also trade shows in which groups or sponsors will have booths that they set up to promote the products they sell.

In all of those instances, there is an opportunity for representations to be made about the products that are sold. And I don't mean to focus solely on drugs, because while that's the easiest example to offer, and the one that is most often talked about,

certainly, these rules play out with respect to devices, biological products, foods, et cetera. But what I want to be clear about is that there is all sorts of representations that are made for the products that FDA regulates, that aren't necessarily written down, that aren't necessarily kind of clearly a television ad. They can be oral representations that a drug representative makes to a doctor, or someone who works in a doctor's office. And, of course, the Agency has a regulatory interest in making sure that the products are not promoted in a way that potentially would mislead people into prescribing or using the products for purposes for which they are not approved.

Now, in the real world this gets complicated, and sometimes messy, because as Nancy pointed out, certainly, the Agency honors the practice of medicine, and recognizes that physicians are going to prescribe drugs for off-label uses, and by

"off-label" we mean uses that have not been approved in the four corners of the FDA's approval of an application. And so, one of the things we're going to talk about in a moment is exactly how the FDA tries to wrestle with what it recognizes is the important public health policy, and end accomplished and achieved by kind of legitimate exchange of information to help doctors who prescribe products off-label to know the most current information about those products; and, yet, at the same time, try and inhibit what we would characterize as kind of the inappropriate promotion of a product for a use for which there's no kind of substantial evidence, or substantial clinical experience to suggest that the product is effective.

Now, I've talked to you about kind of basically five themes or buckets, if you will, types of speech we regulate. There are a couple of cross-cutting themes that emerge from this, that I think are important just to

keep in mind. In the first instance, FDA requires that certain words be used in association with an article. We just talked about that. In other instances, the Agency prohibits certain language from being used in association with an article. In still other instances, the Agency would allow certain language to be used in association with an article, but it would have to first be pre-approved. An example would be a health claim for a food. And a health claim is basically a risk-reduction claim that is associated with a food, and those are pre-approved by the Agency.

Depending on the intended audience, FDA can sometimes prescribe the manner in which the language appears. And the example here is the OTC drug facts labeling, or the Food Facts label that you see on foods. It's a standardized kind of format in which information is communicated. And the reason for it is to empower consumers, so that they

can fully understand what's on a product label, and also compare product labels meaningfully.

The Agency prescribes the format by law in which those labels are organized, and the way the information appears on them to enhance the consumer's ability both to understand, and make these kind of comparative evaluations, so they can make the most informed choices with their consumer dollar.

So that's basically in a nutshell kind of the basics with the cross-cutting themes here, and the idea that FDA does regulate a broad area of speech with respect to the products it regulates, and so it begs the question, well what are the limits of FDA's jurisdiction?

And as I said a few moments ago, the Agency's exercise of authority in this area has to be consistent with the First Amendment to the United States Constitution. And the slide that appears behind you

basically lays out Article 1 to the United States Constitution as it speaks to free speech, and it makes clear that "Congress, the government, shall make no law respecting the establishment of religion, or prohibiting the free exercise thereof, or abridging the freedom of speech."

Now, this term "freedom of speech" is commonly used. People just kind of kick it around, freedom of speech. Freedom of speech is a protection, what does it really mean? Well, the courts have told us that basically it means the right to speak, the right to receive information, the right not to speak, freedom from being compelled to speak, but the courts have also showed us that the right is not absolute. At least it's subject to certain limitations where there can be a kind of co-existence of government regulation, and a recognition that it can be consistent with Constitutional protection.

The slide here basically talks

about the way the courts have evaluated speech, and the protection that's accorded. The highest level of protection, and this is an over-simplification, I should be clear, of a very complicated area. But the highest level of protection goes to political speech, literary speech, scientific exchange. And scientific exchange, of course, is a very important part of this analysis for our purposes, especially as it relates to risk communication. The idea is, the court is saying that if there is true scientific exchange from one scientist to another, that that is the sort of speech that is afforded the highest protection under the First Amendment.

Now, moderate level of protection would be commercial speech, even if it's potentially misleading. And then there's some speech that really has reduced, almost no protection at all. That would be defamation, obscenity, proposing an illegal activity. And

when we talk about proposing illegal activity, basically we're talking about speech that would promote something illegal, like counterfeiting, drugs or prostitution, something of that nature.

The area is kind of jurisdictional interest, and the area where it is most involved in the regulation of speech is in the area of commercial speech, and so it begs the question, what is commercial speech? Well, commercial speech typically involves speech that proposes a commercial transaction, and the factors that we use to identify it most commonly are whether the nature of the communication is promotional. Is it offered in relation to a specific product? Is there an economic motivation?

Now, I compare that to or contrast it with what I said a moment ago, which was this idea of scientific exchange. Now, the reality is that it's easy to kind of put these different categories on a piece of paper, but

in the real world, it becomes complicated.

Imagine a meeting purely scientific in which two scientists are talking about an off-label use of a product, scientific exchange, the sort of speech that the courts have said gets the highest sort of protection. Imagine a discussion in which a drug representative is offering his or her scientific views about a drug for an off-label use to a scientist, that's more commercial in nature. What about a situation in which two scientists are talking at a symposium, but it's been sponsored by the manufacturer of the drug? It gets very complicated.

I just want to take a moment to tell you a little bit about the current test the Supreme Court uses to evaluate whether or not the government's regulation of speech is appropriate under the First Amendment. The test is set forth in a case called Central Hudson, and it's a four-part test.

The first part of the test is

really just more kind of a finding, if you will. The idea is that commercial speech is not entitled to First Amendment protection if it promotes an illegal product or activity, or if it's false or inherently misleading. And a distinction needs to be drawn between false and inherently misleading, versus something that's potentially misleading. Because as we'll talk about in a moment, the question with potentially misleading is whether or not that potential confusion could be cured through some means, like a disclaimer.

If the government chooses to regulate speech, and, as I said, the Food, Drug, and Cosmetic Act does regulate commercial speech in the context of FDA regulated articles in many, many instances, the first thing the courts will ask is, does the government have a substantial interest in the speech at issue? And the courts generally think that promoting public health and safety, protecting consumers from fraud, is a

substantial governmental interest. So as a general rule, the Agency in basically executing the laws, and implementing the laws that Congress has enacted in the Food, Drug, and Cosmetic Act, do not run afoul of this criteria.

The next factor is whether or not the restriction directly advances the substantial interest asserted by the government. Typically, the government has to point to evidence to demonstrate how this works. Let me just give you an example, and this is a pure hypothetical, but let's say the Agency decided under the authority set forth in the Food, Drug, and Cosmetic Act that every over-the-counter drug container should be powder blue. Because the Agency decided that we think well, if something is blue, and you put the black text against it, that's a really great way to read, and it will enhance consumer understanding.

Well, there's no question that the

government would have a substantial - well, I would say there's no question, others might quarrel with this - that there's no -- certainly, the government has a reasonable argument that it has a substantial interest in making sure that consumers understand labels, that they're meaningful understood and read. But the question would be, how can the government justify that having every box, or every container appear in a powder blue color, how does that advance that interest? If the Agency can't defend that it directly advances its substantial interest, then its effort will fail under this factor of the Central Hudson test, and, in turn, be held to violate the First Amendment.

Now, the final part of this four-part test is a question of even if we agree that the Agency's initiative, that the law directly advances a substantial government interest, is the restriction on speech more extensive than necessary? And as the slide

here makes clear, this does not mean that the restriction must be the least severe factor that will achieve the desired end. But the courts will ask themselves whether or not there are less restrictive alternatives. And this has been an area that has been tough, frankly, for FDA and the laws that it implements in recent years.

Since 1998, there have been several significant First Amendment cases litigated about whether or not certain aspects of the Food, Drug, and Cosmetic Act, or the Agency's implementing regulations, or the guidances that its promulgated in support of those regulations violate the First Amendment. Four of those cases are listed for you on this slide, and three of them, the courts held that there was an unconstitutional restriction on the speech at issue because the Agency's efforts failed to satisfy the fourth prong of the Central Hudson test. And let me just give you an example.

Pearson v. Shalala, which is a very interesting case. In Pearson, a dietary supplement manufacturer came to the Agency and tried to get pre-approval for a health claim, actually four health claims for its dietary supplement. Now, when the Agency evaluates and pre-approves a health claim, it does it against a significant scientific agreement standard. And the Agency held that well, you've -- the company submitted a lot of interesting data, but it wasn't enough to meet that standard. The Agency declined to authorize the health claim on the ground that the evidence that the company had offered in support of its claims did not reach the significant scientific agreement standard.

The company sued, and the court held that, "While it might be true that the evidence submitted did not meet the significant scientific agreement standard, nevertheless, it appeared to reach a kind of credible evidence standard", and wasn't it

possible that this claim could be put on the label with some kind of appropriate disclaimer indicating that it might not have reached the higher standard, but, nevertheless, it had met a credible evidence standard with a disclaimer to make it clear that it wasn't quite -- had not quite reached the same level of certitude as other claims that had been pre-approved. And so, the products were allowed to bear this claim with this disclaimer.

Again, it gets at this question of, does the government have a substantial interest in regulating speech? Absolutely. The court said it absolutely did, and that it was absolutely appropriate for the Agency to be concerned about consumer fraud. But the question was, how "paternalistic" are the regulations? Should we allow more or less in the way of free speech in the marketplace, in the marketplace of ideas?

And so, with that, I really just wanted to kind of wrap this up by saying kind

of two things. First of all, it's very clear that the Agency regulates commercial speech in a variety of ways. Speech is required in certain instances, it's restricted in others. And one thing that I really want to impart and share with all of you this morning, as you think about risk communication, and the kinds of messages that you are going to help the Agency craft, or think about, is that the Agency's exercise of authority here, the speech it both offers and restricts, has to be consistent with the First Amendment.

So with that, I thank you very much for your attention, and we're going to move on to the second presentation, which you may be horrified to hear, is going to be from me, as well. And this all seemed so slick when it looked like I was going to be doing one presentation before a break, and then another afterwards, so you may ask yourselves what did you all do wrong that you're going to hear from me twice in short order, but I want to

talk to you a little bit now about kind of the flip-side of what we just talked about. The flip-side of this discussion of the speech that FDA regulates is the speech that FDA generates. And the one thing I can promise you is this will be a much shorter presentation.

We just talked about the ways that FDA regulates speech, and its concerns with commercial speech, and the complicated factors that it considers in trying to regulate speech, particularly the need to be consistent with the First Amendment.

As a general rule, kind of these same concerns apply when the Agency is generating speech. The Agency, as Nancy mentioned, communicates with a variety of stakeholders, in a variety of ways, through a variety of mediums. And, of course, the communications cover a wide range of topics, but for our purposes, the most important is the communication of risk information.

Now, FDA uses several methods to communicate risk to the public, and Nancy touched on several of them, and so I won't belabor them again in this presentation. But I do want to make clear, as I think Nancy referenced, that in some instances, the Agency crafts messages that are for the consumption of the general public at-large, and in other instances, the messages are tailored to more specified communities, like the healthcare professionals. And so, at times, as the Agency is thinking about the messages that it's developing, and the message that it wants to disseminate, it will conscious of the different audiences that it's speaking to. And this gets at a very good question that came up earlier in the context of Dr. Von Eschenbach's remarks, about how is the Agency trying to communicate more concisely and effectively with the public at-large, and use language that is accessible to everyone? And that's obviously an area that is going to be

the subject of much discussion, and we welcome your collective thoughts on.

But let me be clear here that the methods that the Agency uses to communicate with the general public are many. The Agency uses Public Health Advisories, which are basically a form of kind of press release where the Agency will go out and communicate about important information, or significant health-related information related to one of the products it regulates. The Agency also offers press releases about the products it regulates, and risks associated with those products in the normal course.

The Agency also tries to communicate to the public at-large through partnerships, and information networks. The most kind of obvious of these is the Med Watch program, in which the Agency, when it learns about kind of breaking information about risks associated with any of the products that it regulates, will disseminate that information

throughout this entire kind of partnership network, and individual citizens have the opportunity to access that network from any computer, and learn about the kinds of issues that are of concern to the Agency in real time.

The Agency is also developing more and more public service announcements, and these range anywhere from kind of public service posters that appear in common areas, to working with other organizations and non-profits in kind of joint partnerships to develop messages about the products that we regulate, messages about ways to promote and protect public health that we try and disseminate through a variety of vehicles, whether it be in print magazines, or in bus stations, or in common areas of federal buildings.

One thing I want to talk to you about, which is a fairly recent development, is the use of patient information sheets. The

Agency, on its website, particularly in the context of drug risk, has been using patient information sheets as a way to communicate with the public about basically what drugs are approved for, what their risks are, side-effects, et cetera. The patient information sheet is something that the public can access on the Agency's website, and it's a concise summary of information about a drug in terms that hopefully the general public can understand.

It may be that we need to revisit how understandable those terms are, and certainly that's worthy of discussion, but the idea is that the Agency is cognizant of the need to communicate more effectively and broadly with the public, and the patient information sheets represent a recent effort to do this.

The Agency also communicates, as I said, risk information to healthcare professionals directly. As I just mentioned,

there's the patient information sheets. The Agency also has been working on healthcare professional sheets, which are sheets which appear by class of drug, or drug-specific on FDA's website that will basically use kind of more clinical terms to communicate with healthcare professionals about drugs. And, most importantly, in the instance of healthcare professional sheets, about emerging risk information that the Agency is aware of with respect to those drug products.

The Agency is also involved in partnerships and information networks to communicate with healthcare professionals directly. One example would be what's called the CAN, the Counterfeit Alert Network. When the Agency learns of a counterfeit issue, and we're concerned about the integrity of the drug supply in some part of the country, or country-wide, we will try and disseminate that information to those members of this CAN partnership, and make sure that healthcare

professionals, pharmacists, doctors, are aware of the risks that we've identified in the domestic drug supply.

Another way we communicate to healthcare professionals is through professional labeling for prescription drugs. As I said a short while ago, the Agency in the process of pre-approving prescription drug labeling, or restricted device labeling, or biological labeling, will evaluate all sorts of information in there. When they're prescription products, the labeling that the Agency approves is generally directed to the healthcare provider, the practitioner who will be prescribing the drug.

In certain instances, the Agency has also developed its own professional labeling in the absence of any particular application to communicate the safe and effective use of drug products to the terms under which a product may be safely and effectively used for a specific indication to

practitioners. An example would be in our regulations, in 21 CFR, is a listing of the professional labeling for the prescription use of aspirin for cardiovascular risks.

Other means of communication, very briefly, the Agency is also involved in working with stakeholders to help them craft their messages. We work with sponsors in their voluntary recalls, and we help fashion the message that they disseminate. And Captain David Elder of the Public Health Service will talk to you more about that tomorrow.

We also are involved in helping firms with Dear Doctor letters, which is basically a form of communication that sponsors will send to healthcare practitioners to advise those practitioners about risks that have been identified with a drug. The Agency is involved in working with the sponsors to get that message appropriately crafted and out to the healthcare community.

Now, just to be clear, the Agency considers a number of factors in crafting its message. And I won't go through all of these, but I do want to just highlight a couple of them. First of all, as we look at the reliability of the data at issue, when we're communicating risk, is it strictly anecdotal? Is it based on adverse events? And, if so, how much do we know about those adverse events; or is the risk we're communicating based on adequate well-controlled studies?

Obviously, the degree of certitude we have about the risk and the causal relationship, which gets to kind of the next bullet here, the relationship between the risk identified and the product will affect the message that we send out. We're also interested in the magnitude of the risk. Is this a life-threatening situation, or less so, that will affect the urgency, and perhaps the breadth with which the Agency communicates. The extent of exposure. Are we dealing with a

single lot of a product? Are we dealing with an entire class of drugs where we recognize that there's a problem? That will, of course, affect the nature of the Agency's communication.

Does the risk affect clinical practice? Is there a particular message we should be crafting for clinicians and healthcare practitioners? And, if so, we need to make sure that that becomes part of the risk communication, and that it becomes -- that we use the appropriate language.

We also need to kind of consider whether or not we are just simply going to offer facts by way of education, or whether the Agency is also going to communicate advice. It's one thing to say the Agency has learned of several adverse events that may or may not be related to a product, but there looks to be a signal there, versus saying we have identified a risk, and we're so concerned about it that we are going to advise

practitioners not to prescribe the drug. You can, of course, appreciate that qualitatively those are different messages.

Finally, I just want to make clear to you that there are also a couple of factors that we need to consider, one that deals with patient personal privacy. The Agency by law can't disseminate information, whether it would want to or not, that would compromise or jeopardize the privacy of an individual. This most often comes up with respect to kind of HIPAA-type issues, or if we have adverse events, or hospital records that might disclose the identity of a patient. Those have to be appropriately redacted. The Agency has to be very wary, understandably. The Agency certainly believes this is the right thing to protect the privacy of individuals and patients.

I also want to be clear that the firms that the Agency regulates also often have proprietary interest in the information

that they have shared with the Agency, so the Agency may become aware of something that is actually the trade secret property of a company, or represents commercial confidential information, and so the Agency may be prohibited by law from actually disclosing certain aspects of that information to the public at-large. And that also clearly impacts the way we craft our messages.

So the short of this presentation was really just to let you know that the Agency certainly, in addition to regulating speech, is also involved in disseminating and generating speech. And there are a variety of factors that impact the way the Agency crafts its public health message. And as you guys move forward with your important work, we just wanted to make sure that you at least had some of those factors in mind, and some understanding that there is a lot at play when the Agency crafts even a one or two-sentence message that it shares with the public at-

large.

So with that, again, thank you all for being here. I'm very grateful that you've offered us your time and expertise, and I appreciate your attention very much. Thank you.

(Applause.)

DR. FISCHOFF: Thank you very much. We have two other talks on legal issues, and then we'll have a general discussion. This will also give you a chance to sit for bit. Thank you very much.

MS. DUPONT: Hi. I'm going to do this very quickly so that you can get to the next speaker. I want to make sure I have this positioned correctly, and I'm going to apologize in advance. I did these rather rapidly yesterday, and I noticed as I'm sitting there looking at this that there is a typo in here, and I'll explain it as I get to it. In fact, it ought to cause some amusement as we get to the last slide. But what Nancy

had asked me to do was to go through some obligations that have been created by the Food and Drug Administration Amendments Act of 2007. And the first thing you could do is figure out the best way to communicate the title of this, but we are now calling it FDAAA. It has gone through many changes, but this is a very massive act that was passed last September, and has -- and if you look through this -- it was enacted September 27th.

I'm going to tell you now, I'm going to need those lights back on so that I can actually see the slide from here, so if somebody could maybe make that a little clearer, it would help. Thank you.

What this particular Act did, we had a number of re-authorizations of Acts within this particular big Act, including the PDUFA fees, the Medical Device User Fees, Best Pharmaceuticals for Children Act, and the Pediatric Research Equity Act. In addition to that, there are quite a few different

provisions, several of them which deal with drug safety issues, and that's been the primary focus. But the overriding focus of a lot of the sections that were implemented, such as the Clinical Trials Database, the Post-Marketing Safety, some of the recall provisions for food safety, all focus on a lot of communication issues, and informing the public, and letting the public know certain things, and what extent should they know.

And throughout the entire Act, what they did was, is put a number of different provisions that either mandated the consultation with the Advisory Committee, or suggested that it would be advisable to consult with experts on risk communication. And since you all are considered the experts for the FDA at this point, that there may be opportunities over the next couple of years at which you will participate in assisting those particular activities in implementing this Act. Some of them are mandated, as I pointed

out, some of them are just a request, or you might be doing it. We're not sure that you absolutely will.

What I'm going to do is -- what I did was, so that you could have this as background, I'm not going to sit here and read you these particular sections, but I wanted to cite some of them very specifically, and I gave you the specific page number of the public law so that you can go back and read these at some point, if you would like. But I'm just going to go briefly through the different ones that are mandated.

The first set we have are the mandated ones, and the first one is in Title 9, and there are a couple of different reports; in fact, there are many, many reports throughout this whole Act that we have to give to Congress. One of them is due quite early on with respect to some of these, but the first one I have here is one that's due in 24 months, and it's a report with respect to

Direct-to-Consumer advertising. And in the bold and italics you can see where it says, "Shall utilize the Advisory Committee on risk communication in order to study this Direct-to-Consumer advertising." And this one particularly has to do with sub-populations, and how do we increase the information to sub-populations.

The next one is Section 901, and this one -- this is a continuation of the one. It specifically says the type of recommendations we're supposed to make, and what they're supposed to cover. So some of these provisions do limit what they want you to look at. That doesn't necessarily mean we have to only look at those type of things when we're doing this type of report, but there are some mandates that we're supposed to cover in the report itself.

The next one is 906(b), and this is the one that is due in March. And, generally, what this one is supposed to consider, the

statement that is another part of the provision, which I've put in brackets at the very end, and determine if this statement is appropriate for inclusion in television ads.

Well, as we all know, it's very difficult to do an adequate study with respect to that, a good scientific database study in that short of time, so we've been looking at trying to determine what is needed in a study, and bring that eventually to the Risk Communication Committee, and let Congress know how we would proceed with a very adequate scientific-based study on that.

The next one is in the section with respect to the -- I'm sorry. Section 917 is actually the section -- hold on, I'm sorry. These slides are getting confused here. 915 is the Post-Market Drug Safety Information for Patients and Providers. This has to do with the provisions that were implemented with respect to different types of things we're going to be asking sponsors to do with respect

to their post-market activities in promotion, advertising, in their warnings to consumers, that type of thing.

In part of that, they put some obligations on us. And FDA is supposed to put a very comprehensive -- we're supposed to review a very comprehensive website, and put this on the web. We already had a lot of things, and as Bill pointed out earlier, we have a lot of things we already put out. But this is designed, as you can see, there's some parameters. And what they're asking is that the Risk Communication Advisory Committee conduct an annual review, or a review of this to see if we're doing it right. This one is -- they're in the process of redesigning our web pages, and all of this is kind of tied into that, so at some point these will be brought forward to the Committee.

The next one is Section 917, and this is the provision, and I'm sure Nancy has pointed out, this is the provision that

actually set up the Committee. This happened after the Committee had actually been established by us, but they, basically, in effect, indicated that this is what they really wanted, and this is the type of things they wanted the Committee to look at. So they're duties of the Committee, they're encompassed, basically, in the charter that you all have, so there's not anything really new in this particular provision. It's just the authority for setting up this particular Advisory Committee.

The next set of slides are just -- they're not actual mandates, and they may be something that you may never get involved in, but you may also be asked to get involved in concerning certain decisions that we have to make, or that we have to evaluate with respect to this. The first one is in the Pediatric Research Equity Act, which is one of the provisions that deals with research for children. And in the particular provisions,

there are a number of things that we look at in determining whether or not certain absence of labeling poses a risk, or a significant risk to the pediatric patients.

We've been dealing with this over the past couple of years before it was even re-authorized. This is an issue we've dealt with, and we have an Office of Pediatric Therapeutics, and we have a Pediatric Advisory Committee, but there may be an opportunity where we may have difficult situations where they may seek to ask some assistance from this Committee in looking at these particular issues.

The next one is a little more complicated. It's Title 8. This is the new Clinical Trial Databases provision. And I don't know if many of you have heard about this, but, as you know, there's a Clinicaltrials.gov database that NIH, the National Library of Medicine, has operated for a number of years. This originally started

out as an effort to let patients know about trials that were being conducted for significant serious and life-threatening diseases, and for which they could then find a way to participate in these particular trials. And it was an easy way to go on the web and see what there was.

This has now sort of evolved into not just something for patients, but it has evolved into a database where Congress wants a lot of information on there because of the belief, the feeling, the whatever, that there has not been as much honesty as they wish from the drug companies with respect to their particular clinical trials. So this has been expanded significantly to include quite a lot of information. And in that expansion, FDA has also been tasked with a number of different responsibilities in different provisions.

There are several different provisions in here. Now just let me point

out, this is NIH's primary responsibility, and NIH on this one, particularly, on this slide, has the primary responsibility, but they're also supposed to consult with the expert in risk communication. We have a Risk Communication Advisory Committee, they don't, so there has been discussion already with them about whether we'd use this Committee for this particular task, because we are cooperating with them on this.

There are several other provisions in the Clinical Trials Title that you should look at that have to do with a number of different things where, again, it suggests that we should consult with experts on risk communication in determining what the required elements in the database should be, some additional provisions. There's also some very significant issues with respect to adverse events. They want a table posted of certain adverse event information, and there's a significant discussion, and we have a working

group about what should that entail so that it can be provided to consumers in a way that they will understand, and not over-react in the context of what the adverse event is. And, so, there's a working group on that, and it certainly is an area that we would probably want to consult with the experts in risk communication.

The next one is Title 9, again, which is -- I had already pointed out before some of the other ones, but there's some in here that are not mandates, but they're just suggested ones. I've listed a couple of these, and you can certainly go in and look at these. A lot of them deal with what are called now the REMS, the Risk Evaluation and Mitigation Strategies, that we are dealing with with drug approvals. And in those, each of these sponsors have to develop certain communication-type plans. And in those communication plans there may be an opportunity to review those particular plans,

or to determine whether or not these safety issues are being adequately covered in these particular REMS plans. And there are several provisions that talk about using Advisory Committees other than the ones that we have set up for these particular issues. And, clearly, the Risk Communication Advisory Committee could be used for that.

The next one, Section 901, is, again, another preview of television advertisements. And that's similar to the previous ones, and the Direct-to-Consumer advertising has a very specific requirement with respect to the type of thing we're supposed to put in the ad, whether it's a clear and conspicuous and neutral manner. Now some of this is going to entail legally figuring out how to do this, but it also is something that we're going to have to have the Risk Communication Advisory Committee potentially look at and evaluate as to what we can do in this arena. We also are supposed to

do regulations that will come out of the work that we have figured out, whatever study we do, regulations are supposed to come out of that.

904, again, it's Benefit-Risk Assessment issues. And this has to do with how to communicate to the public the risk and benefits of new drugs, and how the new REMS provisions are working with respect to that. Again, in part of the provision it says the Commission may consider including in labeling and any Direct-to-Consumer advertising unique symbols, so this is a new issue of would a symbol indicate something that's riskier, as opposed to just the labeling of the words? Is it appropriate to use symbols? As you know, and maybe you don't know, we've proposed a rule with respect to suntan lotion, that has proposed using symbols, and there's a significant discussion going on about that. Is that more adequate for consumers than something else? And so the same concept is

being asked to be looked at with respect to drugs.

And then, again, Section 905. This has to do with respect to collaborating with private entities on certain risk communication issues. And, again, there are opportunities for that. Then the second part of the provision that set up the Risk Advisory Communication Committee also suggests partnerships for risk communication, and there's opportunity for you all to probably participate in what we set up, how we set it up, and what will be useful to get data out.

Now the last slide is the one that I'm embarrassed because I wrote the wrong title. Obviously, it's not just the Safety of Pet Food. It's the Insuring Efficient and Effective Communications During a Recall, and it's Pet and Human Food. So this one, particularly, has to do with how do you communicate this information?

As you know, this came out of the

pet food problem with Melamine that was discovered and a number of pets died. And there was concern that there wasn't the same type of system for pet recall communications as there are with food, human safety food communications. So there's an effort to set up a website, to set up a network, that type of thing, and also to insure that there is a effective way to let people know how these recalls happen.

Although it's USDA's responsibility on the meat one, there's a huge discussion going on. I think there's a hearing tomorrow, or even today, with respect to that, about how much do you tell the public? Do you go down to the distributor? Do you tell the retail? What is the level of information?

Some of it, again, is a legal interpretation about what we can reveal. As Bill pointed out, there's trade secret, there's all sorts of other issues that come into play during this, but there will be

opportunities for this type of discussion. So that's it.

DR. FISCHOFF: Thank you very much. The next speaker will be Steven Bradbard.

DR. BRADBARD: Good morning. I'm Steve Bradbard, and I am the Team Leader for the Consumer Studies Team in the Center for Food Safety and Applied Nutrition in FDA. And I lead a group of eight social scientists. We're a multi-disciplinary group that contains psychologists, sociologists, agricultural economists, public health and public policy experts, and we do the bulk of the social science research in CFSAN and also provide consultation services across the Agency in terms of social science.

Dr. Neuhauser said earlier today that her interest is what we know from good research and communication. Our interest is in doing good research and communication, so I think we actually have some common things here. And at any given point, we have a

number of different studies at various points in clearance and in the field that either would directly inform or indirectly relate to risk communication. I do hope that we have the opportunity at some point to discuss that with members of this group, because we're very proud of our risk communication portfolio. But that's not why we're here today.

Actually, the title of my talk is FDA Research: Clearance requirements and implications. I guess it could be titled why does it take so damned long for those social scientists to do their research in FDA? And that's what I'm hoping to enlighten you on today.

Okay. I'm hoping that at the end of this presentation you'll have an appreciation for the different hurdles that we go through in terms of developing our social science research, and clearing it, and getting it out. And I hope that you will understand that this is why there is the length of time

between when we propose a project, and when you actually see some results coming.

For those of you who are in academia, it's quite a different process, I think you'll see. And the studies that you might be able to do in a three to six month period, could take us a year and a half, to two and a half years to do. And I assure you that it's not because we're lazy, inept, or under-motivated, that, in fact, we have a very competent group of people, but that we do have certain things that we have to do when we're using taxpayers dollars to do research.

Just real quickly in terms of the importance of social science research to FDA. Our survey research, for example, provides us with population estimates on consumers awareness, understanding and reported behaviors related to food contaminants and pathogens, such as methyl mercury, salmonella, E. coli and listeria, and these results are used then to inform our policies and rules, as

well as our public information, and education outreach that's intended to promote safe food handling and food preparation.

We do experimental research, as well, and that kind of research provides us with important data on consumers understanding of nutrition information, such as the nutrition facts label, health and nutrient content claims, and dietary guidance statements. This experimental research further provides empirical findings that the Agency can use in its decision making, or even in litigation to assert that a claim or a statement may cause consumers to make erroneous judgments, or inferences; that is, mislead consumers.

We often use our qualitative research, such as focus groups, to fine tune the message content for our consumer advisories, education, and risk communication. Our social science data are also used by the Agency's economists to inform the regulatory

impact analyses that they must complete as part of any government rule making.

Now, all of our research is funded with taxpayers' dollars, and supports the Agency's regulatory and policy needs and priorities. We function largely as a research support service within our Center, and across the Food and Drug Administration, and the Department. At times, we provide research support to other government agencies, as well, so we collaborate with the Federal Trade Commission, the Environmental Protection Agency, the Department of Agriculture, and the Centers for Disease Control. So we get our direction from a number of different internal and external entities and stakeholders.

Now, our typical research methods fall under the broad headings of quantitative and qualitative research, surveys and experiments being the quantitative methods that we most often use; focus groups, interviews, and mental modeling are the

qualitative methods.

Let's get into the extramural research process, because this is where it's important for you to understand the various steps that go into almost every one of our studies, and why it is that time lines are the way they are. So this is the general order that we follow in the extramural research process.

Now, extramural studies refer to those in which we use an outside contractor to collect data. Now, you can use an outside contractor for services beyond data collection, at least within CFSAN, our social science group, we design all of our own protocols, we do our own data analyses, so we typically use an extramural contractor as a field service.

Now, don't take the order of these bullets too seriously, because, in fact, it is not a lock-step approach that we follow. It's often a two steps forward, and one step back

approach. Sometimes it's a one step forward, and two steps back approach. We get a request, and have to then get funding in place to conduct a study. We then have to contact our contractor, get them -- give them a head's up, get them to do all of the paperwork necessary to provide a technical proposal, and a cost proposal to the work that we're requiring. That can then require negotiations back and forth between us, the contract's office, and the contractor.

We then collaborate with the Program Offices, for example, one of our frequent collaborators is the Office of Nutrition Labeling and Dietary Supplements at CFSAN to actually design the protocols. And this is not just a single sit-down, and oh, this looks good, let's go. We're talking about repeat iterations of the protocol, oftentimes taking weeks, sometimes taking months. And if there are emerging issues that occur, such as information coming from the

public or industry into the Program Office, protocols change. They're very, very dynamic.

Now, before we clear the protocol with the Center, and FDA, and the Department, you can almost put a sub-bullet in there, because it's not something we always do. There are times where we are asked to actually peer review the research protocol. Now, many of you may be familiar with peer reviewing findings from a study, but this is peer reviewing the protocol itself. And why are we asked to do that? Well, at times, if it seems that the results from our study will be used in litigation, or in rule making, they want to make sure that they have some outside experts look at it and say yes, this is how the study should have been done. We do approve the protocol.

We don't, typically, find our own reviewers. That's done at arm's length, so we then have to contact a sister agency, such as the Federal Trade Commission, and ask the

Federal Trade Commission to identify three reviewers for us. We then have to see if we have money available to pay those reviewers, or drop to our knees and beg them for free reviews. After we get those reviews back from the peer reviewers, we can then move the protocol to approval through the Center, and as needed, through the Agency, and the Department.

As you might imagine, the more sensitive the topic, the more approvals are needed. We have a whole set of guidelines for what types of topics require what types of approvals, so that will determine how long it could actually sit at one particular level of approval before moving to another.

Okay. So once we finally get approval of the protocol from our own people, we then go out to OMB, and we have to get approval from OMB, and also from our Internal Research Involving Human Subjects Committee, which is our IRB. And I'm going to talk a

little bit more about that.

After the period of time required to secure both OMB and risk approvals, which can take typically several months to a year and a half, we then can get into the field, and begin doing cognitive interviews, and pretesting. And from this point on, things move pretty quickly. We do our cognitive interviews and pretesting with a contractor. We then go in the field to study, and then things start to slow down again a little bit.

We do our analysis of the results. But, of course, if these results have a significant impact on -- and significant is defined as a dollar impact on the public and on industry, those results have to be peer reviewed. So, once again, we go out to peer reviewers, maybe the same ones, maybe different ones, to peer review our research findings. And then after that entire peer review process is done, we have to go through, again, Center clearance, Agency clearance, and

possibly Departmental clearance. So this is why it's not two, three months and a cloud of dust. There is, as you can see, quite a process. Let's move on.

OMB - the government is a world of acronyms, as you all know, so I'm giving you some of the ABC's of OMB here, and I'm not going to belabor any of these. Let's just sort of discuss OMB a little bit up front. OMB is the Office of Management and Budget for those of you who have not heard of it. It is an Executive Branch Office that helps the President oversee the preparation of the budget, and it oversees the administration of the budget across the different agencies.

OMB is really the watchdog. It safeguards how the money is spent. And it's up to OMB to determine that the money is really being spent in the interest of the taxpayers, that what we're proposing is not any kind of a duplication of effort, and that what we're proposing does not place any kind of an undue

burden on the public. So to that end, OMB gives great scrutiny to the materials that we send to them. We typically send them a large justification for our research. Then we send them the protocol itself, and then go through a long period of time where we go back and forth with them, as I'll mention in the different notice and comments period.

All of this comes under the Paperwork Reduction Act, and this was enacted in 1980. It was re-authorized in 1998, and it created OIRA, and OIRA is the group within OMB that actually reviews all of our protocols, and it also required that each agency have its own information policy office, and an information officer to carry out information resource management activities. So you've got OMB, you've got OIRA, then you have the person in OIRA who's the desk officer who's assigned to your agency, the OMB desk officer. Then you the Agency's information policy officer, but then you have within each center a policy

person who relates to the information policy officer, and the person in the center doesn't relate directly to the desk officer, so communication goes step-by-step, because, in fact, these are the standard operating procedures for communicating with OMB.

Okay. These are just some of the duties that OIRA has, and let's not spend much time with those. They do, by the way, just the fifth one, they do have, in addition to scientists, social scientists, economists, have statisticians there, as well, so they will spend a lot of time looking over the statistical worthiness of your protocol, your planned analysis, why you're choosing, the end you're choosing for your surveys, if your power analysis is adequate, and so on.

Okay. So what does all this really mean for us? Okay. The Paperwork Reduction Act says that agencies must seek public comment on proposed collection of information through 60-day notices, communicate to OMB

that we made the efforts to reduce the burden of collection to the public. And, also, as I said, have a person in place to do the review, and we have one inside CFSAN, as every center does, of the information that goes to OMB.

Each time that we propose collecting information from ten or more people, you have to file an Information Collection Request, and have it approved by OMB. You want to do nine cognitive interviews, you don't need OMB. You want to do one focus group with eight participants, you don't need OMB. You want to do ten focus groups with eight participants, don't try it. I tried it. No, that's not considered ten individual data collections with ten or less people. They actually add those people up, so no, you can't do that.

Okay. So, as I said, everything we do has to go through our Agency person, and then up through OIRA. And then it has to be announced in the Federal Register as a 60-day

notice. You publish a notice saying you intend to do this research. You make the protocol available to the public, and the public is able to provide comments to an open docket during a 60-day period, called the 60-day comment period.

The Center then that's requesting the information collection, at the end of 60 days responds in writing to these comments in a way that is satisfactory to OMB. Now, fortunately, we can electronically watch the docket during this 60-day period, and watch some of the activity, and some of the questions so we could be prepared for that.

Okay. So after OMB determines that we have adequately responded to these public comments, and any other concerns that OMB has, we then republish in a 30-day notice. And, again, we invite the public to comment on our response to comments, and also any revisions that we've made to the protocol.

Now when this comment period

closes, we again review the comments that the public offered, and we provide OMB with a written response to these comments, and answer any questions that OMB has remaining.

Now, you might say, oh, 60 plus 30, that equals 90, three months. No, that's not exactly how it works, because there is this period of time after comments are collected, that the docket is closed. OMB then provides you with all of the comments. There is a back and forth type of thing that can last anywhere, truly, from weeks to months in terms of the negotiations that go back and forth. So it is certainly not typical that we would get something that requires full PRA through in any time less than seven or eight months, and oftentimes it's gone a year plus before we actually secure OMB approval from the time that we submit a protocol.

Now, here's the good news. Not everything has to go through standard PRA. Focus groups and interviews do not have to go

through full public notice and comment. We have an agreement, a generic clearance agreement with OMB that says we can provide them with our protocols, and with our justification, and they will look at that without asking the public, and give us information as to whether they feel our study is needed, making sure there's no duplication of effort, no outrageous burden on the public in 10 days, a 10-day turn-around.

Now this is a very nice thing. And, actually, this has worked extremely well. Sometimes 10 days becomes 15 or 20 days, but that's not too bad. So we can actually turn around focus groups and interviews pretty well. We do, though, have some very strong stipulations on the use of the data, which I think probably most of you would agree with in terms of it being qualitative data. We have to say in our supporting statement to OMB that this data will not be used to inform any kind of rule making or regulation, and qualitative

research data really shouldn't be used for that purpose.

We also have a couple of other vehicles that are available to us, one that recently was approved by OMB is the generic clearance, is the rapid response survey vehicle, but this is for limited purposes, and also a limited end. You can't collect more than 200 data points using this particular survey method. And there are some stipulations on what you can actually collect.

Finally, there's a 30-day emergency clearance, and this is not something that you can say well, you know, we had some delays around here, so we'd really like to push this thing forward. OMB doesn't really care about your likes. You have to have a good reason for why this research needs to be approved on an emergency basis. And what they will do in that situation is suspend the 60-day notice, and just go out with a 30-day public comment period. So that is what we have in terms of

our OMB requirements.

And just real quickly, most of you are familiar with IRB requirements, and our's may not be too different from your's, but I did want you to know a little bit about what we do. As you can see, according to the Code of Federal Regulations, there is a stipulation that we have an IRB to review Human Subject Research. This applies to studies that are conducted, supported, or funded in whole, or in part by FDA. So if FDA is involved in a grand, or some kind of outside activity, and has a significant contribution to that, it has to go through our IRB. It's not just the studies that we own within the Agency, so if we're working with universities, or we're working with a center of some kind, it has to go through our IRB.

Let's see. Here's just some more information about studies that require IRB. All studies, studies involving focus groups, tests or surveys, that the others don't really

apply to us as social scientists, except private database information. If we, in fact, are using data from another study that used live human beings, and most of our studies do, we are required to go through our IRB, as well.

Now, as I said, our IRB is actually called the RIHSC, the Research Involving Human Subject Committee, and that is FDA's institutional review board. Every FDA center has a RIHSC liaison who reviews the packages that are submitted in support of the human subject research, and this process typically proceeds concurrently with OMB review, usually taking a lot less time.

The RIHSC liaison forwards recommendations to the RIHSC Committee with the statement that the study be exempt from review, or be considered for expedited, or full review. Fortunately, almost all of our social science studies are considered to be exempt from review. Now that doesn't mean

they're not reviewed, and it also doesn't mean that you can self-review. It means that the RIHSC has determined that it doesn't have to go in front of the full committee in order to be exempt.

Now, the exceptions would be if we're dealing with a particularly sensitive topic, or if we're doing social science research in a high-risk population, such as pregnant women, or in a population of - I guess we call them non-adults - I guess that makes them children or teens. That has to go through at least the regular, if not full, review.

Okay. Just lastly, beyond OMB and the RIHSC, there are other factors that influence the time line for social science research in FDA, one of which is funding cycles and budgets. And just to give you an idea, for those of you who may have followed this, just recently, the federal budget, the FY 2008 budget, which began on October 1st, the

money was actually made available to us. So in the middle of 2007, we started making our request for fiscal year 2008, which means that we submitted for review different research ideas that we had. And these ideas were approved before the end of the fiscal year, September 30th, because the new fiscal year begins October 1st. They were approved, but we didn't have any money for them. It's not until you actually get the money that you can do the research. The money has just been made available for the research that was planned last summer, so there are these funding cycles in budgets, and it's very important to keep this in mind, that unless you've got some discretionary funds available, you typically can't just go and say okay, we're going to do it now. Even a focus group, unless you can find the money somewhere, but, normally, there are agency budgets, and you have to take that into account.

Other factors, as I said, internal

collaborations. For example, on our health and diet survey, and food safety survey, it's not even a matter of just collaborating with a single program office. You have to collaborate with multiple program offices, and the document goes around and gets signed off from each.

Sensitive topics, as I mentioned before, can slow down the research process. Emerging science and new research. We had a research study that we originally had approved back in late 2003, and while it was sitting at OMB, there was some new research that came out from industry, and from academia that actually made us go back to the drawing board. And so we had to pull what we had from OMB. We had to redo the protocol. We started the process again, and we recently did that study. Okay? So there can be factors that go into slowing things down.

Finally, the SOPs at the level of the Center, Agency, and Department, depending

on the issue, itself, can have a real strong effect on the time line of the research that we do. And that's all, and thank you very much.

(Applause.)

DR. FISCHOFF: Thank all three of the speakers, and I think this is going to be extremely important in us understanding both what we can and can't do. Could I ask you to come up? We have a fairly rigid schedule in that we have a public response period beginning at one. I'd like to give everybody an hour for lunch, but if maybe the three of you could come up, maybe find one more chair and join Nancy at her table. That will at least give you a mic, rather than having you stand near the rostrum. And let's see if -- if you're willing to have a few -- since there's no mic over there, so maybe you could sit over, maybe join Nancy. Yes, I just thought there was a mic over there, and I think the transcriber would like -- okay. All

right. We had a tech fix for that.

Okay. So we have eight minutes for questions. Let me start off with a question, see if I understand. So you may not want to do this, but let me ask if this would be a strategy that would fit within the law. So Commissioner Von Eschenbach said that we're beginning the Sentinel - the Sentinel program is being developed. Seems to me, the Sentinel program will be producing a set of signals from the field about post-licensing, post-marketing effects, some mixture of good and bad news. The general structure of that good and bad news one can predict, some known effects will out to be smaller or larger than we thought, so there will be some totally new effects. Those will come out, and you will have very little time to respond. So one could imagine, I'm not committing you to doing this, but one could imagine within these constraints that you're under, kind of developing prototypical protocols, field

testing them in sufficiently diverse audiences, letting the other people worry about the dissemination channels. And then, perhaps, using this response, this rapid response to do kind of the quick testing, the 200-person constraint is actually a fairly severe constraint, because if you think about different populations who might -- if you wanted to do it in two or three languages, that's 200 in total. But is that a kind of structure that you're capable of working in?

DR. BRADBARD: I think it is. And just keep in mind, as well, that things -- that is a structure that I think we can work with. And, in fact, the recent rapid response survey approval was meant to give us some flexibility to adjust to changing needs. And OMB is open to our coming to them and saying you know what, this is what's happening right now in the world, and we are operating at a deficiency in terms of being able to provide some quick data to the people who need it.

So, in fact, we can come up with a proposal to OMB to say increase the end in surveys like that. There are things that we can actually do to try to get OMB to be responsive. But yes, that type of thing certainly would work for what you're discussing.

MS. MAYER: A point of clarification about advertising, speech in advertising. It was my understanding that for the purposes of promotional advertising, off-label use, even if it was supported by substantial evidence, was not permitted outside of an indication. Do I have that wrong?

MR. McCONAGHA: You've hit on a very tough issue. I think the Agency generally takes the position that the advertising should not discuss indications that have not been evaluated by FDA, and approved by FDA, with respect to prescription drugs. Nevertheless, the regulation does point to the idea that the -- whatever claims

are made about the drug should be based on substantial evidence, or substantial clinical experience, and so I think there's some in the regulated community who take the view that that doesn't necessarily equate to FDA approval. And, so, I don't -- I think that in the interest of getting it right, and not misleading you, that what I should probably do is try and get you an answer that I can disseminate to you guys through Lee, or Dr. Ostrove. But I think it's one of these areas that is complicated, and because it gets at the heart of kind of First Amendment issue, and its relationship to the regulation.

There are some who question whether or not the indication needs to be FDA-approved, if, indeed, they possess substantial evidence, or substantial clinical experience to suggest that a product is useful for an off-label use. And, so, that's kind of a non-responsive answer. I think what I would really say is that it's really a complicated

area that's at the heart of the First Amendment debate right now.

One thing I could commend you to is the fact that the Agency just put out a draft guidance this month to deal with the dissemination of kind of reprints, or peer reviewed articles, which isn't exactly on point, but I think helps dramatize the way the Agency is trying to draw appropriate distinctions between what is appropriate for scientific exchange, and what needs to be limited by virtue of the fact that a certain indication is not FDA-approved. And, so, I would urge you to read that, and what I can do is go back, huddle with some of the lawyers at FDA, and get you a more precise answer in that days to come.