UNITED STATES OF AMERICA

DEPARTMENT OF HEALTH AND HUMAN SERVICES

FOOD AND DRUG ADMINISTRATION

CENTER FOR DRUG EVALUATION AND RESEARCH

FDA'S COMMUNICATION OF DRUG SAFETY INFORMATION

WEDNESDAY, DECEMBER 7, 2005

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The meeting came to order at 8:00 a.m., Dr. Paul Seligman, Chairman, presiding.

PRESENT:

PAUL SELIGMAN, M.D., M.P.H.	FDA
SANDRA KWEDER, M.D.	FDA
SCOTT GOTTLIEB, M.D.	FDA
NANCY D. SMITH, Ph.D.	FDA
DOUGLAS THROCKMORTON, M.D.	FDA
TERRY TOIGO, Rph, MBA	FDA
ANNE TRONTELL, M.D., M.P.H.	FDA

PANELISTS:

KEVIN OUTTERSON	WVU College of Law
RUTH DAY	Duke University
MICHAEL S. WOLF, Ph.D.	Feinberg School of Med.
ELIZABETH ANDREWS	RTI Health Solutions
SIDNEY WOLFE	Public Citizen's Health Research Group
DIANA ZUCKERMAN	National Research Center for Women and Families
RAY BULLMAN	NCPIE
REBECCA BURKHOLDER	Natl. Consumers League
ANNETTA CHEEK	PLAIN
ELLEN LIVERSIDGE	
CAROL ROTHKOPF	Time Inc.

AGENDA ITEM **PAGE**

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

8:14 a.m.

CHAIRMAN SELIGMAN: Good morning and welcome to the FDA's Part 13 hearing on Communication of Drug Safety Information. My name is Paul Seligman. I'm the Director of the Office of Pharmacoepidemiology and Statistical Science at the Center for Drug Evaluation and Research at the FDA. I would like to welcome you all and thank you for being here at what is an unseemingly early hour for most people here in Washington, D.C. Thank you for being here on time and I do apologize for starting a few minutes late.

The purpose of today's meeting is to seek public input on the Center for Drugs current risk communication tools for health care providers, patients and consumers. We are going to, today, have a series of panels of individuals as well as individuals representing organizations who have self-identified themselves to speak on today's topic. I would encourage anybody else in the audience who wishes to speak or to address the panel either today or tomorrow to sign in with Lee Lemley at the front desk. We will have time this afternoon at 2:45 for additional speakers should any of you so desire to

address the panel.

We are also accepting, as well, any written information, any statements, any materials that you wish to submit to the record. Also, at the front desk in addition to a sign in is a packet of information that contains both today's agenda as well as copies of many of the risk communication tools that many of our speakers will be addressing and talking about today.

Let me take then a quick moment and have the Members of the FDA Panel who are here in front introduce themselves, I guess, starting with my right. Nancy, you want to introduce yourself?

DR. SMITH: I'm Nancy Smith. Is this on?

CHAIRMAN SELIGMAN: You have to push it up, so it's up.

DR. SMITH: I'm Nancy Smith. I'm the Director of the Office of Training and Communications in the Center for Drug Evaluation and Research. My office handles most of CDER's communication with the general public. We have the communications with the Trade Press, the toll free phone number and email system that people can write in to the CDER web page and the public service announcements that we develop. Many of our materials are on display out in the lobby

if you would like to look at them.

DR. THROCKMORTON: I'm Doug Throckmorton. I'm the Deputy Director in the Center for Drug Evaluation and Research. I'm also the head of the Drug Safety Oversight Board in the Center for Drugs.

DR. KWEDER: Good morning. I'm Sandra Kweder. I'm the Deputy Director of the Office of New Drugs in the Center for Drug Evaluation and Research.

DR. GOTTLIEB: Good morning, Scott Gottlieb. I'm one of the Agency's Deputy Commissioner.

MS. TOIGO: Good morning, I'm Terry Toigo. I'm the Director of the Office of Special Health Issues in the Office of External Relations in the Office of the Commissioner.

DR. TRONTELL: Good morning, I'm Anne Trontell. I'm the Deputy Director of the Office of Drug Safety in the Center for Drug Evaluation and Research.

CHAIRMAN SELIGMAN: Thank you all. The FDA role here today is to be good listeners and good askers of questions, because we're really interested in the input that you all have today. We hope that you will be giving us an honest appraisal of our risk communication tools and to provide us information that

we hopefully can take back and ways that will help us refine and improve our efforts at communicating important information about the safety of drugs.

One quick final word before we move on with our program, I want to thank the National Transportation Safety Board for allowing us to use this facility. I want to remind you all that no food or drink is allowed in the auditorium.

CHAIRMAN SELIGMAN: I did my job. And also to remind you that because we are essentially two levels underground, you will find that cell phone communication doesn't work very well down here and that Blackberrys actually work intermittently. But we are going to encourage most of you to turn off your Blackberrys because of the fairly sensitive wireless communication system that exists within this facility and we find periodically that use of a Blackberry often gives us some feedback in the communication and electronic system.

With that, I would like to introduce Dr. Steven Galson, who is the Director of the Center for Drug Evaluation and Research to provide some welcoming remarks. Dr. Galson?

DR. GALSON: Thank you, Paul, and thank you to all of you for being here. This is among the

most important issues facing CDER, the other centers and the Agency and this is a tribute to all of the people who planned and put this meeting together. It's very, very important to us and we've got a great panel up here, including one of our Deputy Commissioners, senior leaders from the Commissioner's office and CDER. We're listening very carefully.

This is an area that I think is very dynamic in the center, the Agency, the Government as a whole and the pharmaceutical industry. I really can see us making changes and improvements in this system in what we do to communicate to the public over the next few years. And this meeting is a very, very important part of making sure that we hear from all of you about your ideas and how effective you think the systems that we are currently using are.

As you all know, CDER approves human drugs and CBER, biologics, when it has been determined that the benefits of the products outweigh the risks for a specific intended population. Part of this process involves deciding on acceptable product label language. But once these products hit the marketplace ensuring the safe use of drugs and biologics becomes a shared responsibility of the whole health care system of the many, many partners that work together.

These partners include health professionals, patients, care givers, manufacturers and others that you are all aware of. I think it is very clear to many of us working in the drug safety area that a great deal of the individual adverse events related to drug use and larger drug safety issues that impact many groups of patients can be traced to one of many types of flaws somewhere in the interdependent web of communications in the U.S. health care system.

Although, we all share responsibility for ensuring that risk communication information is timely, accurate and easily accessible, there really isn't a broad agreement about which risk communication strategies and methods are most effective and efficient and which don't work, particularly the ones that we are currently using that may not work very well.

Many questions remain about how to best convey risk information to an increasingly ethnically diverse population and increasingly older population and many among us with limited literacy skills. I know we look forward to hearing your views about many of these matters over the next couple of days.

Stepping back a few steps, in May 1999,

FDA published "Managing the Risks for Medical Products Use," which laid the framework for our efforts to reduce the risks associated with the products that we regulate. And then in February 2005, HHS Secretary Leavitt announced plans to expand existing risk communication channels and establish new mechanisms to provide targeted information to the public. You all are very, very familiar with many of those steps.

I would like to briefly highlight the current tools, the major current tools that FDA uses to communicate about drug safety information to the public. They include the newer patient information sheets and health professional information sheets, talk papers, public health advisories, press releases, our longstanding MedWatch Listserv Safety Updates, our patient safety news, video presentations, our targeted CDER educational campaigns that Nancy mentioned quickly, and our all important millions of hits per year CDER Internet site.

Over the next two days, we are interested in hearing about your experience in using these tools to get risk information about the products that we regulate. For example, are the tools that we have just listed user-friendly, accurate and timely? Do you believe that the risk information that is

communicated is appropriate and helpful to help and assist health care professionals who make prescribing decisions?

Is the information presented useful and appropriate for consumers? Is our Internet home page and the sub-pages easy to navigate and is the information presented on the Internet site easy to understand? How can FDA improve outreach to special populations, including the elderly and non-English speaking populations? How can we convey information more effectively to those with limited health literacy skills?

Even though we have two days to listen to your comments, we have some topics that are outside of the scope of this public hearing for one or another reason. First, because there may be a separate process underway to get public input about them or we have just decided to define them outside of the scope, so that we have enough time to talk about the important things that I have mentioned already.

The first is the useful written consumer medication information, CMI. These are the sheets that are handed out in pharmacies, industry promotional materials, including direct consumer advertising. I think you all know that we recently

had a separate Part 15 hearing on this issue. In addition, drug labeling, including medication guides and patient package inserts will not be discussed here. Again, there is a very separate, a highly regulated process that goes into producing those materials.

And the draft guidance that we put out in the end of the spring on FDA's Drug Watch for Emerging Information. As you know, we had a public process on that. We got a lot of comments in and we're currently in the process of summarizing those and then we will make an announcement about changes in that draft guidance.

Dr. Seligman, in a few minutes, is going to present the questions as posted in the Federal Register on September 26, reflect some of the things that I mentioned already. Once again, it's really my pleasure to welcome all of you, to thank those of you on the FDA Panel and the public panel for the time commitment that you are putting into this really critical area in public health and drug regulation. And I'm really looking forward to hearing about the important testimony that is going to be presented today and tomorrow. Thanks again. Paul?

CHAIRMAN SELIGMAN: Thank you, Dr. Galson.

Let me just take a quick moment then to review the questions that were published in the Federal Register that really serve as the basis for our two day hearing with the hope that both panelists as well as members of the public will directly address these.

The first question relates, as Dr. Galson already mentioned, to the strengths and weaknesses of the communication tools. Let me just ask, there you go, you should be able to see that on both screens. These include the patient information sheets, the health care professional information sheets, public health advisories, press releases that we use, the MedWatch Listserv Safety Updates that we provide through our listserv as well as our partners' program, the use of the patient safety news vehicle along with our colleagues in the Center for Devices, as well as any comments that you have related to the use of our Internet and websites.

We're clearly interested in learning what information and data are available regarding the awareness, use and perceptions of the effectiveness of these communication tools by health care professionals and by the public in general. Do these tools provide the right kind and amount of risk information or other information that health professionals need in making

informed decisions about whether to prescribe a drug product and that the public needs to make informed decisions about whether to use these products?

We also ask and are interested in knowing how easily accessible and understandable are the FDA's Internet-based sources of drug information, since the Internet is increasingly used as a vehicle for disseminating and providing information to a wide range of practitioners as well as patients. We are clearly interested in understanding to what extent FDA's patient focused communication tools provide useful information for people of low literacy skills.

And finally, we're interested in learning what mechanisms our offices should consider in conveying risk information to special populations, particularly those who don't speak English, the elderly and other individuals.

With that, we will start by introducing the first speaker, Dr. Outterson from West Virginia College of Law. Dr. Outterson?

DR. OUTTERSON: It feels a little strange to have my back to you, so if you don't mind, I'll do this a little bit. My topic is on limited English proficiency and some of the material is a little broader than just the risk communication strategies.

It would apply also to drug labeling and some other issues, but I'll focus mainly on LEP.

Because there's a lot of people in the United States that are limited English proficient and there may well be an issue under Title 6 of the Civil Rights Act, if you go into a hospital in the United States today in an urban center, you will find that they have to provide translation in dozens of languages. And yet, when these same individuals walk out into a community pharmacy, try to fill a prescription, they get it in English, even if they don't speak English at all.

The amount of linguistically isolated households 11.9 million, this is census data, these are people in which no one in the household speaks English, you know, to any significant degree. You can see how LEP is going up, and I'm assuming that you are getting this on your screens. Good, good, all right. The companies are responding, especially in the area of Spanish. Then this is what Nexium puts up on their site in terms of contraindications for Nexium. They do have something in Spanish.

They don't have it in other languages, as far as I was able to find. One interesting issue is that this is not, obviously, a drug label, so they

don't have to run this through the MAPP process for FDA. But if you compare the contraindications on the Spanish site to the English site, you notice on the English site the label itself talks a lot about the interactions with antibiotics, whereas the Spanish site, and that is the complete contraindication section of the Spanish language site, doesn't.

So there are differences. They are not exact translations and there's questions that you may want to think about. But I also put this up here thinking that perhaps not all of you are fluent in Spanish, and if you can imagine being faced with this, an Urdu or an Arabic, how difficult it would be for you and that's the sort of situation people are facing who are LEP in the United States.

CHAIRMAN SELIGMAN: Just to interrupt you, you get a free coupon on the Spanish site.

DR. OUTTERSON: Yes, you get it on the English site as well.

CHAIRMAN SELIGMAN: Okay. Okay.

DR. OUTTERSON: But I wasn't able -- the English site is a macromedia flash and I couldn't copy and paste it, whereas the Spanish site -- you know, who knows why. All right.

LEP and health, and I'll do this very

quickly, you know, we know from a lot of data that we need people to be able to understand what the doctor is saying in order to get an accurate diagnosis and care and follow-up treatment. A lot of studies, many more than I have cited here, on the connection between limited English proficiency and the lack of access to health care and the resulting impact on health.

Less has been said about the impact on prescriptions. And there's three studies here I want to talk about briefly. 25 percent of the LEP patients didn't understand the prescription instructions. There was a study on Vietnamese and Chinese patients who were particularly expressing difficulties in getting this data. And in the Northeast, I believe this third study was in Boston, when they did provide interpreters to patients who were in an in-patient setting and about to go out-patient, the number of scripts tripled compared to the baseline and the number of filled scripts tripled.

Now, you would think the companies would take this as a tremendous marketing opportunity. The understanding here is that these people were being under-filled, under -- you know, not getting the scripts that they should be getting, because they were LEP.

One interesting thing just from the law side, I am a law professor, is that these LEP issues are not really dealt with in these documents that, you know, LEP issues for prescription drugs. The Health and Human Services has a broad document, but it doesn't talk about LEP access in the context of risk communication strategies, drug labeling or any of the things that we are talking about today. It's not mentioned at all in that document, which is very extensive.

It's not mentioned in these national standards. And the only dual language thing that I could find, and I may be operating under ignorance, as you spoke at the beginning, you may well have programs in other languages that I'm not aware of, is that under MAPP 6020.7, you do permit dual language, you know, labeling. But it needs to be an exact translation. The companies provide the translations and the certification.

That doesn't extend to encouraging the companies to do things in other languages nor does it extend to things that are not labels, you know, the other risk communication strategies, the other DTC strategies, which I know isn't the focus today, but all of these issues there is no guidance, as far as I

can tell, from FDA or HHS on LEP issues with prescription drugs.

There is an interesting intersection with importation. And this is a quote from William Hubbard, a lot of the drugs that are coming into the country, when they to the FDA seizures, they find that they are labeled in foreign languages. And that makes them illegally imported in the United States. It is very difficult to get data here on who exactly these customers are. We have in our mind the 68 year-old person from Minnesota going on the bus, but, you know, I suspect that, and this is an area that I have tried to get data from IMS, they really don't have it when it comes to the immigrant population.

But I suspect that a proportion of these people illegally importing are actually bringing drugs or having drugs shipped from their home countries. We have 47 million people in the United States who do not speak English at home. We have an immigration boom in this country. There is a lot of people who are first generation immigrants. And what if somebody from the Philippines is bringing -- who doesn't speak English well, is bringing in drugs in Tagalog approved by the National Drug Regulatory Agency in the Philippines, you know.

I'm not a fan of unrestricted importation, but that's an interesting issue that these people are actually looking for linguistically appropriate, culturally appropriate labeling and drug information. They are not getting it in the United States. They are resorting to a potentially very unsafe means to go get it. So there are some cross issues here.

These are the countries when the FDA did their, you know, countries of origin and if we look at these, you'll see a lot of these connect back to the top LEP languages in the country and these were -- they didn't seize in Los Angeles, for example. I believe that one was in the northeast. If they had done it in Los Angeles, they probably would have seen a different mix of languages coming in.

Here are the top 10 LEP languages: Spanish, obviously, is the big one. And the companies and the FDA, I noticed a couple of the brochures out today on the table are in Spanish. People are doing good efforts there. But there are a lot of other languages and these are the people who don't speak English at home and either speak English not at all or very poorly. And these are the numbers based on the 2000 census.

Okay. And these languages that we might

expect, you go to the next 10 and it begins to, you know, track into languages that I can't even begin to tell you anything about. I suppose Gujarathi, yes, I guess it's a language from the subcontinent of India, but you can see these are significant numbers. Now, you may think 20,000 Hindi speakers is not sufficient, we shouldn't be too concerned about that.

But the Office of Civil Rights, the Title 6 regulations which control what hospitals have to do, for example, in terms of translation, their safe harbor if there is 3,000 patients or more, they have to translate all their documents into the appropriate language, if that hospital faces 3,000 people or more in a given year to satisfy the Safe Harbor. This is the Health and Human Services Office of Civil Rights Safe Harbor on limited English proficiency.

So if you scroll back up, every one of these languages in terms of drug manufacturers and then it turns to the FDA companies. I mean, exceeds the threshold at which translation is required under the Safe Harbor. It's an interesting issue, one that I'm not aware whether our Health and Human Services or FDA has really looked at in the past.

The question what does your PhRMA companies do in terms of their advertising and the

support they can get from FDA, you know, the MAPP document that I referred to earlier could be seen as a restriction on their ability to do non-identical translations. And also, it imposes a question of what should FDA and the Center for Drugs do as well?

One place maybe to look for some guidance, the White House had a mini-conference on health literacy and health disparities this year. Some of their, let's see if this works -- some of what they recommended happened in terms of prescription drugs and LEP. They want translations. They want it available in various languages. And they want CMS to track the availability and accuracy of patient education in multiple languages.

You know, that document is available. It might be something that could help you look at what experts are saying in this area. Just another example, I went on the Wal-Mart site, one of the biggest pharmacies in the country, and Wal-Mart, if you dig through it, you eventually get to the ability to click on espanol. And when you click there, there is a third-party provider who does this information. You get it in Spanish.

I tried hard to find any other language on the Wal-Mart site and I don't think there is. I could

be wrong. But if it took an English speaker looking for an hour, you know, and I couldn't find it, then imagine somebody who spoke Urdu or Japanese or something, they wouldn't be able to find it.

So efforts are being made and they are being made in the largest category. My suggestion is that the Civil Rights Act of 1964 actually requires federal contractors and Health and Human Services to evaluate these issues for limited English proficiency. The OCR's Safe Harbor is 3,000. We would see that with at least 20 languages, and as far as I can tell not much is being done.

So some options. Revise LEP regulation that came out in 2003 to look at compliance by the drug companies for Title 6. That would also require, in essence, that the FDA revise MAPP 6020.7, you know, to permit and to require, you know, other languages to come in, you know, in addition to what we do currently with Spanish and perhaps something in addition to the identical translations of labels, which is what I think is permitted under 6020.7 at this point.

I want to be careful on number three. What I'm really talking about is that, you know, these patients see themselves, you know, possibly as not having good options on importation. One possibility,

you know, one place that we can get culturally and linguistically appropriate labeling information in Tagalog today is from the Philippines National Drug Regulatory Agency.

And one possibility would be to permit, and a lot of these would be through ethnically specific pharmacies, the parallel distribution, not only of the English language materials and risk communication materials, but also to permit the Tagalog materials or the Urdu or the Arabic materials from the appropriate NDRA, you know, in the foreign country to be provided as well or to be offered as well.

It wouldn't require the FDA to reinvent the wheel. It wouldn't require massive translation. It would require some flexibility or at least evaluation of these issues. I suggest monitoring what the drug companies are doing in the foreign language materials, you know, particularly ones that are not approved either by you or by the National Drug Regulatory Agency in the foreign country. Maybe in that as well encouraging them to provide these materials.

And all of the above, I think, needs to be in consultation with the communities themselves that

are involved in this. I don't represent any of these communities, you know, and they certainly should have a strong voice in what you think about and what you do in this area. Paul?

CHAIRMAN SELIGMAN: Thank you very much, Dr. Outterson. We have a moment if there are any questions from the Panel? Fine. Thank you.

DR. OUTTERSON: All right. Thank you.

CHAIRMAN SELIGMAN: And we'll hopefully have questions at the end of the session. The next speaker is Dr. Ruth Day from Cognition Laboratory at Duke University.

DR. DAY: Good morning, everyone. Our topic is risk communication. Risk communication takes place within a wider system. Within this system, we have to consider the prior knowledge of the user, be it the health care professional or the patient or consumer. Perceptions of risks that are now presented to the person, their comprehension and how their mental representation is then affected can then affect prior knowledge and so forth.

So in order to understand how to communicate to people, we need to know more about this entire system. The basic question is how do people understand risk information? The answer is with

difficulty. Many reasons for this, it's a heavy information load oftentimes, complex/technical information, but we're going to focus on Cognitive IN-Accessibility.

Cognitive accessibility is the ease with which people can find, understand, remember and use drug information and hopefully in a safe and effective manner. Cognitive inaccessibility occurs when people have trouble with any of these processes.

In our lab we study a variety of type of drug information from TV ads, Internet to hardcopy and look at a variety of risk communication tools and today we're going to focus on the ones under study for this meeting. Our basic research approach is to do some cognitive analyses of the existing information, obtain quantitative measures and calculate cognitive accessibility materials, and then develop enhanced displays of these same information based on cognitive principles and then perform experiments to test the effects of the original displays versus the enhanced displays on various cognitive processes, including attention, comprehension, memory, problem-solving, decision making, behavior and ultimately health outcomes. All of this is based on a variety of cognitive principles, a few of which we will focus on

today.

So load, how much is too much information? How many risks can we present? Most people look at numbers, number of risks, pages, words and so forth. The important thing is the cognitive load. Have we presented the information in an enhanced way that reduces the amount of mental work? Then the absolute number of risks and other types of information doesn't matter as much. It's the cognitive load that counts.

Let's look now at one type of risk side effects or adverse events. Underlying this domain of side effects, there are two underlying principles or dimensions: severity and frequency of occurrence. Within severity, we could have risks that are serious, moderate, mild. Frequency of occurrence could be common, less common, rare and so forth.

Current practices to reduce information load often focus on just the serious ones and the common ones. So we might ask how serious is serious? How common is common? The answers depend on where we look. We can look at all kinds of data, but we can also look at the perceptions of the health care professionals and the public. So let's look at some typical terms used to describe severity.

Our basic approach extracts severity terms

from existing drug information sources, both professional, such as the PDR, and consumer, such as the CMI or pharmacy leaflets. We then perform semantic analyses on these terms, have people judge the terms and then compare public versus professionals on this. We find there are two basic semantic categories for severity terms. A descriptive term, such as serious or mild, and action terms, what to do if a certain side effect occurs while taking a drug, such as call the doctor immediately or monitor symptoms.

Does it matter? In order to answer this and other questions, we use the following procedure. Participants see a term and then judge its severity. We imbed the terms in a sentence frame, such as this side effect is and then plug in a severity term or if this side effect occurs, plug in the action term. People then judge severity terms in one of two conditions. In the numeric condition, they write a ballpark number from 1 to 100, where 1 equals none or no severity and 100 is maximum severity.

In the visual line condition, they place a term along the line. We actually have a physical line on a cork board and they tack on a little card with the name of a side effect on it. The same anchor

points. And here are the results in terms of clusters from maximum to none. In the top cluster of perceived most severe is rush the emergency room, fatal, life-threatening, get emergency help with no differences among them. The next cluster, the next, next, next, and we can now number these clusters from 1 to 5 for most to least perceived severity.

So now we can ask how serious is serious? The answer is well, kind of in the middle category here. If you think about the FDA definition of serious and complex, you can look at many places and in one Institute of Medicine report here were some of the indicators. Results in death, life-threatening, require hospitalization and so on. We have just seen that the public perception is quite different. So there is a mismatch in understanding of what serious means.

Obviously, there are implications for how we communicate risks. Was there a task effect between the numeric task and the visual task, the number of people either rate the term giving a number or they place the side effect along a visual line? And the answer is they are identical and that's very interesting, because there are implications for people of low literacy, low health literacy and low numeracy.

What about frequency terms? We use the same approach and here are just the semantic categories we identify. There is a big category of frequency terms like common, infrequent, frequent, likely and so forth. There is one of degree, less, more, somewhat. Occurrence category, observation, reported, observed, noted. Causation, probability, number, experience and then that catch-all category which is empty of any information and it just says side effects include.

All right. Here is our procedure. You see a term and judge a frequency. Again, there are sentence frames that are appropriate to the semantic categories. People judge frequency using those same two conditions, one or the other. And here are the results of the frequency clusters from always to never will occur and people's perception. Causes is way at the top. Then there is another category and they go like this from 1 to 6 from always to never.

So how common is common? Well, right there, it's in one of the middle categories. Again, implications for risk communication. We have looked at the severity and frequency terms. Now, let's look at the side effects themselves. In experiment one, we preselected side effects to fit certain severity

categories, life-threatening, dangerous, troublesome, variable.

And then people would see an individual side effect, one at a time, and judge in the severity. This time it was a numeric scale from 1 to 5. And we used both the descriptive terms and the action terms. Does it matter? Well, here we are plodding perceived severity from least to most for each category of side effects and, as you can see, the results are identical. And that's great because this says that we have multiple options for how we communicate the severity of side effects that might be used with different populations.

What about prior knowledge? The same experiment, same setup, but now we compare laypersons, which I have already shown you, with experienced individuals. And these in the first display are pharmacy students and you see two things. One is the overall patterns are exactly the same and the second thing is that the more experienced participants have severity ratings that are higher, perceived severity is higher.

By the way, this goes up as the amount of experience in pharmacy or other health care professions increases. So, in general, laypersons

underestimate the severity of side effects. And by the way, they overestimate frequency of occurrence.

So now, in another experiment on side effects, we took those same four categories of side effects and we added in some technical ones, such as anaphylactic shock and defined each one. And now participants would see a side effect and judge the resulting health state that a person would be in if he or she experienced these side effects. And this was a scale from 0 to 100 from death to perceived health.

And here now are the severity clusters. And I'm showing them to you in a slightly different way. These are the first four clusters and then all of them. And notice they run from the worst health state at the top down to the best. In blue, we have the technical terms, which sound pretty bad, and so we would expect them to be high perceived severity. But look at the red ones from the predetermined life-threatening category, and especially those in the next to the last cluster.

The public really does not understand the severity and consequences of these and we found this repeatedly in different kinds of studies. For example, unexplained bruising. Most people would just discount and not be too interested and even slurred

speech as well. So perhaps educational campaigns could be fashioned around public understanding of such information.

Now, let's turn to the issue of representation. What do we mean by this? Well, we mean external representation, the design and display of information, be it electronic or hardcopy, and then how that gets represented in people's minds. It could be similar, it could be quite different. The risk communication tool kit we have been asked to talk about today has many different types of information, mostly electronic, mostly hardcopy, most of them both.

Here is an example of a patient information sheet for Adderall and just to blow it up a little bit, it starts with two FDA alerts. Let's look at the second one. And I have just highlighted some of the terms we have been talking about. Sudden unexplained death sounds pretty bad, so we'll have those kinds of things in red. But look at the frequency terms. Has been associated with, reported in a small number of cases, reported, can cause and it continues over it may lead to, etcetera.

So now, let's see, yes, all right. The rest of this patient information sheet then has a bulleted list and the green arrows show those

questions that are user-friendly and seem to come from the medication guide design, which is very good. And we have done research that shows that people do understand these kinds of things in the medication guides and they work here too as well most likely.

So in green you have the bullets and you have the side effects in the red there. And we start seeing some of those terms, can result in and the last one is particularly interesting, so it says possible decreased growth and weight loss. That's the name of the category, that's a very good thing to do, that's called coding, and then describe what the category is. And where it says Adderall may decrease growth and cause weight loss.

So is it less likely to decrease growth, because it says may, and is it much more likely to have weight loss, because it says cause? So consistent use of these terms would be very helpful for conveying the right kind of communication about risk. So as you look at the overall design of the rest of this, it looks very good. There is a lot of cognitive principles being observed.

But if you look at the readability of the different portions, when people lapse into text, the readability goes way up. It's 12th grade and beyond.

The metric doesn't go higher than 12th grade. And the bullets tend to be much lower. This is between 8th and 9th grade reading level. So something to think about. Also, the use of passive, when people lapse into text, they tend to write impassive. There is huge research literature in psycholinguistics showing that people have trouble processing passives quickly and efficiently and accurately. So there are implications now for comprehension, memory and behavior from all of this. And that will then drive how we provide risk communication tools.

So let's talk now about alternative ways to represent information. We could think about using linear orderings. We have already seen that people can determine, you know, linear arrays of severity from high to low severity, high to low frequency, high to low health state or good to bad health state. We could have a representation that looked like this where you have the mild side effects for something on one side, life-threatening on the other.

Please, do not misunderstand, however, I am not recommending these pictograms. No one would be happy and delighted to have diarrhea or drowsiness and nausea, I presume. And if you put a life-threatening pictogram up, it's not necessarily the case that

that's going to happen. There's only a certain probability. So those would be misleading. We could use other kinds of pictograms. I'm a little reluctant to use them without testing, but at least here the face on the left looks like the person is in discomfort as opposed to the one on the right in distress.

So you could start providing even with just a simple line or with indicators on each end along with indicators of what to do. Everybody recognizes an EMS truck, so that could be an indicator as well. So here are implications for persons with low health literacy or limited English. And perhaps educational campaigns could be fashioned around understanding risks from different types of representation.

Another type of representation is the matrix and here we have the two underlying dimensions with high and low frequency, high and low severity. And here we can see that although there are some very serious health risk for a particular hypothetical drug like chest pain and slurred speech, that at least a user can see that well, it's very severe, but there's a very low chance it's going to happen.

And seeing the picture of how these

different risks are displayed across different drugs can be very informative. So keep in mind here what we are talking about. We're talking about alternative representations of the same information. The representation will be text, bullet lists, linear ordering, matrix, lots more that we have studied in our lab and others.

And all of these lead to cognitive consequences. Each form of representation has cognitive consequences. That means, in fact, some perception, attention, comprehension, memory, problem-solving and ultimately behavior and health. So in our previous research with other types of risk communication tools, we have learned some lessons and here is the basic lesson, and that is in the original or currently used risk communication tools, comprehension of risk is very low. It is often around the 20 percent level.

However, once we use the exact same information, but provide it in a more cognitively enhanced way, performance goes up significantly or even dramatically. So I think it is time to think anew about alternative representations for providing risks. There are a variety of educational campaigns that can be launched around this for side effect

severity highlighting some of these ones that the public does not understand, such as unexplained bruising.

And also how serious is serious for maybe selecting another term. And how common is common for selecting another term? Actions to take if side effects occur and working with alternative representations across populations.

For health care professionals, I think it is very important to understand what the public perceptions of risks are like. And then in providing information to patients, very often the patient counseling tools of various risk communication tools tell the provider what to say and there is not enough attention to how to say it and to use translation equivalence for the same term where appropriate. And also, alternative representations to the health care professionals will help them speak in a more natural way or provide visual information in a way the patients can really get.

So in terms of the risk communication tool kit for today, it's time to look at the report card, as a university professor that's getting towards the end of the semester here. And so in terms of the cognitive report card, the variety of risk

communication tools we have been asked to look at is just wonderful. The intent of each is terrific. As for the execution, it is variable across the different tools and within a given tool and even within a given example of a tool as we saw with the Adderall example today.

In terms of the terms that are used, the consistency of the terms, even within the same sentence, translation equivalence, alternative representations, readability, etcetera, etcetera. So the time is of the essence. It's at the end of the semester. We need to provide great risk communication. We have done quite a bit, but there's still time to go back in and make some adjustments before the final report card is issued, so to speak, which will never happen, of course. Thank you very much.

CHAIRMAN SELIGMAN: Dr. Day, are you willing to give us a grade on that last slide?

DR. DAY: To be continued. All the homework has not been submitted yet.

CHAIRMAN SELIGMAN: Just one quick question before we go to the next speaker. I think two or three slides before the end when you talked about cognitively enhanced materials, one of the bars

showed the potential for 100 percent comprehension.

DR. DAY: Yes.

CHAIRMAN SELIGMAN: Is that just an example or are there --

DR. DAY: This is not hypothetical.

CHAIRMAN SELIGMAN: It's not hypothetical?

DR. DAY: No. It depends on what task you use, so we use a variety of cognitive tasks from free report, people study materials and then report what they can remember or by looking at the materials what they can understand. We have a recognition task where we give them a bunch of risks and say was this in the materials you just studied and so on and so forth.

The one that I have shown here at 100 percent is a very interesting task and it is a number estimation task. After studying the materials, we say to people oh, about how many risks or side effects, we generally say side effects, are there associated with this drug or did you just study? And they give a ballpark number. And for example, in a study where we looked at pharmacy leaflets, there were over 50 side effects and people grossly underestimated. They said about 6 or 7, something like that.

And then when we gave them an opportunity to restudy that information in original form and then

asked them again about how many side effects are there, they still didn't improve. There was a 2 percent improvement. But on a random basis, half of the people got the same information in a new representation that was more spatial in its layout and they improved by, in this one study, 80 percent. And then when we did the same thing with medication guides, they then improved. So they went up to not only the percentage improvement, but 100 percent correct.

And the one that is shown here is actually for Accutane. The Accutane medication guide has 100, it's a little over 100 side effects sprinkled throughout the document. Something like 107, I'm a little bit off on that, but over 100. And after studying it again in a new representation, they know how many there are as well as increased performance in what they are and so forth.

So to answer your question, this slide is not a hypothetical. These are based on real data.

CHAIRMAN SELIGMAN: Thank you. Other questions? Dr. Gottlieb?

DR. GOTTLIEB: Do you have examples of organizations or entities that you think discipline their communications and take account or take measure

of the kinds of principles you talked about today? And are there any qualities that you can speak to about how they approach communications that enables them to do this? If you're not going to give us a report card, maybe you can let us see some others.

DR. DAY: You could name just about any organization and there would be implications. And I look at the materials provided by companies. I look at materials provided by FDA, consumer groups. Everything that has been talked about this morning is in the tool kit. Any time you are trying to communicate to people, you want to enhance materials so that they can get it. Get it quickly, accurately, understand it, remember it and know how to use it.

So I've done research sponsored by the USP. I used to put out a lot of patient information. I recently attended an American College of Physicians Foundation conference where some of this came up. I think all the stakeholders need to provide risk information in a cognitively enhanced way so people can get it and know what to do about it.

If you would like to mention a couple of other domains, were you wanting me to comment on how well these different groups are doing?

DR. GOTTLIEB: Some examples of -- not

necessarily examples of some of the groups who are doing well, I don't want you to out anyone, but just what you think their approaches are internally that enables them to take measure of these principles. How do they discipline their process?

DR. DAY: Well, I guess the groups I know the most about are within FDA and I'm --

DR. GOTTLIEB: Fair enough.

DR. DAY: -- delighted, generally, at the openness and eagerness to adopt this evidence based on cognitive principles and use them. Unbeknownst to me after presenting research in various settings, some of the medication guides have been revised based on the cognitive principles and other things as well. So I'm delighted the FDA is tremendously open and proactive on this.

Within companies, I think there are different issues. A lot of times documents are serving multiple needs. There is a legal need. There is a regulatory need. There is a communication to whoever the users are need. And very often, I think that the legal need then drives putting in more risks, just so the company is covered should anything happen. But then how do you handle that increased load? It's not necessarily the case you should leave most of them

out. But there are ways to present them in more cognitively enhanced ways.

And when it isn't provided well, people often ask me well, why does that happen? Are they trying to hide things? And I don't know the answer to that, but I do know that unless you know quite a bit about how mental processes work, you don't really know how to provide the information in cognitively enhanced ways. It is very easy and I've used the term today lapsed into text. I was surprised I said that this morning. I hadn't planned to. But it is true.

It's a nice way to say it that when we lapse into text for a communication tools, then it is as if we have to be very professional and erudite or something. And then if you look at the sentences that are provided, they get longer, more complex, more passive, tense and so on. So everything I showed this morning was not very favorable towards text, but you can write text more in an oral mode of communication with shorter sentences and some repetition of words that link successive sentences and so on.

So I think that perhaps all of these groups, consumer groups are often very user-friendly, but still have problems in presenting things, so that people will get them, because the writers and

providers of the information don't know enough about basic cognitive principles to apply them to their specific needs.

CHAIRMAN SELIGMAN: Thank you, Dr. Day. I'm aware, here at the Panel, of at least two or three additional questions for you, but I think what we will do is move on to the next speakers and ask the Panelists to save the questions for the time designated. Our next speaker is Dr. Michael Wolf from the Institute for Health Care Studies and from the Program and Communication Medicine at the Feinberg School of Medicine at Northwestern University. Dr. Wolf?

DR. WOLF: Thank you. I would like to first thank the FDA for hosting this public forum. I'll be presenting, oops my slides are jumping ahead of me, a summary of findings of the work that Drs. Terry Davis and Ruth Parker and I have conducted related to medication risk communication. The topic is actually going to cover a little bit more. We're going to go to the warning label, which is actually something that has been constantly ignored for the many decades that they have been used, but compliment what is in the patient information leaflets.

This we view to be both a patient safety

and health literacy concern of national importance. And for today, the focus again will be on the development of these warning labels and how they are used and if at all we determine them useful.

The broader question we are looking at is do patients understand how to safely take their prescription medications and how do they get that information? Our team has long studied health literacy, which over the past year has become an issue of national concern with reports from the Institute of Medicine, Agency for Healthcare Research and Quality. It has been something that has been included in Healthy People 2010. And the body of literature over the past decade has grown to about nearly 200 publications in professional journals.

Health literacy at the individual level is defined as the capacity to obtain process and understand basic information and services needed to make appropriate health decisions. At its very essence, it's can you understand and use health information? According to the Institute of Medicine, which is based off of the National Adult Literacy Survey, the findings of which are going to be released very soon for the most latest wave, that nearly 90 million adults in the United States, that is half of

the adult population in the United States, may have what we call limited health literacy.

They have difficulty understanding and acting on health information. Whether it be that information is received by text, from oral communications with their provider or through other sources, whether it be the Internet or other information programs. These individuals will have difficulty when they encounter complex or unfamiliar text, which is often found on medication labels.

And we have done a lot of research as of recently. Myself and my colleagues recently reported in the September 26 issue of the Archives of Internal Medicine the first study to date to link literacy, low literacy or low inadequate health literacy to poor physical mental health. Low literacy has a comparable impact on poor physical health, physical function, that to a diagnosis of cancer or chronic obstructive pulmonary disease in our study and it is also linked to a higher prevalence of what would be potentially prevented chronic conditions.

The problem here with getting information off of medication labels, in particular, is that -- or even these patient information leaflets, is that the patient responsibility has increased for medication,

self-management in recent years. More medications are issued, so the average U.S. adult fills nine prescription medications a year. The elderly fill even more, an average of 20 prescriptions per year.

And then the question becomes where do patients get information on how to safely administer all these drugs? The problem is compounded in the elderly, so it's not only they are taking more medications, but they are facing a cognitive and therefore literacy decline as well. So this becomes a very significant challenge to address.

So where do patients actually get information? First, there is the physician who is viewed as the learned intermediary and the one responsible for communicating medication information to the patient. However, physicians' time is limited for counseling on specific prescription drug administration issues and studies have also shown, one of ours in particular, that physicians are not adequately trained to communicate with patients on such topics in a manner that patients can understand.

Secondly, there is the pharmacist, whose time and environment is also limited. Research also suggests that pharmacist counseling does not occur to the extent that it should. This might be viewed as a

system issue. As more prescriptions are filled, there is less time to offer such counseling services.

Third, we can focus on the patient information forms. The industry generated forms that are currently available. Most forms -- very few drugs right now have, what would be, the regulated medication guides that offer useful information to consumers. But right now, a lot of the information might be generated by the industry. It may not, it may vary between one pharmacy to the next, as far as what information is provided to the patient.

And it's usually quite dense, filled with text and studies have shown that patients oftentimes throw them out after they use them or read them once or may not even read them at all. In one of the studies that I'm going to be talking about today, less than a third of patients ever looked at the patient information sheet that is attached to the medication package.

Finally, we arrive at the warning label, also known as the auxiliary or secondary label for medications. This is a label that is a second label attached to the medication bottle that often duplicates information or bullets or highlights the information presented by the patient information

sheet. This is what we wanted to direct our attention to as it has been missed by the keystone dialogue back in the late '90s and has really never been of an issue and is currently unregulated.

So what is the value of these warning labels? Well, first off, they display warnings or special instructions on how to administer a drug. They are placed directly on the drug container. They use icons in addition to text to convey the message that needs to get across, which might be useful for many patients with low literacy skills and they also use color to have them be distinguished from the primary label. They oftentimes use shorter messages compared to the information sheets, which is usually dense full of text.

But the question still remains, are they useful to patients? Our team has extensively studied this issue over the past few years and recently this has gotten quite a bit of attention. This was in the New York Times October 25th issue, a story now warning about labels in the Science Times. It was on CBS Early Morning News, ABC News and it is coming up again in Forbes Magazine to tackle the issue of how do you convey warnings across different contexts, whether it be issuing on children's toys to car recalls. But

this was the big focus, that there is this concern about how do we convey adequately this information on warnings.

We represent Louisiana State University Health Sciences Center, Northwestern and Emory Universities. We have recruited and conducted extensive in-depth interviews with more than 500 primary care patients across three different states, and we have targeted patient comprehension of the warning label message, the icon and the use of color.

What we have found is that, overall, comprehension of existing warning labels is poor. Less than half of all patients comprehend existing warning labels and this is, again, in light of the fact that among the same group of patients, they are not getting the information from the patient information sheets.

So what was the issue? We closely examined the problems and found that the text was clearly too difficult. The reading difficulty was beyond that of what most patients could comprehend. There were too many steps per label and icons are confusing and often in discordance and send a different message than what the text does.

So when patients gravitate towards the

icon because the text is confusing, they find something that says something completely different. The example for this was there is a very simple label that says "Do not chew or crush, swallow whole." Well, a lot of patients, a significant proportion of patients, went to the icon and tried to make a combination of the icon and the text and came across with chew or crush before swallowing and came up with something completely in opposite of what you wanted them to do.

The use of color on labels is also random, but patients impute a meaning in what we refer to as a traffic light schema where people think, well, red means really important, danger, yellow means caution and any other color, green, white, blue, that is issued might even be viewed as not as important or more instructional or optional.

And, again, the overall clarity of the message to be conveyed is problematic with unfamiliar terms frequently being used. So even if you got the reading difficulty to a point that was low enough, you still have to look at the terms that are used that people do not understand. Another example for this might be "For external use only," which many patients could not figure out what this meant. And if you have

seen the icon, I can show you later, it is even more problematic.

So the big picture. Hundreds of warning labels are created by several companies and now, we're seeing an increasing trend of companies such as Walgreens and Target starting to reconsider and think about creating their own labels, and Target in particular has created their own new bottling format which seems to be very promising but, at the same time, we need to look at how labels are going on.

There is also no universal set of warning labels because of this. So you can go to the same pharmacy -- actually the head of the American College Physicians Foundation quoted in the New York Times said that her and her friends looked at about -- had four or five different bottles of statins that they all were prescribed from different pharmacies and saw different precautions. Not all of them had the same ones.

Another example of that would be the "Do not take with grapefruit juice," which most patients still didn't understand why that was on there and not all patients got that message as well. So it's very confusing how information is presented.

There are no standards or regulations to

guide warning label development. There has to date been no consumer involvement in how these warning labels are created and the use of color has been random.

Their language concordance still is missing, so most labels do not have an adequate translation. And, as my colleagues have mentioned earlier, the problem also is that even if there is a translation, it's not sure that that is an adequate translation or whether or not it has been used. There is something like a back translation. A double back translation has been used to make sure that it is clearly concordant with what you want to say, and it's also culturally appropriate.

And there is also not any assurances that the best evidence drives warning labels. So do we have a clear route that yes, this indication should be placed into a warning label? How that happens, it's still not very certain. Many people would argue about the issue of having a statement that says "Do not take with grapefruit juice."

Here are some examples we have found of the multiple labels that are available to convey the same message, different icons, different messages. This we feel is likely to be very confusing for

patients and especially for icons, we need to promote the need for one symbol much like a stop sign that can be universally accepted by patients, so they can learn the meaning over time.

Just as a red octagon symbolizes stop, icons can be used. I'm thinking also back to the Mr. Yuck for the poison symbol. People can start to learn what these symbols mean and understand the message that might be conveyed or the icon can become more helpful.

So a road map here. We propose that the process for developing and using warning labels, so that they can be useful and compliment existing patient information forms that this process could also be applied to, we need them to be standardized and regulated.

Message text should be written below a 6th grade level, according to our research, which is lower than what has been issued before and it's also very difficult to get at, but in a very short message and, as Dr. Day pointed out, not thinking just in a text way but how you might speak the language. That might be more beneficial.

The number of steps to be included on a label should be minimized. As many patients impose a

traffic light schema to the use of color, this should be considered for labels. Most importantly, include consumers in the development process. Get feedback from them to confirm the efficacy of these labels. It's clear that we need to go to those who will use them to involve them in the process of developing new and better labels.

Ultimately, for warning labels to be an adequate source of risk communication for medications, we will need universal icons as well as messages for patients to learn over time their meaning. And, finally, warning labels must be part of a comprehensive medication risk communication strategy that is integrated.

These labels should reiterate what is on the patient information leaflet in a similar manner and we need to train health professionals, the physician, the pharmacist, the nurse, on literacy and medication risk communication issues, so warning labels can be complimentary to what is told to patients by their health care provider.

And I have included some contact information since I did a more broad presentation of this. We have much more detail of the studies that we have actually -- are currently under review and should

be published in early 2006. Thank you.

CHAIRMAN SELIGMAN: Thank you very much, Dr. Wolf. I anticipate we'll have some questions for you after the last speaker. The final speaker in this session is Dr. Elizabeth Andrews from RTI Health Solutions. Dr. Andrews?

DR. ANDREWS: Great. Thanks very much. I spend much of my time and I have spent many years of my career as an epidemiologist evaluating drug safety using observational methods and evaluating the effectiveness of risk management programs.

What I have come to learn is the importance and the necessity of saying risk communication is a multidisciplinary effort that must involve people who are experts in communication in psychology, psychometrics, survey research, economics, health policy and epidemiology, as well as involvement of the health care professionals and consumers, as the last speaker mentioned, in order for us to truly develop communication that is understood by individuals and they can act on that information.

What I would like to do is to provide two examples in the area of risk communication and those examples should demonstrate that patients and physicians can understand quantitative risk

information and make informed choices, and that risk perceptions and risk attitudes are highly dependent on the manner in which the risk information is presented.

The first example is of Alosetron or Lotronex which was reintroduced into the marketplace after being removed because of concerns of irritable, excuse me, of ischemic colitis and complications of constipation. It's a drug for Irritable Bowel Syndrome.

It was reintroduced with a multi-component risk management program that also included specific information targeted to patients, so that they could understand the benefits but also the risks and what actions they should take at signs of possible serious adverse events.

That information was provided through physician counseling, also through a physician-patient agreement form that both the physician and patient sign and through a medication guide that is provided both by the physician and by the pharmacist in the actual packaging of the drug.

To evaluate the impact of this risk management program, a number of things were done including an evaluation of both the communication process and the knowledge of patients using a

voluntary patient survey, which involved recruiting patients through their physicians or through the product labeling and collecting data at baseline and in follow-up, and this study has included throughout the re-launch and use of Lotronex 35 percent of all users.

When we look at the process measures for the communication process, we see that there is -- and these are data from December of 2003, but the current data show the exact same percentages. We see a very high level of compliance as recorded by patients on all of these process measures, including did you discuss the risks and benefits of Lotronex with your doctor, did you receive a medication guide, did you read the medication guide?

Now, in addition to these process measures, a number of questions were added to the patient questionnaire based on extensive cognitive testing.

The rest of the questions were also tested, but through a rigorous process of cognitive testing to make sure that patients or people with IBS, most of whom had received Lotronex at some point, could understand the question and understand the response category so we were likely to obtain accurate

information directly from the patient. And, as you saw with the results from the process measures, compliance or knowledge was extremely high on all of these knowledge questions.

Now, what really matters in health care is that patients understand the risks and understand what they are supposed to do in a circumstance where they may be experiencing an adverse event that could be ameliorated or prevented, and that is what we observed through the questionnaires aimed at these patients.

Now, that wonderful knowledge might have been achieved because this population of patients is highly motivated. They are the ones that have the most severe IBS symptoms. Their doctors may be the most compliant because they have signed up to participate in a program and have agreed to counsel patients.

And this excellent awareness and knowledge might also be partly a result of effective communication that has used multiple approaches, including the careful design of the physician-patient agreement form and the medication guide, the consistent messages and the reinforced messages of the overall program.

The lessons we take away from this

experience is that it is incredibly important to carefully develop and test not only the communication tool and set of tools that are intended to be used, but also the measurement instrument for the evaluation of the effectiveness of those tools.

The next example that I would like to present relates to hormone replacement therapy. As we're all aware, the Women's Health Initiative clinical trial was terminated early and the conclusion was that the long-term benefits of hormone replacement therapy in terms of decreased risk of hip fracture were not greater than the health risks of heart attack and breast cancer.

However, that study did not consider the patient perspective on the use of hormone replacement therapy to relieve the motor symptoms, vasomotor symptoms of menopause. Therefore, my colleagues undertook a risk/benefit tradeoff study and that study was aimed at estimating women's willingness to trade risks of heart attack and breast cancer for control over their vasomotor symptoms of menopause.

The study also afforded us the opportunity to test two different methods of describing risk as absolute risks, also as relative risks, to determine whether the method of stating the risk made a

difference in the patient's willingness. The study then estimated the maximum acceptable level of risk that individuals were willing to take in order to achieve specific levels of symptom control.

This was done by conjoint analysis method, which provides a rigorous conceptual framework, and the data are collected through eliciting choices, preferences from patients after being presented with very real life choices.

The study was conducted using a web-enabled survey method and choices to patients were provided in which the efficacy features of treatment were described in terms of the symptom severity, frequency and duration of hot flashes and night sweats. Then risks were described either as relative risk or absolute risks.

The study was designed very, very carefully with lots of testing of the survey instrument and the prior information that is given to the individuals before they begin their tradeoff tasks, and then the study design includes a number of internal validity checks to assure that biases do not exist within the response behaviors. The study included 523 women ages 46 to 60, the vast majority of whom were experiencing or had experienced menopausal

symptoms.

And this, if you can see it, is an example of one of the series of tradeoff tasks that individuals were presented with. They were asked to look at Treatment A and Treatment B and then at the bottom to determine whether they felt that A was better or B was better. And they are presented with a number of attributes of the treatment and different sets of responses or levels of those attributes.

And then in this particular case, risk of heart attack within 10 years is described as a 30 percent increase over their baseline risk. Most of these women said they felt that their baseline risk was the population baseline risk. In the case of the other questionnaire that described absolute risk, that information was presented as a 10 year risk of 65 per 1,000 or 6.5 percent.

So what we can do from the data from a study like this is estimate a curve or maximum acceptable risk curve that shows the maximum acceptable level of risk for a particular event that a patient is willing to take for a particular level of symptom control. So you see the expected pattern of this curve.

And what we show here on the data on

myocardial infarction risk is you see on the Y axis is the maximum acceptable risk and on the X axis the level of benefit. Women who were presented with risk as an absolute risk were willing to accept a higher level of risk to achieve therapeutic benefit than those who were presented information as relative risk. And, interestingly, the dashed yellow line shows the estimated risk, absolute risk level determined from the Women's Health Initiative Study.

When we look at the same graph for breast cancer, we see a similar pattern, that women were willing to accept a higher level of risk to achieve therapeutic benefit if the information was presented as absolute cancer risk. I would like to make three points about this slide.

First of all, the confidence intervals are pretty tight here, unlike the previous graph, showing that there probably is real separation between the types of presentation of the risk data. In addition, the women were much less willing to accept a risk of breast cancer than a risk of heart attack. And also that, at a lower level of benefit, they were unwilling to accept much risk at all.

So our conclusion from this experience was that women had a higher tolerance for risk when the

risk was presented as an absolute risk, and that women were actually willing to accept risks that were greater than the Women's Health Initiative risk estimates to obtain good symptom control for their menopausal symptoms.

And what we take away from both experiences is that patients and physicians can, indeed, understand risk information and make informed choices. However, to assure that happens requires very careful design and testing not only of the communication tools, but also of the evaluation instruments that seek to measure the effectiveness of those, and that evaluation needs to consider the various high risk and special needs of the different populations that are the intended patient groups for particular treatments.

The type of risk that is to be communicated is incredibly important. The media tends to report risk as relative risk and sometimes that can be misleading, especially for events that occur infrequently. For example, a twofold or doubling of the risk of bone cancer sounds pretty alarming, but stated as an increase from three out of a million to six out of a million puts it in greater context.

We also conclude that the patient

perspective on tradeoffs between risks and benefits is an important aspect of the development of risk communication, as well as risk policy, and the consideration of how we make drugs available and whether there are risk management tools that are needed over and beyond the typical tools that we have been discussing today, and that the patient perspective on tradeoffs can actually be evaluated in a scientifically robust manner and a very informative manner.

I have provided the references that I have cited here and also, I believe that you all have a copy of a summary of the report on the HRT study if you would like more details on that.

CHAIRMAN SELIGMAN: Excellent. Thank you, Dr. Andrews. Let me now turn to the Members of the Panel for questions for any of our speakers. Dr. Trontell?

DR. TRONTELL: This will be directed to Dr. Day, but actually I would invite all the panelists to reply because I was struck by some of your clustering analyses around risk and frequency in your testing laboratory.

I have actually seen in your linear scale many pain displays that actually use several

techniques, the smiley faces, color and actually words so that there all three communication mechanisms are displayed often in a chart on the office wall. This is a simple question.

Are we working to one common denominator of communication that we might hope would be well-understood by all or might some of this clustering information lead us to pursue risk communication like marketers do and target maybe a select number of groups that would use, you know, one mechanism better than the other?

DR. DAY: I think my microphone is off.

CHAIRMAN SELIGMAN: The button should be up.

DR. DAY: Yes.

CHAIRMAN SELIGMAN: There you go.

DR. DAY: The answer to your question is yes, yes. That is to say we should take multiple representations and study how people understand them, but all people. We don't know if there is going to be interaction until we test them.

I think that, although I'm a great advocate for having appropriate materials for appropriate people, that some individuals when they try to do this dumb down the information too much or

make assumptions about what is going to work with a certain group of people and use cutesy things or I don't know, just inappropriate things.

So I think the appropriate way to get the answer to your question is to develop a variety of multiple representations, many of which we study in our lab and others as well, and then test each one with appropriate groups of people.

So the highly literate and educated people, the best and brightest, are starting to get left out of the mix now because we do need to pay attention to people with lower literacy and other kinds of skills. But even the best and brightest have great difficulty with some of the forms of representation that are currently used.

So, eventually, I know Dr. Wolf talked about coming to some kind of universal set of icons and so on, and that can be very useful, I wouldn't rush to that immediately. I would take the alternative representations approach which is to develop ones that are principled and reasoned based on cognitive principles and then test them across different groups.

And if there are no differences and the same kinds of enhancements for some forms of

representation then, yes, we could move more quickly to something that is more universal. Otherwise, have different strokes for different folks.

DR. WOLF: May I make a comment?

CHAIRMAN SELIGMAN: Yes, please.

DR. WOLF: I agree with Dr. Day. From a health literacy perspective though, I would suggest that in our studies with understanding how to take medications, we went in with an idea thinking that we wondered if literacy was associated with comprehension of medication risk information.

And we found that but, more importantly, we were struck by how, regardless of your educational level, regardless of your literacy level, lots of patients had trouble understanding existing forms of medication information.

And, that said, a lot of what the health literacy literature would suggest you do is a layering effect, that you have a front lines form of information, whether that be a patient information material, a patient information sheet, the medication label, the auxiliary label that should be -- and I would still probably promote a universally accepted one.

I agree with Dr. Day. It has to be tested

across all groups who you think might have trouble understanding it, but you need to come to some form of front lines, this is the information, and then provide backups, additional sources, web information where you're more likely to find people who are more functionally literature seeking out that form of information.

So as long as they can clearly navigate through how to get as much information as they possibly want on that medication, they can do so. But at least from the very beginning we need that first piece to be something that is accessible to all, especially, from my perspective, by literacy and culture.

CHAIRMAN SELIGMAN: Dr. Kweder?

DR. KWEDER: I have a comment and a question to clarify, that you might clarify, Dr. Wolf. One is thank you for bringing up the point about the warning labels are not always necessarily based on very much. My own experience is that I have taken medication regularly, and every time I pick up my prescription it has a sticker on it that says "Do not drink alcohol while taking this medication."

And I'm pretty literate when it comes to drug information and I can't for the life of me figure

out why that darn sticker is on that bottle. There is nothing in that label to indicate to me that that sticker should be on that bottle, but maybe I just look like a lush, you know, and the pharmacist sees me and pops it on there. I don't know.

But I wanted to just -- you showed on one of your slides a couple of examples of some of these warning labels, most of which have to do -- we don't regulate those. Those are decisions made by pharmacies or, you know, individually or collectively in a chain drugstore.

Most of them have to do with something about how to take the medicine. You don't see warnings about liver toxicity or heart risk. They are about how to take the medicine, designed so that when the patient holds the bottle they see something that tells them don't chew this or whatever it is.

You said something about some of those are even too -- implying that they are too complicated for even a 6th grade level of education. I was wondering if you could give an example of one of those.

DR. WOLF: An example of a label that was complicated?

DR. KWEDER: Yes, because most of them are -- because of the size, they are pretty short and

sweet.

DR. WOLF: We evaluated. In our first round of study, we evaluated eight specific warning labels that, on an expert panel of physicians and pharmacists, they said on the most commonly prescribed medications that we see these are the ones that are most frequently appearing.

So from those labels, we found -- we conducted what is called a lexical analysis that looks at the word complexity and also how frequently it's used in popular literature to gauge the reading difficulty of that specific message, and actually found in our own studies that that was, in multi-varied analysis, one of the strongest predictors of whether or not someone could comprehend.

But in those eight labels we had those that ranged from beginning reading labels such as "Take with food," "For external use only" to those that say something as, you know, multi-step instructions like, you know, "Avoid being in direct or artificial sunlight while taking this medication," which most people couldn't understand if that meant do I not leave my drugs in the sun or do I myself have to get out of the sunlight?

"For external use only," which is at a

less than 1st grade reading level, we found patients regardless of their literacy or education having considerable problems in trying to figure out what that meant.

So I understand that they are different and we also recognize that they are not regulated at this time, and are trying to at least find some way that they can be universally accepted. From a low literacy perspective, we view these things because they are on the pill bottle, because of their location, their brevity, their use of icons and color, that these things could be a great source for providing health information to patients, medication information to patients if used properly, which we feel that they aren't right now. I don't know if I answered your question.

DR. KWEDER: You did.

DR. THROCKMORTON: Yes. I have a question for Dr. Wolf and the rest of the panel as well. A lot of the comments that we heard today I expect were related to print material, sort of holding something in my hand and interpreting it. Obviously, the Internet is increasingly a place people are looking for information.

Does that change? Should that change any

of our thinking here?

DR. WOLF: I don't know if it should change our thinking. I would definitely want a lot of the information that you are planning to put on, you know, that you are providing to consumers in particular on the Internet.

I think it should be recognized that there is maybe an overestimation among patients with lower literacy, the elderly, those that are socioeconomically disadvantaged, that these individuals are not going to be able to access Internet information, so if you solely provide it on the Internet that you're not going to get the full audience, especially those who represent -- you know, who are affected most adversely by health disparities which is of great concern to myself personally.

So I would think that you can't avoid print text, obviously. We need to work with -- I think Dr. Day presented a fabulous method for addressing these print materials and I would seriously consider it and want to learn more myself about what she is doing.

But we need to also work with professionals because, technically, I think in the language that we're understanding is that providers --

a lot of the reasons why nobody pays attention to warning labels and patients tend to forget the information sheets is because they expect it from their providers.

And we know that providers right now are not able, whether it be a system issue or their own training, communications training, to provide that information in a manner that is accessible to the patients.

DR. DAY: I have a comment about Internet providing of information for individual drugs, be it on a company website or FDA or elsewhere. We have done studies to look at a given drug and find out how easy or hard it is to find the benefits versus the risks. And on the product website it is incredible. The risks -- excuse me, the benefits are right there on the front page.

You go to drugname.com, plug in whatever drug name you're interested in, and the benefits are right there. And we actually do a tree diagram of the site. Most site maps don't really show you enough of what is going on, so we do a tree diagram where the home page is on the top and then all the first main buttons that you can click on and then for each successive page.

And then we count the number of points and clicks you would have to do to find all the different risks. And the good news is that some of the risks appear on more than one page, but some of them only appear on one page and if you just adopt any strategy you want of reasonable search mechanisms people use like top to bottom or left to right, that there are -- on some of these product websites, there's only one place where a given risk is shown and it's all the way, if you'll pardon the left to right analogy, all the way to the right and to the bottom.

And so if a person had a search strategy that was in any way resembling that, they would probably have gone to sleep or, you know, be the next day or they would, you know, something worse before they would ever find it.

Now, what FDA seems to be doing is for the patient information, having everything like all on one page and that's good. But within a given page, how easily can someone search and find all the information. And I think that in the patient information sheets it's really good that there is this kind of chunking of all the risks, each one separate, and both the name of the risk and then a description of it.

That's really, really good, but there are other spatial ways of providing so that you can then find out what are the most serious ones without just seeing, having to read the word serious. So there are a variety of different ways to enhance the ease of which people will concentrate more on some and know that the others are there and can come to them later or not be as concerned about them.

So I still think that alternative representations can be used to really enhance the information in the current tools. And although we have talked a lot about patient tools, the same goes for health care providers. Even though they have more information, we have the same pattern of results with the providers as you do with the patients as a function of how you present the information.

DR. ANDREWS: I would like to add --

CHAIRMAN SELIGMAN: Please.

DR. ANDREWS: -- a comment as well about the use of the Internet. And I think it's important to realize that the web offers the ability to present information in different ways that you can't do on paper.

And there is an analogous situation in conducting survey research using the Internet where

you can build in skip logic and help people through logic of information. You can use color and graphics in ways that are more complicated in print and you can also make use of video.

For example, in a study we're doing where we're collecting data on the web and asking people to take a waist circumference measure, that is not an easy thing to get standardized. So there is a little video that shows patients how to take a waist circumference measurement with a measuring tape and it's simple.

So I would encourage you to think broadly about the types, using the Internet smartly and not just to provide something that looks like paper.

CHAIRMAN SELIGMAN: Yes, Dr. Smith?

DR. SMITH: I have a question, basically, to all of you. We have been trying with our public service announcements and the things we're doing for the general public to follow many of the health literacy and other things we have been discussing here.

But the question I frequently get asked is does it make a difference? If we get a public service announcement published in a major magazine, say Good Housekeeping, Woman's Day, the magazines that are read

by the general public, Reader's Digest, we always feel like we have a major accomplishment when we do that. But the question is do these make a difference? And it's not can people understand them. It's do people act on what they understand?

And so my question is have any of you taken your research beyond patient understanding of information to a patient using that information in their day-to-day life and is it really making a difference in the way they use their medications?

DR. DAY: We have gotten quite a long way along that pathway. In a study of EpiPen, which is a drug device combination used for people who have severe reactions to bee stings, latex and so forth and go into anaphylaxis and they need to whip out this pen and inject themselves quickly with epinephrine.

So we looked at the original patient information or package insert and found a lot of problems with it that would create errors, and revised it and the company adopted and it has been out on the web and in the package inserts for some time. They have recently done some additional revision.

And in the laboratory, what we study is we do a regular comprehension study, people study the materials then we test them, but we also do a use

study and we give them an EpiPen which has no needle or drug and assure them of that multiple times. And then we say, you know, they study the information or have it in front of them, say assume you are a person who could have this severe reaction. Please, use the EpiPen and so on.

And we have found that with the original materials they make a tremendous number of mistakes. They inject the wrong end. A pen looks like the sharp end is here. After you take off the cap, plunge it in this way. In this kind of auto-injector and others, as well, that is just the activator that activates the drug and you have to plunge the other side into you and so on.

And we found that with the original materials they were making that mistake and many others, and with the revised cognitively enhanced materials those decreased dramatically.

Now, in order to find out does it really affect health, we have to go into surveillance data sets, and so we're trying to figure out how to really get good information on medication errors or however they are going to -- adverse events using the product before the materials came out and now and it's very difficult. It's difficult, but we're determined to

find out.

DR. WOLF: If I can comment, too. We have a couple studies underway. We have been able to figure out how to improve -- in asthma how to improve the proper use of a metered dose inhaler among adult patients with asthma.

We have a couple trials underway right now for managing hypertension and high blood cholesterol medications for patients in federally qualified health care centers through using enhanced print text forms as well as multimedia forms. But just on a general -- I mean, so I think the data is coming out there.

One comment is that I think we have to be first cautious about -- the ultimate endpoint, sure, is to improve how people act on information, but it's still important to make sure that they actually understand it and that there are so many behavioral individual factors, as well as social and environmental factors, that might impede someone's ability to properly take medication. So that should be -- you know, that is a hard thing to test.

But also that -- and I think that there is a lot of literature that suggests that multimedia print is -- there is a lot of research that we still need to learn. There is a lot of conflicting evidence

on whether or not multimedia tools can actually improve comprehension in low literate populations.

This dating back to 1995 and we have had more things coming out recently that the use of multimedia tools doesn't work with low literacy populations in helping people manage their diabetes medications. Why is that?

Everything that Dr. Andrews said is correct, that these are great opportunities to provide, to help patients choose how they want to learn about their medications not just in a flat text format, but everybody learns differently and multimedia tools do that.

We just still have to perfect how it's presented, I think. We need a lot to learn with low literacy patients being kind of those who don't fit the mold that should be tracked to see if they understand it at least, you know, for some assurances.

DR. KWEDER: I have one question for you. Despite some of the limitations of the Internet's reach, and I certainly know a lot of people who don't have access to it or wouldn't choose the Internet as a source for information, I would like to know how many of you on the panel have attempted to look up information about a particular drug on the FDA website

and what your experience was as people who I am assuming are comfortable with Internet use and trying to find that information.

CHAIRMAN SELIGMAN: Am I supposed to answer that? I'm sorry.

DR. KWEDER: That panel.

DR. WOLF: I mean, I have actually gone through it. I mean, I think that a lot of information is very promising currently on the website. And a lot of what is out there right now is, I think, very promising and very good. Sure, there's opportunities for improving it or at least going back, since a lot of materials haven't really taken a systematic approach to make assurances by literature and culture that they are appropriate, to confirm that.

And, also, it's an issue that we need to keep putting Internet stuff out there because access issues might be diverted. What we're doing at Northwestern Memorial Hospital involves using the electronic medical record terminal that is in all of our -- I mean, it's not in all hospitals and obviously not in federally qualified health care centers, but since there is a computer, you know, monitor in the doctor's office with web access, using that as a video screen, so priming patients on how to take their

medications or other chronic disease self-management issues while they are waiting for the physician.

We're doing time in motion studies to figure out how much time they actually would have before going in there. All that stuff is a way to give access to patients who may not have it at their home and that could be the future. So keep doing what you're doing. Make confirmations that it works for the right people and see how access can be improved in the meantime.

DR. KWEDER: Dr. Wolf, I think you missed your calling. You didn't answer my question. I will give you a minute to think about it and see if somebody else wants to take a shot. Dr. Day?

DR. DAY: I have different experience in finding things on the website as a function of where I'm trying to do it from. When I'm in my office with all of the latest bells and whistles at the university, I can find things and navigate.

At home I confess to having a not up to date system, which I'm trying to replace, but there are a lot of things I can't access. I can't get the videos or, you know, things happen and I go to places that should be all right and page not available.

So over and beyond my particular computing

problem, I would just say that whenever there are new and exciting things that are then incorporated into the website, do not assume everybody is going to have the equipment and the software to get all of that.

DR. KWEDER: Have you tried to look up a drug on the FDA website?

DR. DAY: Oh, many times.

DR. KWEDER: And how did you do?

DR. DAY: Well, it depends on how I try to do it.

DR. KWEDER: Okay.

DR. DAY: If I just go to the original home page and type in a drug name, that is one way. Another way is to go on the patient side. There are patient information or consumer buttons, whatever they are, and all the experiences are different. And sometimes I have been a little frustrated.

DR. KWEDER: Okay.

DR. DAY: And, you know, it depends. There's multiple -- oh, that leads me to another suggestion about all these tools we're supposed to talk about. They are wonderful and I regret we didn't have enough time to talk about all of them, each of us, but at first it's kind of a dizzying array.

I like the array, but it's a dizzying

array, what are these and what is a press release and what is a talking point and what is a da, da, da, da? And, yes, there's always buttons for them. Well, now, the good thing is is that when you're in a given tool, there will be appropriate links and then, you know, they say something. You can click on them and try them, so that's good.

But getting an overview, I would like to have one page that shows all the different risk communication tools in some kind of a spatial overview, whether it's a hierarchy or something with a little description beneath each as to what it is and what it's for. I mean, what is the difference between a press release versus a you know.

So I would like to -- and I wanted very much to show a slide on that today and I didn't have a chance, but that's one of the navigation problems, you know, knowing where to go as a function of what kind of thing it might have popped up in.

DR. WOLF: Can you direct your question to the panel, Dr. Kweder?

DR. KWEDER: My question is have you tried to look up a drug or information about a drug or risk on the FDA, using the FDA website, and what was your experience?

DR. WOLF: I mean, I think I'm less familiar with the FDA website specifically in getting the drugs and I guess I was going to inquire, because it sounds like part of the question is that you might be suspecting that there is a navigational problem with the FDA's current format.

DR. KWEDER: I'm asking you if you think there is one.

DR. WOLF: Yes, yes. I think I'm probably not as informed to actually answer that for the FDA specifically. I know other sources that are out there that are pretty good, but I think I'm going to have to go home today and actually take a handful of drugs and see what I get out of them.

DR. SMITH: If I could modify Dr. Kweder's question a little. Have any of you used the drugs at FDA site specifically and did you find it useful?

DR. ANDREWS: Is that on? I use the site fairly regularly and find that there is an amazing amount of information, and I really applaud the FDA for making so many documents available in the public domain that contain lots of very useful information.

But I'm not accessing the website as a patient so often for specific drug information, so I can't really answer that question. But I would say

that there is information that I would like to have access to that is sometimes not -- it's not there because it's not in the public domain and I think that's a pity.

DR. SMITH: That's different.

DR. ANDREWS: Yes.

DR. OUTTERSON: I spend a lot of time on your website and, not as a novice user, I find it to be very helpful and there is a lot of information. But a lot of my work is in health disparities and, you know, there is no representation that it's good for a mass audience.

I think that CMS right now is experiencing what a mass audience looks like on Medicare.gov and with the Part D benefit, just the issues that they are facing on that particular interface is probably a great learning experience.

CHAIRMAN SELIGMAN: Dr. Outterson, I have a quick question for you regarding the existence, availability and quality of information in other languages and the degree to which other national regulatory drug authorities have that information, I presume they do, the European Union, Canadians, Japanese, China, etcetera, and the degree to which that information either in terms of professional

labeling or in terms of information for consumers not only exists but might even be available on websites and what the quality of it is, given that some of these products are sold by multinational pharmaceutical companies that clearly have, I presume, some interest in high quality information.

DR. OUTTERSON: There's a reason for my suspicion that a lot of the personal importation from what we would call a developing country, there is a lot of, I think, very serious issues. Within the European Union they have had a lot of experience with the single market now at 25 countries, 20 different languages, major languages within the Union, on the parallel trade.

You know, what happens when a drug picks up in Spain and moves to Germany and the repackaging and the dual labeling? And so I would probably not be an expert on that issue myself. The European Union has a lot of experience in this kind of dual labeling, multiple language labeling issue within the Union. So it's not drugs from Thailand. These are drugs from within the community.

CHAIRMAN SELIGMAN: I guess we have time for two last questions. Terry?

MS. TOIGO: Dr. Day, in your studies you

say that people overestimate the frequency and underestimate severity. Is that the way we're presenting the information that is being presented or do you have some thoughts on why that is?

DR. DAY: Okay. So the question is the observation first that people underestimate severity and overestimate frequency. Do I think that's based on the way the information is presented? That is your question?

MS. TOIGO: Yes.

DR. DAY: Yes. It's based on that and it's based on prior knowledge. Well, they may have experienced it or heard that somebody else had it, a side effect and so on, but definitely the way it's presented and the mixing up of different terms within the same message can cause some of it.

But I think a lot of it has to do with prior knowledge and that's why I recommend a public education campaign about side effects and what ones are, you know, just about all the time, you really ought to get some medical attention right away versus others, you know, could be, maybe not, but it would be good to check versus these are other things that are kind of mild and, you know, just monitor them. If they persist and bother you, by all means do such and

such.

So linking severity with action would be a good way to do this, but there is just a lot of problems with prior knowledge of not understanding the likelihood of something happening and being able to work with the numbers. But going to what Elizabeth was talking about, a little bit about absolute versus relative numbers, so what does common mean? Does it mean out of 100?

And if you give people a scale from, you know, 1 to 100 people might experience this, they use a scale. But if you give them a scale 1 in 1,000 or one in a million, then it's framing it in a different way. And so then the likelihood -- and you can do the same thing with severity.

So it's really an interaction between prior knowledge and the way that things are presented, but I think that changes in the way of things that are presented are going to dramatically help prior knowledge. So that is why my little diagram I kept showing with the arrows going around and around. They keep affecting each other.

MS. TOIGO: Thank you.

CHAIRMAN SELIGMAN: Last question, Dr. Trontell.

DR. TRONTELL: For all the panel. One theme I have taken away from your presentations this morning is the need to test communication materials and, clearly, that may have potential regulatory or economic consequences.

Could you briefly comment how extensive this should be, how diverse the populations should be included in that, how sophisticated in terms of prior cognitive testing of the comprehension instrument itself? Could you give us some idea of what we might be looking at if we were to pursue some of these testing ideas?

DR. WOLF: I can actually maybe direct you to a woman who presented last week at the American College of Physicians who has done something very similar at least in establishing kind of a standard protocol for the testing in diverse populations or what might be viewed as at risk populations, and that is a woman, Yolanda Partida, who developed something called Hablamos Juntos to develop better signage and health messages for patients to help better navigate health care systems.

And her website, which I do not have, but I can actually send it to you after this meeting, has been fantastic as far as showing here is a very

concrete process which, to answer your question, seems to be quite, I think, intensive and I think Dr. Day's methods are clearly, you know, wonderful, but it's the mucky muck.

You have to do some of this stuff and it is very time-intensive and you do need to have an adequate number of people represented in those that you think are, what I would say, people who are reading at a 6th grade level and below to be involved in the study to see if they can understand it.

And I also think you also need a culturally diverse representation of patients, as well, to see if there are semantic differences in how they -- you know, in what Dr. Day refers to as what representations they have of the medication. So, overall, I think that you shouldn't cut corners and just realize that this is something that should be integrated into the process and that should be -- and it will be I think intensive.

DR. DAY: I have a radical proposal. Yes, we should test these tools with multiple people, but I get very upset when testing happens where you have to have a balanced representation from every geographical, socioeconomical, age group and you have to be representative across all of that.

Eventually, we need that much, if not all, of that information but for a given tool, a new type of tool or, you know, you can test almost anyone to begin with. And although they are convenient and a much maligned group, college students are very interesting and that is because they are relatively smart and they like to do tests and so on.

If you do a study with them, sure, the overall level of performance is going to be very different from people with low literacy skills and with professionals who have much more content information. However, across every single group of people you generally find the same pattern of performance. Some things are harder to understand, remember and use, Nancy, and other things are easier and they vary by these different representations.

What is lost in all of this "be representative" testing is that all people are people. They have basic cognitive processes. Barring any disease processes, such as Alzheimer's Disease, etcetera, we all process information in similar kinds of ways.

Of course, there are individual differences and some people prefer this way and that way and so on, but we have been able to take people

who maybe don't prefer a certain form of representation and give it to them anyway and they do more better, if you'll pardon the term, than the other things that they think they prefer.

So why don't we, not every time but often, start with the base population. It doesn't have to be college students. It could be just some base average group of people, see how it works, get the pattern of results. And then what happens next is an iterative process. You go back and change the tool because you see what's going on, and after a couple of iterations, then farm it out specifically to the other groups.

But this mass testing of everybody and everything right away I think is costly, expensive, time consuming and is not productive enough.

DR. ANDREWS: I would like to echo Ruth's comments and say I think it's more important to have some testing for everything, rather than extensive and highly representative testing for only a few things. I think we could make huge strides. But I would also say that I think that the most important thing is to really know the patient population that a particular product is intended for and to know if there are some special issues.

So, for example, if it is an injectable

product that is to be used in an elderly population, then I think special testing needs to be done in an elderly population that has a variety of levels of mobility, comprehension and care giver reliance. So that would be the only thing that I would qualify from Dr. Day's comments.

DR. DAY: And I just wanted to agree with that. I should have included the specific patient population. Absolutely.

CHAIRMAN SELIGMAN: Dr. Outterson, I will let you have the last word.

DR. OUTTERSON: The 6th grade reading level assumes you can read English. 47 million people don't speak English at home. About 20 million are linguistically isolated. They do not speak English either not at all or not well and there is no one else in the household who speaks English at the good or well level.

So where are these people getting the information? You know, when they are at the hospital, Title 6 requires that we give them translation. When they go home and when they go to the pharmacy and when they get their drugs, there is no one that gives them the appropriate information.

So I am suggesting an overlay within, not

disagreeing obviously with anything that has been presented, but an overlay that you have a basic obligation under Title 6 to provide linguistically accessible information to these people. And, secondly, that outside of the Title 6 obligation, because of the way the MAPP guidance is given from the center, perhaps even just a gentle urging or permission from the Agency telling companies that they are encouraged to present this information in multiple languages, something short of a rule under Title 6, I think, would go a long way to encouraging them on their marketing plan.

They want to sell these drugs to people who speak Thai and Tagalog, but there may be hesitancies just because the Agency has this guidance out there that might be interpreted as restricting them.

CHAIRMAN SELIGMAN: Thank you to all the panelists. It was an excellent morning. I appreciate your responses to our questions as well as your presentations. We'll begin at 10:30 in about 15 minutes with the second panel, so if they will come up to the table we'll try to start promptly at 10:30.

(Whereupon, at 10:18 a.m. a recess until 10:33 a.m.)

CHAIRMAN SELIGMAN: Before we begin, just a reminder again that the National Transportation Safety Board does not permit food or drink here in the auditorium. With that, let's begin the second panel. Our first speaker is Dr. Sidney Wolfe from the Public Citizen's Health Research Group. Dr. Wolfe? You can use the podium if you like.

DR. WOLFE: Okay. Good. Is this on? Yes, it is. Although the other topics from the list of six questions that were posed to us are important in the context of how well a given amount of information is communicated to patients and health professionals, the main question with one final exception that I will focus on is Question 3, which asks about the adequacy and implicitly the timeliness of the content of the communication, rather than the success of the communication process.

And as you read Question 3, just to remind those of you who focused on Questions 1, 2, 5, 6, do these tools provide the right kind and amount of risk and other information that health professionals need to make informed decisions about whether to prescribe their products and that the public needs to make informed decisions about whether to use these products?

George Santayana is frequently remembered for his statement, often misquoted, but I think that we got the right quote here, that "Those who cannot remember the past are condemned to repeat it." The critical part of risk management and communication is remembering and learning from past mistakes. The FDA, because it appears largely incapable of doing so, will inevitably continue to repeat the kind of mistakes that a careful "post-mortem" examination and course correction would have prevented.

I remember back about 30 some years ago after the disaster of the antihypertensive drug Selacrin, Bob Temple said we need to do a post-mortem on this. It may or may not have been done. We never heard about it. I think it was sort of canceled midstream. And in the overall population, the autopsy rate has gone from about 45 percent after the second World War to about 7 or 8 percent.

The autopsy rate whatever it was is very, very low right now or at least as far as the public is concerned. We have never heard the FDA acknowledge that there was some regulatory mistake made, which has an impact on this Question 3.

Along with the FDA though, back to Santayana, the public winds up being "condemned" by

the inadequate actions of this Agency, the Public Health Service. So I'm going to through some various categories of failed risk information, again focusing on what the information is, rather than, which certainly the first panel focused on given what it is, how well does it get out there.

And the first example is approving drugs whose preapproval risk clearly outweigh the benefits. When a drug is approved, the public and health professionals clearly get the message that the FDA has decided that the benefits outweigh the risk. And if drugs where it is clear, not just in retrospect, but at the time that the risks outweigh the benefits are approved, the public gets exactly the wrong message in every way, shape or form that they try to, whether it is on the FDA website or anywhere.

So that when this mistake is made, the misleading message communicated to the public is that the benefits outweigh the risk, which is the opposite of the above. And so as with these other four or five examples, I will give the case study is Trovan or trovafloxacin, an antibiotic.

Another drug also approved in 1997, the painkiller, Duract, bromfenac, now off the market because of liver toxicity, there was also clear

evidence of liver damage caused by Trovan in animals and humans before the drug was approved in December 1997. In one preapproval study in which the drug was used to treat prostatitis, 10 percent of the men given the drug developed evidence of liver toxicity, 14 out of 140.

With eight other drugs in this fluoroquinolone antibiotic family available in the U.S. and a leading expert in infectious disease, when I called them before, we asked the FDA to ban Trovan, would the public or physicians be harmed in any way by the removal of this drug from the market, he just immediately said absolutely no. No unique benefits. So with all these other drugs as well as dozens of other safer and equally more effective drugs for infections, the removal of Trovan from the market by the FDA would not have deprived doctors or patients a drug that could possibly be considered indispensable.

Instead of banning Trovan in 1999, again, this is a case example mainly that shouldn't have been approved, but it kept going after approval, as was done everywhere in the world, the FDA chose to limit "its use" in the United States to patients who were either hospitalized or in nursing homes.

At the time of our 1999 petition to ban

the drug, there were eight cases of liver failure, including five deaths and three liver transplants. There were as of December 31st of last year a total of 58 cases of liver failure, including 29 deaths and nine transplants. This is especially alarming since for the past several years there were a total of only 350,000 prescriptions filled in the whole country. This is over a three year period.

A sales wane following the 1999 market withdrawal in Europe, but more and more cases of liver failure and death occurred. Pfizer quietly without announcement discontinued making the drug in 2002, but the FDA didn't really ban it. During the latest year for which U.S. sales data are available, there were still 18,000 prescriptions filled. So the message here is: (A) It shouldn't have been approved.

The second category is failing to promptly ban drugs when there is post-approval evidence that risks clearly outweigh benefits. I mean, we would add to the first category Crestor, which we think based on preapproval clinical trial data should not have also been approved.

So in the second category, failing to promptly ban when there is post-approval evidence. As I said, Trovan is an example, because preapproval and

then massive amounts of post-approval evidence leading the drug to be banned everywhere other than the United States. The other example in this category is Rezulin, approved in March of '97, and within a few months the drug was taken off the market in the UK, largely because of toxicity in U.S. patients, 130 cases of liver damage and six deaths.

By July of '98, we at the Health Citizen's Group petitioned FDA to ban Rezulin. By then, 560 cases of liver damage, including 26 liver deaths. And in March of the following year, '99, an FDA Advisory Committee met to think about this and discuss it. By then, 43 liver deaths. Early in 2000, some FDA physicians, not for attribution, said the drug should be taken off the market. And in March of 2000, almost three years, two and a half years after it occurred in Britain, it was withdrawn in the United States. By then, 63 liver deaths.

Another example is Baycol or cervistatin. One year before it was removed from the market in August of 2001, its manufacturer, Bayer, using FDA data, data it had gotten from the Agency on other statins, found that Baycol had 20 times more reports of rhabdomyolysis, often fatal destruction of muscle, per million prescriptions than Lipitor.

An FDA official feebly excusing FDA's belated ban stated that "We weren't aware, at that point, of the difference between Baycol and the other similar drugs. Our expectation is when a company becomes aware of a specific problem with their drug, they come to us." Now, of course, the companies data had come from the FDA. By the time Baycol was banned, there were 1,899 cases of rhabdomyolysis, a significant number having occurred between the time there was unequivocal evidence that FDA should have banned the drug and when it was actually banned. So another example of failing to ban promptly.

Now, with Baycol, there were no preapproval cases of rhabdomyolysis. There were eight with Crestor. But once it came on the market, the cases abounded.

The third category in this Question 3 is the information on risk benefits adequate? Is failing to promptly warn the public with black box warnings when there is new risk information of sufficient concern to merit black box warnings? And the case example here is Vioxx Rofecoxib. A randomized control study published more than five years ago, November of 2000, found a 4 to 5-fold increase in heart attacks in people using Vioxx compared to those using Naproxen.

There was then and there is now no credible evidence that this enormous difference in risk can be explained by protective effect of Naproxen as the company and some people in the FDA would like to have done, rather than by the heart attack provoking risk of Vioxx. As a result of this study, we asked the FDA for a black box warning, almost five years ago in February 2001. Although such a box warning would have greatly reduced the toll of tens of thousands of heart attacks, according to Dr. Graham's estimates from his study, occurring between then and Vioxx's withdrawal.

The Agency to the pleasure of Merck rejected a black box and chose not to adequately warn the public, even the minor label change was delayed a couple of years because of bickering between the FDA and Merck. Many lives were thus lost.

Another very current example of failure to warn the public adequately with a black box warning and all that goes with that are the erectile dysfunction drugs. 50 reports of ischemic optic neuropathy usually resulting in irreversible unilateral blindness in men using these drugs, Viagra, Cialis or Levitra have been received by the FDA by March 2005. But the FDA and the companies have

downplayed the link between these drugs and ischemic optic neuropathy stating correctly that the disease also occurs in men with cardiovascular risk who do not take erectile dysfunction drugs. We don't dispute that. But implying that the cause is cardiovascular risk, not the drugs.

To test this, we compared the rate of reports of ischemic optic neuropathy per million prescriptions filled in those using these ED drugs with the rate in those using Lipitor. Both groups having presumed increased cardiovascular risk. With Viagra, there were 18 times more reports of ischemic optic neuropathy per million prescriptions than for Lipitor. And for Cialis 25 times more reports per million prescriptions. Thus, it is very likely that the drugs actually cause blindness in some people.

We, therefore, petitioned the FDA to immediately require a black box warning on the labels for all these three drugs and to require an FDA approved medication guide and to begin a registry of all cases. I mean, we have spent a lot of time over these 34 years with this issue of communicating information risk/benefits and our whole petition is on our website, which is worstpills.org.

Dr. Howard Pomerance, the neuro-

ophthalmologist, who first published a report of this disease in a man using ED drugs and has added 13 further published cases, joined our petition to the FDA. So the person who really identified this problem is in back of FDA taking action. They have not taken action.

The fourth category is failing to require FDA approved medication guides for all drugs, even failing to provide them for all drugs with black box. 24 years ago, in 1981, and in terms of guaranteeing information going out, it's hard to beat this, I mean, yes, a lot of people don't have Internet access and so won't have to think about ways in which everyone affected is going to get warned.

24 years ago in 1981, a carefully researched field tested in a diverse group of people a regulation requiring patient information leaflets approved by the FDA to be dispensed was canceled by the Reagan Administration just before it was to have gone into effect at the behest of drug companies, pharmacy organizations and some physician groups.

And private sector leaflets not approved by the FDA known as PIL, Patient Information Leaflets, thereby continued and continue to be the norm for virtually every prescription. When you go to a drug

store, the piece of paper you get, with the exception of 75 drugs, is not approved by the FDA.

The FDA, obviously, has authority to require these if the drug is one for which patient labeling could help prevent serious adverse effects, if it is one that has serious risks relative to the benefits, which patients should be made aware, because information concerning the risk could affect patients' decisions to use or continue to use the product. And third, if the drug product is important to health, in other words, it should stay in the market and patient adherence to directions for use is crucial to the drugs' effectiveness.

The other thing that is required, and this is again part of this larger picture of informing people, is that when FDA decides that there should be a medication guide, the pharmacist is obligated to hand it out every time a prescription is filled. The FDA commissioned a study at the University of Wisconsin a few years ago to look at the extent to which these private sector initiatives of giving out information, not approved by the FDA, when a prescription was filled was going on.

And they found that yes, 89 percent of consumers are getting something or other, but that the

information that they were getting was pretty pitifully deficient. As measured by eight objective criteria, the overall usefulness was about 50 percent. According to the author, "the majority of leaflets did not include adequate information about contraindications precautions and how to avoid harm." The notion that consumer drug information would be 50 percent useful is unfathomable.

And finally, the last category is on this issue as well and it's a study that we -- a colleague of ours, Dr. Larry Sassik, a PhARM D, who many of you know and have worked with, has conducted just in the last week. And the question it asks is even in the relatively small number of instances where FDA has said yes, there should be a medication guide, is it being given out?

On June 15th this year, FDA announced the requirement that all non-steroidal anti-inflammatory drugs should be accompanied by an FDA approved med guide, particularly different information in here, although there was no med guide at all before, was this cardiovascular risk, which is most clear with the COX-2 inhibitors, but there are some concern, not in our view as much for the other NSAIDs.

Because of previous evidence from the

birth control pill, one of the first drugs for which FDA required a med guide, the equivalent of a med guide 30 years ago, there was evidence that it just wasn't getting out to women. Dr. Sassik did a study in Erie, Pennsylvania of pharmacies to see the extent to which this now six month old requirement for a med guide for Celebrex, one of the NSAIDs was being done.

The preliminary results of the survey of 13 pharmacies are summarized very simply in a table, which I have given out here. Of 13 pharmacies, only one of them was giving out a medication guide. None of them explained, as they are supposed to, what the medication guide is for. All of them handed out the non-FDA approved patient information leaflet.

Ironically, the unregulated drug information leaflet produced by one of the vendors contained the statement "Read the medication guide provided by your pharmacist before you start using Celecox inhibitor each time you get a refill." Yet no medication guide was distributed by that same pharmacist and no information concerning the existence of medication guide was communicated by the pharmacist to the purchaser.

In summary, the answer to Question 3, "Do these tools provide the right kind and amount of risk

and other information that health care professionals need to make informed decisions and the patients need to make informed decisions," the answer in too many situations is no, because of really regulatory failures. And unless adequate communication -- well, I think that when we go back to these other five questions, the only way that you can say that this stuff is a success, the various things on the FDA website, which I think is a good website, the main feelings of it, other than some difficulty doing some maneuvering, are that the information is right.

So the only way one would consider a lot of these categories as examples that were cited in the Federal Register notice as success, unless adequate communication of too often inadequate information is viewed as a success. Thank you.

CHAIRMAN SELIGMAN: Thank you, Dr. Wolfe. Our next speaker --

DR. WOLFE: I'll answer afterwards later.

CHAIRMAN SELIGMAN: Yes. Our next speaker is Dr. Diana Zuckerman from the National Research Center for Women and Families. Dr. Zuckerman?

DR. ZUCKERMAN: Thank you very much. I am Dr. Diana Zuckerman, President of the National Research Center for Women and Families. And our

organization works to improve the health and safety of adults and children. So the topic today is one of great interest and importance to us. How do you let the public know what the risks are for drugs that they may be interested in taking or may already be taking?

We have reviewed a lot of the information that is available on CDER's website and we have some comments about some simple and yet very critical improvements that could be made. Let me actually start out by saying I was very impressed with some of the graphics and these very nice information that was available today outside this room. You have a lot of beautiful simple messages. I really like this antibiotics one, for example. But I didn't find it on the website.

Okay. Okay. Here we go. Here is CDER's home page. It has an incredible amount of information. And, of course, a lot of people do use the web and could use the web to get that information. So the question is how easy is it to understand it, to find what they need? Let's think of some parents who have a depressed 16 year-old and they are trying to decide whether that child should take antidepressants. And they have heard all this controversy in the news and they are not sure what to

do.

Where would they go? They would look on this website. Maybe they would use the search box, which you can see in the middle. And if they did that, let's say they didn't know which antidepressants to put in the search box, so maybe they would just write antidepressants. They would just be totally overwhelmed with information. They wouldn't have any idea what to use.

They would really have to go to information about specific products, specific drugs. So they are looking on here and they are trying to decide where to go. Maybe they would go to the Drug Information Pathfinder. Maybe they would think that. Well, it's drug information, that sounds like what we want. What happens if they go there?

Well, they get all of this writing. You get an idea of how difficult it would be to maneuver and how to get this information. It would just be overwhelming. It's not clearly organized and it's not really clear who is this for. Is this for consumers? Is this for doctors? Is this for policy folks? Is this for nonprofit organizations? And I think the truth is it's supposed to be for everybody and because of that, it might not be too clear for anybody.

So if consumers were going here, they really wouldn't know what to do. What about health care professionals? Maybe health care professionals and maybe even patients would be more likely to find some useful information on the next site. Oops, not working. I can't seem to make it change. Oh, there we go. Sorry.

Okay. This is the Index to Drug-Specific Information. We like the format, but our biggest complaint is that it's inconsistent. That if you tried to get information on this website, it would be inconsistent. For each drug, the type and the reliability of information is completely different. And for some reason, only some drug information includes links to MedWatch and, of course, we think everything should have links to MedWatch.

Now, here is the next one, the patient information sheets. Of the, approximately, 250 drugs on this website, we have calculated only 41 percent have patient information sheets. And we think these patient information sheets are important. We think the design is pretty good. The content is quite good. We do think it's a problem that the date is often missing, so the patient is left or the person looking at it is left not knowing exactly how up to date this

is. And so we think that the date should be very clear to the reader.

I just have some samples here to give you an idea of what it looks like. About 26 percent of the drugs listed on this website have health care professional information sheets or alerts, like this one. But as with the patient information sheet, we think the date should always be very clear. And obviously, these things are not really attractive. You know, it's very dry information. People need to be highly motivated to look at it. It doesn't have, you know, oops how did that happen, sorry. You know, it isn't all that engaging.

But here is an example of why that information is so important. If patients are stuck getting information from their magazines, they are getting information that looks like this. It's really impossible to read. So, obviously, what's on the website is a big improvement compared to this. But it's not nearly as good as it should be and could be.

And let's remember that FDA drug labels can be very long, sometimes 50 or 60 pages long and people are not going to read it. So how can we get information to them that's readable, understandable and, you know, some kind of length that makes sense?

This is an example of a drug information page that a person might access through the index of drug-specific information website. And the available documents in this include the FDA drug label, which is 62 pages long, a Q&A information about the FDA's announced revision to the drug's label, an FDA press release about its plans and reasons for changing the label and a consumer information sheet that has not been updated since August 2003.

This is Ortho Evra, in case you can't read it, and, of course, that's something that has been in the news lately and people might want to know information. And yet they are kind of again overwhelmed with a lot of information. So there may be risk communication on this website, but how are you going to find what you really need?

What we found is that frequently the FDA website really focuses on the FDA process. You can find the whole history of a drug, you know, when it was approved and changes to the label. But, of course, the consumer isn't interested in that. They want to know what it is they need to know, the most up to date information. And if they want risk information, they want it simple and up to date and they don't want this enormous process and all this

detailed information.

Okay. Now, in this case, you can see we have -- this is again Ortho Evra, and you can see the date on this, so this is up there. It's the side effects of Ortho Evra, but it was posted in 2002 and it was revised in 2003 and yet that's the information that's up there today.

Again, there is another piece of information. If a person was looking for the information they needed, they would have to read through all of these choices. It's very hard to find the link that they really need to get the information that they really want.

Here is a public health advisory. Again, there is no date. Once again, the risk communication materials, we just don't know when they were written and we think that date is really important. And if this information here on these advisories is important, it's equally important to know when it came out.

Oops, I don't know why this keeps doing that. Sorry. Okay. So again, this one has no date listed and, actually, the incorrect year is listed on the website. Here it's listed as an advisory from 2005, but actually the actual date is June 9, 2004.

So, I mean, mistakes can be made but sometimes with some products, you really want the most up to date information and it's very important.

And if the FDA website can't figure out what year their own material is written, that's a sad state of affairs. This one is an example that does have a clear date and we think that's really important to do that. Again, another one with a clear date and, again, why shouldn't they all look like that?

So just in conclusion I want to say that the risk information may be there, but who in the world is going to be able to find it and understand it and figure out what really is true, the most recent information that is possible to get at this point?

And if the FDA website is supposed to be for consumers, the way it is right now, I think it's very difficult for most consumers, except possibly the most educated consumers, to use in some kind of reasonable way. And my guess is that even the most educated consumers aren't going to be able to find the information they want easily.

So why not have a website that is just for consumers? Why not have something that instead of focusing on the process, of the FDA approval process and all the changes in labeling and so on, that really

just has up-to-date information about the risks and benefits? Obviously, patients are getting a lot of information about the benefits from other sources, but not enough about the risks.

And why not use some of the information you have and the knowledge you have about how to communicate to consumers, like you show in your written materials, why not have that on a website that patients can easily access? Thank you.

CHAIRMAN SELIGMAN: Thank you very much. Thank you very much. Our next speaker is Ray Bullman from NCPIE.

MR. BULLMAN: My name is Ray Bullman. I am Executive Vice President for the National Council on Patient Information and Education. It's a nonprofit coalition of over 100 organizations representing health care professionals, voluntary health groups, consumer and patient groups, businesses and Government agencies.

I have worked for NCPIE for 21 years in various positions, most currently as Chief Staff Executive since January of 1995. Please, note that my comments do not necessarily reflect those of all of the individual members of NCPIE, the National Council on Patient Information.

I would like to first thank the FDA for convening this meeting and for allowing NCPIE the opportunity to comment today. The Agency is to be commended for its efforts to increase transparency and to get emerging information to health care professionals and to consumers in a timely manner.

My comments relate primarily to the development of FDA-produced patient information sheets, PIS, that for some approved drug products are currently posted on or linked to the Agency's drug watch web page. Additionally, since there is a relationship to FDA's patient information sheets and FDA required medication guides, which are required for certain drug products, I also have a few comments in that regard as well.

Regarding the Agency's patient information sheets, I would provide both caution and advice to the Agency regarding the messages included in those consumer-directed documents. Since the knowledge base for those drug products targeted for inclusion on the drug watch page is incomplete and emerging, the message to consumers via a patient information sheet or other such vehicles needs to be constructed in a way that is informative and helpful, but does not overstate what to do or create undue fear in patients'

minds that their medicines' risks are greater than their benefits to the extent that patients will not take the medicine without talking with their health care professionals, which patient information sheets have potential to do.

I would ask FDA to clarify the development and the utility of the patient information sheet, including its relationship to other written information consumers routinely receive with prescription medicines at community pharmacies.

Additionally, since the Agency continues to expand the list of medicines for which a medication guide is required to be dispensed with the medication at community pharmacies, for example, along with the aforementioned written consumer medicine information leaflets, FDA is urged to develop and publish for public comment a research agenda to evaluate the impact and effectiveness, including possible unintended consequences for both patient information sheets and medication guides.

I would also like to ask what criteria the Agency is using to develop its patient information sheets. The producers of written drug information for consumers in the private sector are mandated by federal law, PL104-180, to use criteria for usefulness

contained in the action plan of the provision of useful prescription medicine information for guidance on development of clinical content, design, layout and readability of written information.

A consortia of nearly three dozen multidisciplinary stakeholder groups, consumer and patient organizations developed this action plan criteria in 1996. The action plan was subsequently reviewed and accepted by the Secretary of HHS in 1997. FDA is, therefore, encouraged to draw on the action plan for guidance and producing consumer-friendly, balanced with respect to risk and benefit and quality of life information and useful patient information sheets.

I would also ask what is the purpose of patient information sheets? As reported by FDA in July 2002, nearly 90 percent of prescriptions dispensed by community pharmacies were accompanied by written consumer medicine information. That percentage is likely closer to 100 percent today.

Does FDA plan to develop and conduct an ongoing national consumer awareness campaign to encourage consumers to visit the FDA website and then to download and print patient information sheets as a supplement or perhaps serve as an alternative to the

written drug information that is routinely disseminated with new and refill prescriptions dispensed by community pharmacies?

Are patient information sheets intended to supplement or replace such existing information, and how does a patient information sheet relate, for example, to a medication guide? I would also ask how will patient information sheets be promoted and disseminated?

Although access to the Internet continues to expand, significant numbers of consumers, as we heard on the first panel, and particularly older adults do not have such access. Primary reliance on the Internet to access the patient information sheets cannot ensure equal access by consumers to emerging risk and safety information. Encouraging health care providers to download and print patient information sheets is problematic, given the time and expense of so doing on an ongoing basis in various medical and pharmacy practices, for example.

There currently exists a nationwide pharmacy information delivery system with the capacity to disseminate written consumer medicine information with every prescription dispensed by community pharmacies in the U.S. How this existing nationwide

capacity to deliver timely and authoritative information to consumers can be enlisted, equipped and enabled to support communication of emerging drug safety and risk information is a more reasonable question to consider than how FDA can compete with such a system?

I would also ask why produce a patient information sheet for every drug product when, as stated in footnote number 5 of FDA's recent draft guidance on its drug safety initiative, our ultimate objective is to develop patient information sheets for all approved drugs, most of which will not have an emerging safety section?

This implies that FDA will become a drug information publisher in addition to its regulatory functions in competition with drug information publishers in the nonprofit and private sectors. It raises questions such as does FDA have resources and expertise to sustain this unique ongoing function?

How will FDA continuously update and distribute patient information sheets to consumers with every prescription dispensed and, lastly, why would a patient information sheet be necessary for every drug product and especially for those drugs without a narrow therapeutic index, i.e., safer drugs?

I would also ask how the patient information sheet relates to or differs from medication guides? FDA currently requires pharmaceutical manufacturers to prepare and disseminate or to establish the means to disseminate medication guides for select drug products that the Agency believes poses a serious and significant public health risk in the absence of such labeling information pursuant to 21 CFR 208.

Since the patient information sheet is going to be prepared for every drug product, that would include those drugs for which a medication guide is required, I assume. Is the patient information sheet duplicative of a medication guide or is it intended as an abbreviated medication guide or a med guide light, as it were?

Another question this raises is how specifically do patient information sheets and med guides differ not just in content, but in intended use and purpose? I would also ask how FDA plans to evaluate the effectiveness of patient information sheets singularly and in relation to their impact relative to existing written drug information and medication guides.

In a 2002 presentation entitled

"Communicating Risks and Benefits Through Labeling and Leaflets," Dr. Lechter of the Food and Drug Administration addresses the need for research on medication guides. At the time of that presentation in 2002, there were 10 drugs and biologics for which a medication guide was required. Currently, there are many times that number of drugs for which a medication guide is required, including two recently dispensed prescription drug classes, antidepressants, NSAIDs/COX-2 drugs.

Areas of research on medication guides, and I would now add patient information sheets, called for by FDA in Dr. Lechter's presentation are perhaps more relevant today than in 2002, given the expansion of the number of drugs for which a medication guide is required and the planned introduction of a patient information sheet for every approved drug product.

FDA is, therefore, encouraged to publish in advance for comment its planned agenda for research and dissemination of such research related to patients receiving medication guides and patient information sheets. If not, why not? Do patients read medication guides and patient information sheets and if not, why not?

Do patients understand the information,

especially low literacy patients? If not, how can the information be improved? Will patients heed the information? If not, why not? Do medication guides and patient information sheets reduce risks and increase safe and appropriate use of medicines? If so, which combination works best and why? How can risks be conveyed without discouraging patients from using a drug that has a favorable benefit versus risk profile for them without discouraging patients?

Earlier this year, the FDA conducted a national survey to obtain insight of licensed pharmacists' views of the availability and usefulness of drug information tools for communicating drug risks to patients entitled "The National Survey of Pharmacists to Assess Awareness of Drug Risk Communication Tools."

FDA's research found that only 70 percent of respondent pharmacists were familiar with the term medication guide, this after medication guides have been required for some medications since 1999. Of these respondents, only 30 percent stated that medication guides were very effective in communicating drug risks. Additionally, only 30 percent of respondents correctly answered that medication guides are required to be dispensed with both new and refill

prescriptions.

Among pharmacists who have dispensed the medication requiring a medication guide, nearly a quarter, 23 percent, reported that the patients have complained that a medication guide was not understandable. Nearly two thirds of pharmacists familiar with medication guides rated them as somewhat or not effective in communicating drug risks to patients.

Given these findings by FDA and the added complexities of introducing a patient information sheet for every drug product that would work synergistically with the drug information already available to consumers, FDA should reconsider its policy on patient information sheets and focus such time and resources on creating awareness about medication guides for high risk medications and encouraging health care providers to mediate such information with patients at the point of prescribing and dispensing.

Very limited time remains for FDA to ensure that drug information publishers' efforts to produce balanced, useful written information is conveyed with new and refill prescriptions by the end of 2006 pursuant to the Action Plan for the Provision

of Useful Prescription Drug Information.

One way that this national effort to develop and deliver useful information to consumers could be advanced by FDA is by FDA actively reviewing and commenting on the content of information produced by private sector publishers to ensure that it meets FDA's threshold for risk and safety information, for example. The Agency could be providing ongoing guidance on the development of content of drug information in the marketplace in this way.

Instead, the FDA, as recently as October of this year, notified major drug information publishers through NCPIE that it will not assist publishers in this manner, noting that there is ample information available to data vendors and pharmacies to help guide them toward producing and distributing information to consumers that meets the criteria set forth in the action plan.

I would suggest that, in this particular instance, collaboration can best ensure delivery of balanced risk and benefit information to consumers. Thank you very much for your consideration.

CHAIRMAN SELIGMAN: Thank you. Our next speaker is Rebecca Burkholder from the National Consumers League.

MS. BURKHOLDER: Good morning. The National Consumers League is the nation's oldest consumer organization and our mission is to protect and promote social and economic justice for consumers and workers in the United States and abroad.

NCL has worked extensively on issues surrounding communication of information to consumers about the drugs they take. NCL was one of the participants on the Steering Committee for the Action Plan for the Provision of Useful Prescription Medicine information.

Furthermore, NCL convenes a coalition of over 80 organizations called SOS Rx which is dedicated to improving outpatient medication safety. We also serve on the board of directors of the National Council on Patient Education and Information, NCPIE, and we support many of the comments made by NCPIE here at this hearing this morning.

NCL is pleased to be able to comment today on FDA's current risk communication tools for prescription drugs as outlined in the Federal Register notice. While we commend FDA for undertaking this effort to improve risk communication for drugs marketed and sold in the United States, we have identified several areas of concern.

I will be focusing my comments today on the patient information sheets and addressing some of the questions posed in the Federal Register around the following issues: Coordination of all information sources, harmonization of information format and content and communication of helpful risk information.

First, coordination of all FDA information sources. NCL believes it is vitally important for the FDA to coordinate all of its patient information materials. This is necessary both to avoid overloading consumers with vast amounts of potentially conflicting or duplicative information, and to ensure that the information provided is readable and understandable.

If the patient information sheets are going to be produced for all approved drugs, even those that do not have an emerging safety issue, it is important that their purpose and utility is clarified. As NCPIE just stated in it's comments, and I quote, "We would ask FDA to clarify the development and utility of the patient sheet, including its relationship to other written information consumers routinely receive with prescription medicines at community pharmacies."

If, however, the patient sheets are

properly integrated with other sources, they could provide consumers with a valuable tool. Consumers would be well-served, for example, by having access to a single web source with a complete and frequently updated and consistently formatted information sheet for all medications. The sheets could be searchable by indication, class or specific product name and would facilitate consumers' ability to compare medications across a variety of important domains.

The FDA has also asked specifically about strengths and weaknesses of the patient sheets. While we commend the FDA for developing the medication information summaries that are, we believe, for the most part understandable and easy to read, we have noted several weaknesses.

First, we ask that the FDA ensure that each patient information sheet has the same format for conveying information. The sample patient sheet referred to in the Federal Register for Adderall did not contain a section of what patients should ask of their health care provider. Other sheets did not specifically contain a section on what are the risks.

It is helpful for consumers to have a similar format for each medication, so they will know what information can be expected and that certain

questions will be answered. In cases where a specific section is not relevant, it is better to have the category left blank with notes acknowledging as much, as opposed to altering formats.

Secondly, there appears to be no mention of additional resources or references to which patients might turn for more or related risk and adverse event information. For example, a patient may not understand or appreciate the potential risks associated with renal failure or liver failure and should, therefore, be directed to a resource where they can learn more about these risks.

Third, the patient information sheets do not encourage patients to report their adverse events to the MedWatch system. Given the woefully inadequate information we have about how drug products perform on real populations once approved, FDA should be encouraging patients to use MedWatch to report their adverse events.

The current MedWatch system which relies primarily on adverse event data reported by drug manufacturers and, to a lesser extent, physicians is under-used. FDA has admitted that the present system yields only a small percentage of the total adverse events experienced.

In order to obtain a more realistic rate of adverse events, the FDA should actively encourage reporting directly from patients. To achieve this, FDA needs to add a consumer portal to the existing system and then promote the system's new features to consumers. As part of this effort, FDA should revamp both the telephone and Internet interfaces to make them more user-friendly and develop a separate reporting form that is easier for consumers to use.

The patient information sheets provide an excellent opportunity to promote the MedWatch system. These sheets could direct patients to report adverse events to their health care professional, but would also provide consumers with the MedWatch web address and toll-free number to encourage direct reporting.

The FDA also asked in the Federal Register "Do these tools provide the right kind and amount of risk and other information that the public and health care professionals need to make informed choices about whether to use the products?"

First, to address this question of whether it is the right kind of risk information for the public. As with all patient medication information, it is important to convey the risk information in a way that does not create unreasonable fear and result

in patients not taking needed drugs. Patients need to understand that the risk for an individual person will vary depending on whether certain risk factors are present, and their health care provider can help them determine what is right for them.

However, upon reading that Advair may increase the chance of asthma death in some people and without defining who some people are, it is likely some patients may immediately stop taking the medication. FDA may want to consider adding a statement in the patient information sheet after the alert information that patients should not stop or change medication until they have consulted their health care professional.

We have recently heard firsthand how when risk information is misinterpreted, the results can be harmful to patients. This past October, NCL held a symposium on communicating child health risks and the challenges of conveying and understanding research findings related to often controversial child health issues.

For example, we heard from a physician about her frustration when pediatric patients suddenly went off Elidel, a skin cream used to treat dermatitis that was linked with skin cancer. While the

children's skin condition became much worse and they suffered tremendously, doctors were frustrated because the risk of cancer from the use of Elidel was, as FDA stated, uncertain.

There was consensus among the researchers, journalists and others attending the symposium that all parties, including the FDA, need to do a better job of explaining that our scientific knowledge base with respect to particular drugs and diseases is never static. We are always adding to our knowledge, but have to make the best choice possible based on existing research.

To help communicate this level of nuance, the Agency might wish to provide more information in the patient sheets about the studies that serve as the basis for the FDA alerts and refer patients to other sources, such as the health care professional sheet and/or other partner sites that contain more detailed information on the studies. Ideally, one would like to be able to point consumers to a centralized NIH-managed database of all completed clinical trials, but that is really for another day.

Now, to address the question of whether it is the right kind of information for health care professionals. The health care professionals should

be an integral part of any patient education process, including education on medication use and associated benefits and risks.

In our work with the SOS Rx Coalition, a coalition of over 80 organizations focusing on improving outpatient medication safety, the health care professional is an integral part of an education campaign focusing on a high risk medication, oral anticoagulants.

To better understand the challenges, patients, clinicians and care givers face when managing oral anticoagulants, the coalition conducted focus groups and surveys of patients on this medication, as well as clinicians and care givers. The research revealed that there are gaps in health care management of patients on oral anticoagulants that expose patients to serious and often many risks. Clinicians indicated that better patient information and more time spent on patient counseling could help reduce these risks.

Based on this research, the SOS education materials for health care professionals will be integrated with the patient materials. Patients will be educated about the key questions they need to be asking their health care professional and, in order to

respond appropriately, the health care professional will have patient education material in order to answer their questions.

In the same way, the FDA's patient information sheets must be integrated with the health care professional sheets. The professional sheets should specifically refer the reader to the patient sheets and, more importantly, include specific questions and answers that the health care professional should share with their patients, such as do they know the risks associated with the medication, what other medications and behaviors can affect them.

After reading the patient information sheets, patients may very well ask questions that are posed on the sheets and the health care professional should be prepared to answer them for the individual patient in a way that is clear and understandable.

We remind the FDA that one of the stated goals of Healthy People 2010 is to, and I quote, "Increase the proportion of patients who receive verbal counseling from prescribers and pharmacists on the appropriate use and potential risk of medications." Prescribers and pharmacists could be encouraged to use the patient information sheets as a basis for verbal counseling of their patients.

Finally, FDA asked for comment on the specific mechanisms it should consider using to convey risk information, particularly to special populations. First, it is unclear how the Agency plans to get this information out to the general public, let alone special populations. Will the sheets be printed off at the pharmacy, given out by physicians or only accessed through the Internet?

We once again ask the FDA to coordinate the patient information sheets with other medication information, given that only having access to the patient information sheets through the Internet will limit its utility and effectiveness for some of the populations that need it most.

Seniors are taking more drugs than ever and are often on multiple prescriptions, not to mention OTCs and dietary supplements. Although Internet use is expanding, as we have heard, less than a third of seniors ages 65 and over have ever gone online. FDA should not just rely on the Internet, but use pharmacists, family care givers and health care professionals to convey information to seniors.

FDA may want to consider running public service announcements on radio and television announcing the existence of a new centralized resource

for consumers to get information about the prescription medications they take. The PSAs could point people to the FDA website, but also mention FDA partner organizations and resources that would help people get information that they need.

In closing, NCL is encouraged that FDA is seeking to improve risk communication to patients and we thank you for this opportunity to comment.

CHAIRMAN SELIGMAN: Thank you very much. Our final speaker on this panel is Annetta Cheek from PLAIN.

DR. CHEEK: Did it already. Okay. I will wrestle with the system. Is the page up? There we go. My name is Annetta Cheek. I am not a health care professional. In fact, I am an archeologist, but I am the chair of an interagency group of federal employees called the Plain Language Action and Information Network and we struggle daily to get our agencies to communicate more clearly.

When our group decided to take this on, I also talked to Susan Kleimann, who is the executive director of a relatively new nonprofit private sector organization, the Center for Plain Language, and we decided to divvy this up so that I will be talking about the website and she will talk about specific

documents.

So I decided to visit the website as a consumer might and what follows is my thought processes as I walked through the CDER website. This is a legitimate way to test the website where you get someone to take on a task and walk through a website and tell you what they are thinking as they go along, so I was basically the tester and the testee at the same time. And if we run out of time for my slides, that's fine, because that tells you something, too.

So, first, let's look at the home page. You have seen that already. Here is the top. Here is the bottom. This is obviously a complex site with lots and lots of information on it, many different entry points for information that all appear similar to me. I had no clue which might be the best link to go to.

I also wondered what CDER was. The term was all over the website and I found this neat program that lets me highlight things. And I had no clue what CDER was since I wasn't a health professional, but I decided I didn't really care. It didn't matter to me. It was just sort of "background noise" in the information I was looking for and I suspect that most consumers would have the same feeling.

So then I decided to look for information about risks, because that's what this was supposed to be all about. And the first thing I saw was this big, red drug safety button which was great. That's great, right in the middle, bright red, easy to see. So I clicked on it and I went here.

Now, this page is a little complex and, of course, I'm not showing you the whole page. Again, there is lots of material on here and I really have little idea about which one to go to. The very first one looked promising, so I clicked on it and guess where I went? I went back to the home page. I don't think that's where you meant to take me but that's where I went.

So then I took the next one and guess where I went? I went back here. So, at that point, I decided that the website probably had a few problems and I decided instead of looking for risks that I would look for information about drugs. Maybe my doctor has recommended a drug to me and I want to find out more about it, and I thought maybe as I did that I would come upon the risk information.

So I go back here and I see Quick Info Links. Well, that's good. People that are web users, and I do have to say I am a very heavy web user, so

I'm not a novice at using the web as many of your customers really would be, but Quick Info Links is an attractive link to go to.

So I picked the first one and I went to drugs at FDA. That seemed like a good thing to go to. I came to an alphabetical list. That's good. I like alphabetical lists. Picked one, went to it and then I got overwhelmed. If I were looking for this drug, you know, which of these, I wouldn't know. I picked one. I went to it and decided this isn't the information I'm looking for. This looks more like it's for your health professional or, you know, not your customer.

So that was a dead end, so I went back to the home page. So I decided I was going to stick with the Quick Info Links a little bit longer, see if I was more successful the next time with the Drug Information Pathfinder.

So we go there and you have seen this page before. Dr. Zuckerman showed it to you. And, again, this is a sort of overwhelming page. There's lots and lots of stuff on it, but I do see -- here is the bottom of it and I did see one thing that explained to me why drugs at FDA wasn't the right link for me because it's listed under drug approvals now. So, apparently, it's something for industry. At least

that's what I would get from drug approvals as a heading, but I didn't know that based on what I saw on the home page.

So there is this other link that looks promising, but that is also under drug approvals, so at least for now I rejected that. I don't want to deal with this complex page. Let's see if I can find something else on the home page, so back we go.

And this time I move to the middle column and I see this about safety information for specific drugs. So okay, let's try that. Now, we have a specific alphabetical list. I like alphabetical lists. I read the top though and, as a person who had never been to this site before, I got very confused.

What is the difference between these, among these three types of documents, particularly when the third one lists the first two as being contained within it? Very confusing to me and when I look down at the list, there is no clue about which one of these documents I'm going to get when I click on a specific drug.

So this may be the best site. At this point I'm thinking this may be the best site to go to, but maybe there is something better, because it did confuse me so I'll try one more time. I come back

here and now, I see drug information up at the top.

This is a fairly common problem. I redesigned my own website, plainlanguage.gov. Well, I didn't do it, but people helped me do it and we found that a lot of people don't look up at those navigation items on the top of the page. And, really, I had not seen it until now because the first, that red drug safety thing, had attracted me.

So I drop down the menu. Again, a little complex, hard to tell, but I decide on consumer drug information. That's where I think I should go. So I go here and the first thing that attracts me, and if I showed you this whole page, I think you have seen this, I think this was another page you have seen before, it's a very long page with a lot of complex stuff on it.

So this attracts me and I go here. Hm, this looks familiar. Yes, indeed, it's my three friends, the patient information sheet, the consumer information sheet and the drug information sheet. Okay. So, now, I'm resigned to having to look at this material so, of course, we'll pick Adderall since that's what you guys were talking about, and I get this.

Okay. There is a lot of stuff here. I'm

not finding it right away. I see a PDF on patient information. I go there and I am not impressed with this as a piece of information going to an individual consumer. As someone else said, this is aimed at multiple audiences which, from our plain language point of view, is always bad. You know, each document, each page needs to go to one audience or you don't serve any audience well.

I scroll down. I do see what are the risks over on the right, and so I think I have now concluded the task. I have found the information about risks. It took me a long time.

What is my overall impression? It's hard to navigate. The pages are too complex. The lists are too long. There is similar material, not identical, in many different places. It's impossible to tell without opening a link what audience the document addresses, and you shouldn't make your audience open a link to find out what they are going to find there.

Some web pages and some documents have multiple audiences and there is no place for one audience to go to get all the information that they need. If I were really trying to get information about drugs, I would go somewhere else.

And someone at FDA sent me a link to a news article that came out, I believe, yesterday in the LA Times. I didn't have time to read it all. It apparently links to a study of the effectiveness of sites, and the quote is "If it's drug information you're hunting, skip the FDA's site that can be difficult to navigate." So that's what the LA Times says.

Okay. So I might go here, I might go here. I would probably go here. One thing you have going for you as a federal site is that we do know that federal websites, people give credibility to the information on federal websites. So if I had a bunch of private sector sites, I might reject them and go to someplace like the Mayo Clinic, because that seems like I could trust them. The LA Times article listed something that I didn't see, which was pdrhealth.com as a site to be visited.

So what should you do? Get rid of all that extra stuff. Someone mentioned that a lot of the information on there is your process. The public doesn't care. I mean, every federal website has that kind of stuff on it. You're certainly not alone, but the public doesn't care about that stuff.

The site is supposed to be -- you know,

who is the site for? Think about who the site is for. Every page you should have, when you design a page, who is this page for and have that clearly in your mind. You need a lot of input from your customers. This is a great way to get it and I compliment you on having this hearing. It's a terrific step.

You have the ASCI survey on your website. I know, because it popped up on me several times as I was clicking through, focus groups, useability tests. One thing I didn't list was what are the 100 top terms that people search for on your website. You take those, you make sure that when they search for those 100 top terms they go to a page that gives them the right kind of information for those terms. It's sort of your hot list.

Give each customer group an easy-to-find destination and from that destination, they can get anywhere to any of their information. Don't make them open a link to find out what is there and write each page for one document only.

And thank you for the opportunity to speak. I commend you for doing this and wish you lots of luck. And if PLAIN can help you, Joanne Locke was out there somewhere. Joanne, there she is waving her hand, is your rep on our Plain Language group and we

would all love to help you with this, because it's a very important project. Thank you for your time.

CHAIRMAN SELIGMAN: Thank you very much. At least I know I'm not alone when I try to navigate the FDA website. Questions from Members of the Panel? Anyone? Yes, Sandy?

DR. KWEDER: I want to thank you all for your really thoughtful presentations. These are really -- your comments are really helpful and certainly put before us some daunting tasks to address.

And I wonder if any of you would care to comment on if we had to prioritize, what we would address first. Given some of the things that you said, I think -- Annetta Cheek, I know what you would say, but some of the other folks, I would just kind of like to hear.

Is there one thing that, if we could wave a magic wand and fix this, you think it would give us the best start possible?

DR. ZUCKERMAN: Does this work? Yes. Well, that's an impossible question to answer, of course. But I do think that the website does reach a lot of people and it's very unfortunate that it's not going to be reaching too many people over the age of

65 who probably use more prescription drugs than anybody else but, still, you can reach an enormous amount of people for not much money and, yet, you do have a website that is not useable by consumers, basically.

And so I do think having a website just for consumers that really has only new information, not the process, and information that is clear, you know, in plain English and, you know, easy to navigate would go a long way.

You know, I do agree that it's -- well, I think a lot of people wouldn't know to go to the Mayo Clinic website and I don't think they should go to the Mayo Clinic website. I think they should go to the FDA website. I think that should be the source, you know, the source of information. And, of course, we know if they Google a drug name, they are going to end up on the drug company's website and that is not usually the best place for risk information.

CHAIRMAN SELIGMAN: Dr. Wolfe, did you want to say something?

DR. WOLFE: Yes. Everyone showed the CDER home page but since most people in the country have never heard of CDER and since we're talking about drugs, it would seem that the FDA home page should

have a huge thing somewhere, I mean, as opposed to the small thing that is there that says drugs, devices, whatever else, so that someone -- most people who are interested in the FDA, from a patient perspective, are interested in drugs, and not that other FDA functions are not important, but that's where, A, most of the budget is and where -- most of the regulated products that we are particularly concerned with are there.

So I think that if, on the FDA home page, in one huge place you could direct people, drugs, something else, and when they go to drugs in one huge place, it could say, as interestingly it says on drug companies' home pages, this is for patients or for doctors.

So the route should be FDA home page to drugs and on the drug home page, it should say drug information for patients, big, big, big. And then they go there and in one integrated place, as opposed to 10 integrated places, one can find out the latest and identified as latest, as Diana pointed out, if it is that recent, information because I think that's the number one thing that people are going to the FDA website for, people other than ourselves or health professionals.

And it's not to say that we sort of blow

off or write off these other people, because they can be directed to places, too. So I think that that's just a very fundamental design issue. It's not just on the CDER home page that there is too much information.

On the FDA home page there is too much information and people will get lost or will keep recycling, as another pointed out, back to here and back to here. It's like a catch-22 loop in reverse or something like that. So, anyway, just a couple simple suggestions.

CHAIRMAN SELIGMAN: Other Members of the Panel want to comment?

MR. BULLMAN: I was going to suggest perhaps some advanced information or information gathering and querying of the broad range of stakeholder groups that are ultimately affected or impacted by the programs and policies that are developed.

I know our organization was contacted about the patient information sheets after they were already posted, and we were asked can we help disseminate them. And, you know, the first question is what is a patient information sheet?

And, you know, I recognize that you are a

regulatory agency, but the fact and information gathering process, I think, in advance even to -- almost like focus groups with professional and patient groups with trial balloons, I think, just to find out, you know, what the first level implications are and perhaps avoid some of the unintended consequences after the fact.

DR. KWEDER: I would assume you would apply that not only to the patient groups, but to health care professionals as well?

MR. BULLMAN: Yes.

MS. BURKHOLDER: I would just add that I would agree with what everyone has said, but would just add --

CHAIRMAN SELIGMAN: Could you activate your microphone, please?

MS. BURKHOLDER: Now is it on? Now?

CHAIRMAN SELIGMAN: Yes.

MS. BURKHOLDER: Okay. Sorry about that. Coordinate, coordinate, coordinate which is really what everybody has said, but I still think some of the confusion is the utility of each of these various tool pieces and when it was talked about going onto this site, finally getting to the drug-specific site, there were too many different pieces of consumer

information, consumer medication information, medication guides, patient safety information sheets, to narrow it down.

So, again, it's really what everybody else has said, but to be very careful with the terminology and think about the purpose and utility of each tool.

DR. CHEEK: Yes. I would like to see, I mean, each drug should have one document, one page, one site about it with the different pieces on that and they should all look the same, as someone else recommended that, you know, you need a consistent format.

But, I mean, I still don't really understand what the difference between a consumer sheet and a patient sheet would be. You know, it doesn't seem to make sense. And are you doing duplicate work? You probably are and you can't afford that anymore.

CHAIRMAN SELIGMAN: Any other questions from the Panel? Yes, Dr. Gottlieb?

DR. GOTTLIEB: Towards the close of your remarks, you had mentioned the FDA working with publishers to assist them in some of their risk communication and some impediments to that. Can you elaborate on that? I'm not sure if I missed it or it

was just in passing.

MR. BULLMAN: Hello? That's on? Fairly recently, several of the publishers, third-party drug information publishers, asked, sought input from the Agency on their database of drug information products selectively, essentially as maybe a litmus test or a near rounding third check of their clinical information, vis-a-vis, it's conformance with the action plan. And that was not amenable. That was not seen as something that the Agency would do at this time, and time really is an important aspect right now of this initiative.

CHAIRMAN SELIGMAN: Any other comments, questions from the Panel?

DR. CHEEK: Could I make one last comment? I should have said this before, but information on the web should be designed for the web. What you have up there, as all federal agencies do, is a lot of information that was designed for print, not particularly well-designed for print, but nevertheless designed for print and then you stick it up there in a PDF and it doesn't translate very well to the web. So, you know, the drug information on the web should be designed specifically for display on the web.

DR. ZUCKERMAN: Could I add one thing?

Another real problem, I think, with the website is that so much of the information is out of date and that is partly because you have the whole process. So you have, you know, the advisory from 1999 and then you have the advisory from 2004.

I mean, just as an example, if a consumer was searching for information on Bextra, they might end up with a consumer information sheet that was last updated in November of 2002. I mean, that has been -- there is a drug that has been in the news so much and I know you can't necessarily update everything, but to have a 2002 document on the web and nothing updated since then in that format, you know, it is not just misleading. It's providing really inaccurate information in terms of what we know now.

PARTICIPANT: It's off the market.

DR. GOTTLIEB: Just to follow-up.

DR. ZUCKERMAN: Yes, right. But, still, people might have it. You know, they might still have it in their --

DR. CHEEK: Right.

DR. GOTTLIEB: To follow-up on Ms. Cheek's points, obviously there is a lot of creativity going on in the consumer environment with other websites, many of which are linking to FDA's website as a source

of reliable information.

Do you have examples of some of the websites you think are doing a particularly good job? I think we found out the one website you think is challenged, but what is working well out there?

DR. CHEEK: Well, from the point of view of drugs, I can't really tell you. I guess I would just look at that site that the LA Times suggested was a good site, which was pdrhealth.com, but I haven't even looked at that. I have looked at a lot of other federal websites and I like the sites that have a dual pathway to get to information one by topic and one by customer group.

The Department of Agriculture site is not bad. A little agency called Pension Benefit Guaranteed Corporation, which is pbgc.gov, has a pretty well-designed site. Firstgov, firstgov is a decent effort considering what a huge mass of material they have to try to get consumers to. So those would be some that you might take a look at, but you need some professional help.

DR. ZUCKERMAN: And I would just like to add that it's really important that the information be categorized by type of drug. You know, a patient should not have to know the name of every

antidepressant to look at, you know, what antidepressants are out there. There should be a category of antidepressants that they can look at.

So, you know, currently it's alphabetical by the name of the drug but, you know, what if they want a painkiller and what if they want to look at lots of different painkillers? How are they going to know how to get that information?

CHAIRMAN SELIGMAN: Ray?

MR. BULLMAN: On the first panel it was suggested that the Agency might undertake some public awareness outreach campaigns or public education campaigns. I think it's interesting on the 7:00 p.m. news nightly or weekly or whenever when there is a story about a drug product. There is always talk about the label has been changed, and I would be willing to bet you that probably 99 out of 100 people that you pass on the street would think that is the label on the bottle itself.

And so, therefore, if the Agency is on watch and creating changes to the label on the product that I get, it must be okay because I just got the drug and the label and I know that the change has been made. So, I mean, some of that is glossary but some of it just, I think, creates more confusion as well.

That is just one small point.

But I know recently the Agency announced daily med with the posting of the professional insert on the -- the product insert on the NIH Library of Medicine website. I would think that that would also or suggest that that might be also a good repository for med guides as they are approved and published as well so that people, health professionals and/or patients, could have access to that information.

DR. WOLFE: Just one comment. When we designed our website, worstpills.org, which has now in its present form been up for about a year, we thought a lot about different ways people might approach something having to do with drugs. And so the database that is used when one searches, there are four different ways of searching.

One, obviously, the name of the drug which either a generic or a brand name comes up. Two, the disease that you're interested in or, you know, pain, arthritis, whatever else. You can go that way and get the information. And, three, the adverse drug reaction since a huge number of people are literally being treated with drugs to treat adverse drug reactions, such as probably close to half of the people taking Viagra have drug-induced impotence.

So you can put in sexual dysfunction and 130 drugs will pop up and all the information. And the fourth is just by general categories like drug advertising or whatever. So, I mean, I'm sure it's not perfect but assume as one goes to search, it bifurcates into these four ways.

Obviously, the most common one that is used from the statistics on our site is by drug, but people do have, if they want these other three options, they can go to, you know, and once you have created a database, that kind of thing is not that difficult to do.

DR. ZUCKERMAN: Yes. And I would like to add, I think, that you have some really good models. Just look at direct to consumer advertising and how they present benefits and just try to do risks in simple language, nice colors and, you know, something that people can read quickly and understand.

Of course, risk information is usually more complicated, but still you could go a long way just looking at how drugs are advertised in terms of their benefits and what the comparable risk information would be.

MS. BURKHOLDER: You know, I do think that the patient information sheets are a good start.

There is more that could be done in the formatting, but they are a good start. You could also think of, I'm not sure how you do this, direct to consumer advertising as a way to get people to go to the FDA website for more information on risks and benefits. So that's an idea.

DR. CHEEK: You could always get a domain called druginformation.gov or druginfo.gov and advertise that. I mean, we have, you know, seniors.gov and students.gov and firstgov.gov, and that way you wouldn't have to have cder.faa.gov which no one understands.

CHAIRMAN SELIGMAN: Thank you. Yes, Anne?

DR. TRONTELL: I have a quick question for Dr. Cheek and then one I would really like not to miss the opportunity, after all this excellent input on our website, to ask all these consumer organizations to address the question.

First, the question for Dr. Cheek, which is, you know, when I think you lightheartedly suggested getting professional help, you know, we have just seen the extensive infrastructure that is put in place around print materials and understanding cognition, eye tracking and other matters.

Can you elaborate a little more if FDA was

to seek expertise in this area where we might start?

DR. CHEEK: Well, you could start with usability.gov which is the National Cancer Institute's website, but there are a lot of people, information architects, web designers, a lot of people that do research on usability, web usability specifically. Let's take one example.

What we did at FAA, which is my agency, we selected six customer groups and found three people from each group and then we had a usability professional come in and she guided us in setting up the tests. We developed little -- they are called scenarios in which you would ask the person a question that they might actually ask of your site.

And then they do what I did when I went on the site and you're videotaping them and they walk through the site and they say okay, I would click here because of this and oh, I didn't expect that. And just three people from each customer group gave us a wealth of information.

And we also hired someone who took that data, the results of the search, some actual focus groups and the results of that, we also have that survey, that online survey that have you, and took all of that information and put it together and said,

okay, here is your top three problems, here is what I would start to work on and surprise, surprise, navigation was the number one problem.

And then, at that point, once you really hone in on the problems, then you move on to finding the right professional and I would make some recommendations in private, but it's a little touchy saying, you know, this person versus that person, but we can certainly talk to you more about that.

DR. TRONTELL: My next question diverges from the website. I think everyone has described the elderly as a population that is less than likely to use the Internet and, clearly, this is a very important population to reach.

Can you suggest other cost effective ways that we might best reach that population? For anyone.

MR. BULLMAN: Since timing is everything, I would suggest that perhaps as an opening salvo trying to work out some kind of an either initial and/or ongoing relationship with CMS to provide information to the Medicare population as materials are disseminated not just about enrollment, but as the program rolls on about safe and appropriate use of the medicine, of their medications, and referral to resources and materials available from FDA.

DR. ZUCKERMAN: Yes, I would like to -- well, my parents are in their 80s and I have become very aware of how the older people are and the more medications they are taking, the less likely they are able -- the less likely they are to get the information they need and the less likely they are to be to be able to understand it.

CMS is actually a good example of providing a lot of documentation to patients as absolutely unintelligible. So I would really be a little concerned about going there to partner. Really, their materials are outliers in terms of providing information in a way that cannot be understood.

A different way to reach out to the elderly would be CME courses for their health professionals, and I think that CME courses are actually something that our center has been looking into and we have been shocked to discover that because of the way the CME process, the continuing medication education process, works, the people providing the courses have to pay a lot of money and, as a result, it's almost entirely pharmaceutical company money that is providing this education to doctors.

And it would be great if somehow the

Government was able to be a more unbiased source of information on these products and by educating health professionals who serve patients and who particularly serve elderly patients, I think that would be a great way, you know, to reach out providing useful information.

You would be getting, hopefully, both populations at the same time, the health professionals who are prescribing drugs and giving information about them as well as the patients. So I'm not exactly sure how one would go about doing that in terms of the Government, but I do know that we're really in a situation now where the vast, vast majority of continuing medical education is funded by pharmaceutical companies.

DR. WOLFE: One suggestion on this. The so-called Part D of Medicare is unworkable. The sooner it fails the better, just impossible, and part of the cheerleading for it was done by Dr. McClellan when he was at FDA, as you know, although it wasn't part of his job description.

However, Social Security checks get sent out at regular intervals to everyone in the country and aside from CMS itself or CMS at all, there is an opportunity if you work with the Department of HHS

that sends out Social Security checks to get a simple piece of information included with the Social Security check, which you could design.

I mean, I don't think there should be that much difficulty. You know, rules for safer drug use, whatever you want to call it, things that would be simple, clear, large print and would go with the Social Security check which everybody opens, just something within the department but not depending on CMS with all of its multiple problems these days.

DR. CHEEK: You could also look at IRS, they mail a lot of letters out, and the Veterans Administration. The Veterans Administration might be a good one.

DR. WOLFE: Yes. It's just that Social Security probably includes as many or more people and drug information would be at least a little more on the topic of Social Security than oops, you owe us $30 for a delayed filing or something like that.

MS. BURKHOLDER: You could also specifically target the family care givers. As we know, many seniors are taken care of by members of their family. There are several national family care giver organizations. You could also provide information, because usually these care givers are

looking for help, to physicians or health care providers that specifically target the care givers.

DR. CHEEK: And there is always AARP.

MR. BULLMAN: I would like to also recognize the fact that back in, I mean, I'm dating myself as well, but back in the early '80s the FDA did, as a matter of fact, work with NCPIE and did arrange for a mailing in Social Security checks for an informational booklet about get the answers about your medicines.

And my point about the CMS is not so much to try and insert and integrate text and information about the Part D Program, but that it's a huge mailing list to the appropriate target audience for high risk patients, and I think that collaboratively the agencies ought to or should be working together to make sure that, in addition to information about access to information, there is also either included direct and specific information or references and links or resources to information about appropriate and safe use of the medicine as well.

CHAIRMAN SELIGMAN: I have a question about medication guides. Dr. Wolfe, you talked about the survey that was conducted in Erie, Pennsylvania.

DR. WOLFE: Right.

CHAIRMAN SELIGMAN: And Ray Bullman also talked about the FDA survey which in many ways reinforced what you had to say about the poor awareness and/or poor distribution of the, you know, FDA-approved medication guide and I would be interested in both of your thoughts, as well as other members of the panel, as to how one might improve or remedy this distribution problem.

DR. WOLFE: Well, I mean, the reason we picked this instance of Celebrex is that that has gotten past the decision making, should you or should you not have a medication guide.

There is one and one might argue from a legal perspective, I am just a doctor not a lawyer as I like to say in these legal circumstances, that these drugs are misbranded, because to the extent that the regulations governing med guides go to actually handing it out, not just simply having the FDA get companies to print it.

If a patient is getting a prescription filled that is supposed to have a med guide and they aren't, the drug is misbranded and there is, obviously, the role of the pharmacist in this, particularly if the information is being produced, which we know it is, for these med guides and if it is

being shipped to the pharmacist.

I think that generally the lack of awareness of this program, and partly because it covers such a tiny fraction contrary to what it would have covered if this program had gone through in '81, I think there is a huge problem of awareness. And if the FDA is going to put out regulations and specifically require med guides, there is some obligation to do some kind of survey.

I'm not sure that there has ever been an FDA survey at the level of the pharmacy to check on med guides. There certainly was this survey done by Bonnie Svarstad at the University of Wisconsin on patient information leaflets which had these appalling results.

But there is no reason why very simply and easily, as we were able to do, you couldn't do some checks on the med guides that are going out, which, if nothing else, will increase the sensitivity of the people participating, as in the pharmacist particularly, that they have got to get these out.

If they can just sort of say, well, you know, it's another med guide, we don't have to give it out, then it's meaningless if no one gets it and if they get -- I mean, particularly if you want to call

it humorless, humorous rather, this example I cited where the patient is getting a patient information leaflet that says see your med guide but they don't get a med guide. You know, that's ridiculous.

MR. BULLMAN: One of the things that our organization has been actually in some discussions with the FDA about is making the distribution or the means to distribute the medication guides such that when the medication guide is delivered over the transom, as it were, into the pharmacy that it really is not then literally raining pads of paper or tear sheets of medication guides from various multiple sponsors for the same information.

If the drug information publishers and pharmacy system vendors and pharmacists could affix or append the medication guide and integrate them into their drug information databases, that makes the production of that, the actual physical printing/production of the medication guide, part of the process of filling the prescription on a normal kind of a regular work flow basis.

So I think that's important and that might mean for right now some consideration by the Agency about design and formatting, for example, vis-a-vis the med guide regulation.

But I think also that there is a lot of noise. I'm not a pharmacist, but I think we all on the panel interact with pharmacy organizations. There is a lot of confusion, if not about the medication guide, about the implications of being out of compliance with not providing a medication guide in terms of, you know, if there is a regulation, who is enforcing the regulation, what are the implications of not and, therefore, the implications of the regulation being considered as not being enforced, for example.

DR. ZUCKERMAN: Another option might be if you think about direct to consumer ads in magazines that have usually something resembling the package insert on the back, which I showed the Zoloft one which had like no white space at all and was absolutely impossible to read, why not have a med guide on the back instead?

You know, if you're having advertising in magazines or, you know, newspapers or other print, why not have the med guide for that same product right there?

DR. WOLFE: Only about 1 percent of products have med guides. It's a problem for the other 99 percent.

DR. ZUCKERMAN: Well --

DR. WOLFE: It's a start.

DR. ZUCKERMAN: Well, you would have to have them.

MR. BULLMAN: Right, and the NSAID med guide is almost three pages long. So, I mean, that would be -- you would end up with a not-so-brief brief summary, essentially, at the same time.

DR. WOLFE: It would be more advertising revenue for the newspapers then. That's it.

DR. ZUCKERMAN: Yes, they would be happy. They need it, too.

CHAIRMAN SELIGMAN: Any other questions from Members of the Panel? Well, thank all of you very much for excellent presentations and for responding to our questions. We will reconvene at 1:30 this afternoon, in an hour and 15 minutes. Thank you.

(Whereupon, the meeting was recessed at 12:13 p.m. to reconvene at 1:33 p.m. this same day.)

A-F-T-E-R-N-O-O-N S-E-S-S-I-O-N

1:33 p.m.

CHAIRMAN SELIGMAN: Am I on? Yes. I would like to call this afternoon's session of the Part 15 hearing on communication of drug safety information to order. Thank you all for returning to this afternoon's session.

Let me start by first of all apologizing. We originally had two full panels scheduled for this afternoon but, unfortunately, due to various cancellations beyond our control, we now only have one panel which consists of two individuals.

So the way I would like to structure this afternoon's session is that we will hear from the two speakers who are on our panel, then offer an opportunity for any members of the audience who wish to make a statement or ask any -- make any remarks for the record, and then close after that our open public session. So we'll be finishing early.

Tomorrow morning we will again begin at 8:00 in the morning and then, as it turns out, tomorrow we, indeed, do have a full day of sessions and panelists that will take us through the end of the day. Again, I apologize. Ordinarily, we like to have the first day a little heavier than the second but,

due to circumstances beyond our control, we were unable to accommodate that.

So with that, let me introduce our first speaker for this afternoon, Ellen Liversidge.

MS. LIVERSIDGE: Okay. Good afternoon, ladies and gentlemen and Members of the Panel. My name is Ellen Liversidge and I am the mother of a son, Rob Liversidge, who died after taking Eli Lilly's top seller, Zyprexa, an atypical antipsychotic in October 2002 and of a daughter who is thankfully alive.

I am here today to speak of the FDA's efforts in the areas of drug safety communication, and I would like to say that I speak also in behalf of many parents around the country that have lost their children to psychotropic drugs.

This FDA topic today, that of the Agency's drug safety communication efforts and their successes and failures, has particular relevance for me, because it was the lack of any mention of a warning having to do with drug safety on the Lilly drug, Zyprexa, that caused my son, Rob, to die on October 5, 2002.

In fact, the truth of the metabolic lethal conditions that this drug can cause was so little known by the medical community at the time that the doctors in the ICU trying to save Rob from ultimate

death from profound hyperglycemia tested him for every possible condition they could think of, including AIDS and West Nile Virus.

In fact, after his death I really had no idea why he had died. However, I found out eventually on the Public Citizen website that the truth had been known for some time by the FDA and by other countries, and in other countries Lilly had been required to place a warning label on Zyprexa for diabetes, hyperglycemia and death.

My urgent wish at the time was to get a warning label in this country, so that others might not die, and I was very involved in the first article about this on the front page of the Baltimore Sun in March 2003. The article was about Zyprexa specifically and talked about Rob's death. But, at the time, the FDA was quoted as saying they were not ready to require any warning labels, because they were examining all the atypicals in this class to see if they might also have this problem.

Time ticked on and another front page article about Zyprexa came out in the Wall Street Journal that spring. Again, the FDA said the same thing. People were dying. I have no idea how many, but there was no warning.

A third article came out also in the spring of 2003 on the front pages of the New York Times about the dangers of Zyprexa. All the articles were specifically about Zyprexa. Again, the FDA did not act, repeating that they will still looking at all the drugs in this class. How was the Agency protecting the public health with this reaction?

When the FDA finally acted, over two years after other countries had, it was the fall of 2003 and all the atypical antipsychotics were required to place the same warning even though it was clear that the most dangerous drug was Zyprexa. I heard, at the time, that Lilly was relieved not to have been singled out, not to have anything threaten their best selling drug, even though the evidence was clear that it was the most dangerous.

Rob was 39 when he died. He had been diagnosed with manic depression at age 20 during his sophomore year at Cornell. He had always been a popular, brilliant boy, attaining almost 1,500 college boards, having girlfriends, playing first the drums then, thankfully, the piano with excellence. And he was philosophical and kind.

He took this diagnosis, given following a brief psychotic episode, hard because the first doctor

misdiagnosed him with the label of schizophrenia and said he would never get better. After being in and out of the hospital for three years, I found different care and it was quickly ascertained that he had manic depression.

One clue was that my father had had it briefly before he was killed by electric shock therapy back in its early days. So both my father and my son have been killed by psychiatry.

Rob lived for 19 years with this diagnosis. He had the strength and fortitude along with a caring psychiatrist who didn't just shove pills at him to finish his bachelor's and master's degree, have a love life, work professionally at the EPA, have fun and live fully. The only drug he ever took was lithium.

When he first had to go on Medicaid in Maryland in the year 2000, the overworked psychiatrist gave him 15 minutes of his time for each appointment and put him on Zyprexa, which we were told was very safe. When it came to bring suit, we did not sue the psychiatrist believing that he was uninformed as to the lethal possibilities of Zyprexa, and that the doctor may also have been pressured by the Maryland Medicaid system to use this or another atypical, as

opposed to placing him back on the lithium that had always worked before.

Why? Because of TMAP, a program that started in Texas when George Bush was Governor there that pushed the new, expensive atypical antipsychotics onto the formularies of first Texas Medicaid then many other states.

17 years of life my son had on lithium followed by two years of sliding into death with no warning at all. His death came quickly. On September 30, 2002 he said he didn't feel well and thought he should go to the hospital. He was not exhibiting any psychiatric symptoms and to my eternal regret, I did not take him.

On Tuesday, October 1st, I got a disturbing call that he had been taken to the ER. When I got there, Rob was almost out and all I could do was give him chips of ice to suck. I was helpless and terrified. Just before he went into a coma for good, he said one word. Mom, he cried out in panic and anguish. I believe he knew at this moment that he was going to die and four days later he did of profound hyperglycemia, one of the conditions Lilly denies as having any connection with its best seller.

I hope I never have to meet a Lilly

executive. It's hard enough to be here talking to you, the people who could have but did not save my only and adored son's life. Why did you wait? Why didn't you require a warning on the label?

The FDA has repeatedly shown this behavior with Zyprexa. According to your own Dr. David Graham, you waited three years after knowing to require a black box warning on the atypicals for people with dementia and Alzheimer's and you were still waiting to require a warning for Zyprexa IM even though there has been a warning required for this overseas since last year, a warning of potentially fatal adverse effects.

What do you do while you are waiting to require these warnings or deciding to pull a drug from the market? Do you wait until there are a certain amount of deaths? According to Dr. Graham, 62,000 are estimated that will have died from atypical antipsychotics this year.

Is this enough deaths to consider banning them from the market? Have you analyzed which of the atypicals are causing the most deaths, undertaking action to remove them from the market? How many deaths is it going to take to remove the worst of the atypicals from the market?

This presents an opportunity to make my

first point about the success or lack of it with FDA drug safety communication efforts. There must be a system in place and an agreement that drugs sold in this country will automatically get tagged with a black box warning of some sort if a similar action is taken in one or more specified other countries or be banned if another country bans a drug.

It is obvious that several other countries are much more apt to require warnings from pharmaceutical companies than this country, much more apt to act on the side of public safety quickly. If the U.S. had followed the lead of Japan and one or two other countries in 2002, my son would be alive today. Why was this step not taken?

The second point I would like to make is about MedWatch. I earnestly filled out a report about my beloved son's death and sent it right into MedWatch as soon as I knew there was such a thing. I know this sounds terribly naive, but somehow I expected a person at the other end to contact me, ask me about what happened and to express sympathy of my loss.

I never in a million years expected silence. Silence is what I got and what I guess everyone gets who uses MedWatch. Does anyone at the FDA use MedWatch? If so, is analysis done of this

data? Has anyone surveyed doctors in the field about their use of MedWatch?

I read the Canadian National Health site and it is clear that their system is used, used for decision making about warnings, used to give warnings even if a warning is not required to be placed on the drug itself.

The third point I would like to make is about adverse event reports. I received a copy of the Zyprexa adverse event reports from the year the drug was first used, 1996, up until this year through the Freedom of Information Act. Assume these reports are taken from MedWatch, the over 2,000 reported deaths in the report represent a lot of people who have died from Zyprexa if one supposes a 1 to 10 use rate for MedWatch.

Again, do these numbers matter to the FDA as it makes decisions about black box warnings or removing the drug from the market? I plan to get the MedWatch reports for all the other atypicals to compare their death rates. Is this being done by the FDA as well?

The fourth point, who decides? It's my understanding that some of the same people within the Agency and the Drug Safety Committee that decide what

drugs are approved are those that decide that a drug must place a warning or be removed from the market. If this is the case, the practice should change.

Not only who approves a drug should sit on the committee that determines its safety, the needs for warnings or the need for recall. Every person on the Drug Safety Committee should be required to sign strict conflict of interest statements. I have read that some of the people on the committee have close ties to the pharmaceutical industry.

Practicing doctors with no ties to the industry should sit on these committees, not just Government employed non-practicing physicians, and family members should also be represented on the Drug Safety Committee. I believe it is this decision making in the absence of data through other countries, MedWatch and adverse event analysis that causes so much unneeded death and disability from prescription drugs.

We know that the number of suicides in the initial Zyprexa trial, 12, were the highest for any atypical and the number of attempted suicides was not revealed. And what of the fact that 8,000 plaintiffs were paid off by Eli Lilly last June for damage or death with Zyprexa or the KADI study that showed that

Zyprexa had the worst side effects of all of the atypicals studied.

Are these factors taken into consideration by the Drug Safety Committee when it meets to discuss taking Zyprexa off the market or when it decides what to communicate to the public when it is determining drug safety communication?

The sixth point, who finds out? Are there guidelines that require a physician to tell a patient about the major warnings on a drug before a prescription is written? Are there any guidelines that require pharmacies to include black box and other warnings when a drug is dispensed?

In my own self survey, I can report that neither the local pharmacy nor the send-away pharmacy include the FDA warnings when they dispense prescription drugs to me. I have asked for the long, thin sheet about Zyprexa at the local drugstore and there is one there, but similar warning packets are not included in the bag when I pick up my drugs nor in the plastic bag when I receive a three month supply in the mail.

So does this mean that all the effort to have black box warnings is for naught? And the only barrier between a possible deadly side effect and the

person taking the drug is the doctor.

The seventh point, the website, which was covered this morning. I am sorry to say that my impression of the website is that it is confusing, not user-friendly and very bureaucratic looking. One of them, the MedWatch website, states that it is both trustworthy and timely. How ironic a statement is this considering that the FDA is now up against an industry that spends billions of dollars for TV ads with happy, dancing pills.

I would suggest that the Agency look at, for one example, its counterpart from Canada. The Canadian website is clean, clear and appealing. Its categories are separated by plenty of white space and they appear to give good information. It gives off an aura of having made up its mind what its job is, whereas the FDA site does not give this impression.

Perhaps the webmaster could meet with his or her counterpart from Canada and turn what looks like a muddle into a hit that people would turn to and maybe even understand. It's shocking to me to get a warning about maraschino cherries out of the blue when I know that people are dying. A separation of food news and drug news might help.

Eighth point, trust. I know that a lot of

people do not trust the FDA, do not trust that it is protecting the public health. I have followed Zyprexa pretty closely, for example, and found out that Lilly has been required by other countries to place warning on Zyprexa IM for adverse cardiac and respiratory events, including death.

How do you think it makes me feel to know that, once again, the FDA is dragging its feet in this country on this issue while people die? Senator Grassley said the FDA should be about one thing only, and that is protecting John Q. Public. Well, as John Q. Public, I stand before you and say I do not trust you.

I read recently that you have a new woman to head the Office of Women's Health as the previous one quit over the Morning After Pill flap. Might I suggest you add a new office, the Office of the Innocents, I-N-N-O-C-E-N-T-S, the helpless and defenseless who are dying at a frightening rate from pharmaceuticals, those who are mentally ill, the elderly and now increasingly children.

Society is supposed to be judged by how it treats the weakest among it. I would suggest that our track record in this regard is poor and your communications to these vulnerable groups and their

families is poor as well.

Tenth point, communication responsiveness. Awhile back I compared the FDA website to the one in Canada. Both are supposed to be interactive, but I find with the FDA website, which proclaims that it will respond within a very short period of time, that when I bring up drug safety issues, ask if they are being studied, considered, etcetera, there is no response. It takes me right back to where I started in the beginning with the silence of MedWatch.

Is it once again a lack of personnel, the cause of the FDA not to respond to questions of drug safety, or is it an area that is considered somehow confidential? I have emailed Canada's website more than once and heard right back from them.

The final point, tone of the Agency. I believe that my son was killed by two factors, a pharmaceutical company that figured it could get away with a product that can kill and that denies to this day any connection between death and its product, and by a regulatory body that was and remains under-responsive to death and disability due to political and pharmaceutical pressures.

I do not believe the situation will change without Congressional action, which looks dubious

under the current Administration. But you can be assured that I will do everything within my power to work for this change. I lost my son due to what looks to me like a very grim corporate and regulatory situation.

Every time I see Zyprexa use go down in this country, I cheer. When I have the chance to work with my band of brothers and sisters who also lost sons and daughters to psychotropic drugs, I cheer. Whenever I get to meet a whistle blower who has, at the risk of his or her job, exposed an awful truth about pharmaceuticals, I cheer. These are my heroes.

At this point I see nothing to cheer about in this Agency and I hope to live to see the day that I do. When I came here before and testified, only one person spoke to me, Rose Cunningham, who arranged the meeting. She made eye contact, offered me condolences and made small talk. Not one other person in this room did that.

Is that because the culture of this Agency is cold and bureaucratic? Is it policy not to communicate with people who testify? Is my son just a number or a statistic to you even as I am standing here pleading that you protect others in honor of his memory? Is it because you have heard it too many

times?

If any of these things are true, then why are you going through the motions of having a hearing on drug safety communication today? I remember reading in the paper earlier in the year one of your high officials saying that the Division of Drug Safety was broken. Is this lack of general communication part of that?

I have studied the Grassley Bills on reforming the FDA, which now sit in the Senate Health Education, Labor and Pension Committee led by Senator Enzi. I'm sure you have as well. Are any of these reforms mentioned? Can they be enacted without legislation? Will this bill stay bottled up?

I believe that the FDA is now experiencing a very low ebb. I have not been following its fortunes for that long. It has been only three years since my son died, but if it is not held in high esteem, how can drug safety and drug safety communication be taken seriously?

These are serious questions and worries, because the consequences are grave. My family is ripped apart over the loss of my son. He was a fabulous guy and even though he became a person with manic depression at the age of 20, he was properly

medicated for 18 years with lithium, finishing his bachelor's, getting a master's at Cornell, working at the EPA, having a full life until the last two years on Zyprexa.

Though I can't prove it, I suspect he was put on Zyprexa because he had to go on Medicaid finally in Maryland, and I suspect the formulary was heavily weighted with the atypicals. Prior to those last two ultimately fatal years, he was a wonderful person. I want you to know that. He was not a statistic. He was a brilliant person cut down at the age of 39.

I wanted you to have protected him, been the last line of defense, the guardian of drug safety and drug safety communication and you weren't, just the same way you still aren't at this moment for someone with psychosis who is brought into an ER and given Zyprexa IM. Thank you.

CHAIRMAN SELIGMAN: Thank you very much. Our next speaker is Carol Rothkopf from Time.

MS. ROTHKOPF: My presentation today concerns itself with patient communications and I have put the deck together from a variety of industry resources and just a little bit of time and original research. I would like to show that research

demonstrates the need to improve patient communications and the need for more information materials that are easier for patients to understand and act upon.

First, let's look at doctor/patient communications. The National Council on Patient Information and Education requests that half of all patients to get verbal information communicated by their physicians. 60 percent are unable to report precisely what they were advised to do, even one hour after leaving the doctor's office. And only 35 percent of patients received instructions from their physicians on how to take medication.

Let's look at prescription drug compliance in the United States. Of the 63 percent of adults who were prescribed prescription drugs in the last year, 33 percent did not take their medications as prescribed, according to Harris Interactive. I have seen other research out there with a much higher number. Some research that about half of all patients are not taking their drugs as prescribed and there are many reasons for this.

64 percent of the respondents in this survey said they simply forgot to take their medications. 35 percent wanted to save money. But

some reasons that respondents stated show the need for more education. For example, one-third of the respondents did not believe that the drugs were effective. 31 percent didn't think they needed the drugs. And 28 percent said that the drugs had painful or frightening side effects.

Now, let's look at prescription drug compliance in terms of initial prescriptions and refills. According to cutting edge information, between 10 percent to 20 percent of patients do not get the initial prescription filled because the physician has not convinced them that they need to take it. 30 to 85 percent of patients may disregard refills, depending on the disease and the treatment.

And looking at the cost of noncompliance, up to 20 percent of hospital and nursing home admissions and 125,000 deaths annually are attributable to noncompliance.

The last issue I would like to discuss is health literacy, which is the ability to read, understand and act on health information. And this is an issue that crosses all demographic groups: Age, race and income levels. Studies show that the health of 90 million people in the United States may be at risk, because of the difficulty some patients have in

understanding and acting on health information.

One out of five American adults reads at the 5th grade level or below and the average American reads at the 8th to 9th grade level. Yet, most health care materials are written above the 10th grade level.

Now, the next four slides that I'm going to show you are from the MARS 2005 OTC/DTC Study. This is a survey that was conducted by Kanter Media Research via the mail and the sample size is quite large, over 21,000 respondents.

So first, let's look at attitudes and opinions about health care and pharmaceuticals. And if you look at the top row, I have segmented the data by age group. Age 18 plus, 18 to 34, 35 to 49, 50 to 64 and 65 plus. Respondents were asked a series of questions and whether they agreed a lot or a little on the following statements.

The first one, "I research treatment options on my own and then ask my doctor about them." Almost a third of the population said they agreed with that statement. And the numbers on this slide don't vary very much by age group. But on subsequent slides that I'm going to show you, you will see that they do vary quite a bit.

The second statement, "I always read the

small print in magazine and newspaper pharmaceutical ads." Again, almost a third of the population agrees with that statement.

And the last statement here, "The side effects associated with some prescription drugs sometimes scare me off a brand." 52 percent of the population agrees with that statement. So while we do want to make people aware of the side effects and risks, we also have to make sure that we don't discourage them or scare them from taking a drug that may help them.

Okay. More on attitudes and opinions about health care and pharmaceuticals. The first statement here, "Finding information on health treatments on the Internet is very helpful to me." 32 percent of the population agreed with that statement. But if you look at the last column, the age 65 plus group, only 15 percent of the population agrees with that statement. And, of course, that is mainly just to the fact that they don't have very much Internet access.

The second statement, "I am comfortable registering on a website which offers useful information about my health condition." Here we see that across every age group, the numbers are

significantly lower, so there is something that is making people not feel comfortable to register on these websites.

And the last statement, "Health information put out by drug companies and available at pharmacies is credible and useful." 38 percent of respondents agreed with that statement. And you can see that an even higher number in the older age segments agreed with it. For example, 65 plus group, 42 percent of the people agree with that statement. So that may be a good place to reach this segment of the population.

Now, we're going to look at some sources for health care information that respondents said they valued very much or somewhat. And what we will see here is that the numbers are lower in every case for the 65 plus age group. Looking at health care professionals, they were found to be the most valued source in the study, valued source of health information. 82 percent of the population said so. And the number was a little bit lower for the 65 age group at 77 percent.

52 percent of the population values friends and relatives as an information source, but only 31 percent of the 65 plus age group. And I would

have thought that number would have been higher there, because that is the age group that tends to have a care giver.

Looking at place-based media in doctor's offices, half of the population values this information, only 31 percent of the population age 65 plus. Medical journals are valued by 37 percent of the population and by 24 percent for those that are 65 plus.

Okay. Looking at traditional media, we see that magazines, TV and newspapers are valued more than radio is and that crosses all age groups. And the numbers are not that much lower for the 65 plus group.

Now, interestingly, although people are flocking to the web for a lot of health information, these numbers aren't reflecting usage, but they are reflecting what people value very much or somewhat. And according to this study, the Internet drug websites and Internet health websites are not valued as much as traditional media and that does cross every age group.

And now I'm going to show you three slides from Time Inc.'s latest DTC Research Study. It was done in the fourth quarter of 2004 and it was

conducted by Harris Interactive on the Internet. The numbers were adjusted for the fact that it was an Internet study and it does reflect the U.S. population of adults 18 plus. And in this study, we had a sample of 3,570 respondents.

In this chart here, we're looking at a sample size of 1,417 respondents and these were people that were diagnosed by health care professionals in the last two years for seven different conditions: Allergies, arthritis, GERD, depression, cholesterol, hypertension and diabetes. And what we found was the respondents said that 38 percent of doctors gave them samples of medications. However, only 26 percent gave them literature about the condition and only 13 percent literature about the medications.

I know there is a lot of concern about do people read the disclaimer in drug advertising, do they read their package insert, but there is also a concern about people getting free samples and not getting the literature, so that they know how to take them properly or what the side effects are.

In this chart, we're looking at the benefits of prescription drug advertising among the general population. 1,800 randomly selected respondents who were asked a series of questions and

asked if they agreed completely or somewhat on the following statements. And I'm only going to concern us, at this meeting, with two of them that pertain to what we are here for.

49 percent of these respondents said that prescription advertising provides clear information on the drug's benefits and a slightly smaller number 42 percent said prescription advertising provides enough information about the drug's side effects or risks.

And this is the final chart. It addresses the role of TV and magazine advertising. And here our respondents are not just sufferers of the seven different conditions diagnosed in the past two years, but for longer periods of time. There is no time frame. And we asked these people what role each of the media played. And what they said was -- and they had to see advertising in both media, magazines and TV.

If you look at the last column that says "both the same," 40 percent of the respondents said that the advertising in both media played an equal role in providing enough information about the drug's side effects or risks. 48 percent said that magazines did a better job and 12 percent that TV did a better job.

On the second row, and looking at the right hand column, 47 percent of respondents said that prescription advertising in both media does an equal job of providing clear information on the drug's benefits. 38 percent said magazines did a better job and 15 percent television.

So just to conclude, this research found that health care professionals are the most valued source of health care information among patients of all age groups. However, there is a need for additional communication beyond these professionals. Patients forget much of the verbal information communicated by their physicians and prescription drug compliance problems abound.

We also see that many patients are proactive in research treatment options on their own and supplement information from their doctors from a wide variety of sources, such as friends and relatives, traditional media, the Internet and place-based media in pharmacies and doctors' offices.

So our challenge is really how to improve communications among patients who are not proactive, among those who have difficulty understanding health care information and among the elderly. And thank you for giving me the opportunity to present here.

CHAIRMAN SELIGMAN: All right. Thank you for your comments. Any questions from Members of the Panel? I just actually have one question for you, Mrs. Liversidge. I noticed in your testimony you talked about your interaction with the Canadian website. I wanted to know if you could give us a little bit more information about the nature of the question that you asked and the kinds of responses that you received from the Canadian website.

MS. LIVERSIDGE: Should I push this button? Is it on now?

CHAIRMAN SELIGMAN: The button should be up.

MS. LIVERSIDGE: Should be up. Okay.

CHAIRMAN SELIGMAN: There you go. You got it.

MS. LIVERSIDGE: To be perfectly honest, I don't remember what I asked them. But I guess that I did not ask them anything as either technical or perhaps confidential as I have attempted to ask your website. I have been trying to ask questions like, you know, what about it guys? You know, what are you doing about that drug stuff and I'm getting no response back. I doubt I asked anything like that of the Canadian website. But I honestly can't recall.

I would suggest that you take a look at the website. There are some papers in the handout that I gave you that have some emails. I don't know whether they have the content that you want, but they certainly have a nice look.

CHAIRMAN SELIGMAN: Thank you.

DR. KWEDER: I have a question.

CHAIRMAN SELIGMAN: Sure.

DR. KWEDER: I want to ask Mrs. Liversidge a question. First though, let me express my personal condolence, Ms. Liversidge, for the loss of your son.

MS. LIVERSIDGE: Thank you very much.

DR. KWEDER: And assure you that the 700 people who work in my office and the 1,800 that work in the center care very deeply about people like you and your son and are committed to doing the best job we possibly can. It's an uphill battle always, but we're there to do it.

I was wondering, you said that the doctors that were talking care of him didn't have any information on this. And you also said that you were -- that your son was told that the medicine was safe.

MS. LIVERSIDGE: Yes.

DR. KWEDER: Do you think that you -- he might have changed his willingness to take the

medicine if he had more information about the safety risk profile of that medicine compared to the lithium, which is, of course, itself not, you know, known for being -- having problems of its own? I'm just curious.

MS. LIVERSIDGE: He would have stopped in five minutes and gone back to lithium.

DR. KWEDER: And would there be one particular -- I guess, not so much you can never predict that you're going to -- for a rare side effect like that, one can never predict that I'm going to be the one it happens to. But some of the other side effects, was he aware of some of the others?

MS. LIVERSIDGE: No.

DR. KWEDER: Okay. Thank you.

MS. LIVERSIDGE: He got very little information. He was seeing a Medicaid doctor and if you know how it works in the Medicaid mental health clinic, you're in and out before you even know it. And I honestly don't believe, because I talked to my attorney, the doctor knew the lit and I'm not sure even if a private psychiatrist, at the time, unless he read all the literature, there just wasn't that much literature about it.

DR. KWEDER: Right.

MS. LIVERSIDGE: However, other countries had already acted and had required Lilly to put warnings on the label in that country and that was going to be one of my questions to you that I didn't ask. Why wouldn't Lilly have the responsibility to tell you that and have you act on that? I don't understand. If Japan made them put that warning on about diabetes, hyperglycemia and death, which they did, why weren't they made to tell you that and then why didn't you do something about it? That's something I don't understand.

DR. KWEDER: I'm not sure. I'm not prepared to answer it, but a good question regarding that particular product. Companies are required to tell us about regulatory actions taken in other countries, particularly regarding the safety of their drug.

CHAIRMAN SELIGMAN: I have a question for you, Mrs. Rothkopf. There was a lot of discussion this morning about the FDA website and I was curious, you talked a lot in your presentation about sources for health care information. I wanted to get your sense or assessment as to how a governmental website that provided information for consumers might be received, since it's my sense in looking at your data

that you primarily evaluated either drug company or other websites that are presumably in the private sector that focus on health.

MS. ROTHKOPF: I would think that most people, can you hear me, would feel that it was a very credible source. However, I have to say until the hearings, I have been working on this category at Time Inc. for almost 15 years now. I had never heard of the website before. So I think the first thing --

CHAIRMAN SELIGMAN: Maybe that answers the question.

MS. ROTHKOPF: Yes. But I think that just hearing about the site and knowing it's a Government site, people would feel that it was very credible and want to get information from that website.

CHAIRMAN SELIGMAN: Would it be fair to interpret a lot of what you said, is it we really need in this society an approach which provides multiple sources of information?

MS. ROTHKOPF: Oh, absolutely, absolutely. And I also think it's a learning process. You don't get everything from just going to one doctor visit. You learn a little from your doctor and then you go to various sources and it could be friends and relatives and it may be the Internet or media, but you do need

multiple sources. And I think new information also comes out at different periods of time and you have to keep up with whatever your ailment is.

I also think it would be a good idea if people suffering from various conditions were directed to some of the association websites. I can't imagine why if you have something like diabetes or a heart condition that you wouldn't be on the American Heart Association website or American Diabetes Association. And so many illnesses do have a website that has a wealth of information.

CHAIRMAN SELIGMAN: One of the findings in your study that I found a little striking was that a third of the respondents regarding attitudes and opinions indicated that they always read the small print in magazine and newspapers --

MS. ROTHKOPF: Yes.

CHAIRMAN SELIGMAN: -- and pharmaceutical ads.

MS. ROTHKOPF: Yes, I also found that --

CHAIRMAN SELIGMAN: I have a hard time actually focusing on it myself.

MS. ROTHKOPF: Yes.

CHAIRMAN SELIGMAN: Let alone reading it.

MS. ROTHKOPF: I found that a little bit

hard to believe and I also think, too, that there are better ways to ask that question. I know the FDA's earlier research said to people if you were very interested in a drug for yourself or someone that you knew or loved, did you read the information? Because most of the time if that's not the case, you really don't have any interest in reading it.

And then I think you also have to ask people well, did you read a little bit of it, all of it, just a tiny little piece of it? So I think that, you know, Time Inc. does research periodically on this category and I would like to ask that question, but a little bit more differently. And also ask about the package insert and reading that.

CHAIRMAN SELIGMAN: Good. Any other questions, comments from Members of the Panel? Then let me ask if there is anyone in the audience, at this time, who wishes to make a statement or add anything to the record in today's meeting? Again, for those of you who may have missed my opening remarks at the beginning of this afternoon's session, we had a number of cancellations unexpectedly over the last two days, and as a result, we're going to shorten this afternoon's session, because many of tomorrow's speakers couldn't be moved to today.

So we have a full day of panel and panelists and speakers tomorrow. But if there is no one then who wishes to make a statement, I want to thank both of our speakers this afternoon for their input and then call us adjourned until tomorrow morning at 8:00 a.m. Thank you.

(Whereupon, the meeting was adjourned to reconvene tomorrow at 8:00 a.m.)