UNITED STATES OF AMERICA

DEPARTMENT OF HEALTH AND HUMAN SERVICES

FOOD AND DRUG ADMINISTRATION

CENTER FOR DRUG EVALUATION AND RESEARCH

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FDA'S COMMUNICATION OF DRUG SAFETY INFORMATION

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THURSDAY,
DECEMBER 8, 2005

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The meeting was held in the National Transportation Safety Board Conference Center, 429 L'Enfant Plaza, S.W., Washington, D.C., at 8:00 a.m. Dr. Paul Seligman, Chairman, presiding.

MEMBERS PRESENT:

PAUL SELIGMAN, M.D., M.P.H., Chairman

SUSAN K. CUMMINS, M.D., M.P.H.

NANCY OSTROVE, Ph.D.

TERRY TOIGO, Rph, MBA

ANNE TRONTELL, M.D., M.P.H.

SCOTT GOTTLIEB, M.D.

PANELISTS PRESENT:

DOUGLAS McNAIR, Cerner Corporation

CHERIF BENNATTIA, AphaRC

ALAN GOLDHAMMER, PhRMA

JOHN WOLLEBEN, Pfizer

STEPHEN GOLDMAN, M.D., Stephen A. Goldman Consulting Services

JANICE DUNSAVAGE, ISMP

JOE CRANSTON, American Medical Association

SUSAN WINCKLER, American Pharmacists Association

TOM LAWLOR, National Association of Chain Drug Stores

NICHOLAS RATTO, First DataBank

WENDY JEZARIANT, Time, Inc.

JOHN KAMP, Coalition for Healthcare Communication

SUSAN KLEIMANN, Center for Plain Language

PETER MAYBERRY, Pharmaceutical Printed Literature Association

HARRY SWEENY, Dorland Global Health

VANESSA CULLINS, Planned Parenthood Federation of America

C O N T E N T S

P R O C E E D I N G S

(8:02 a.m.)

CHAIRMAN SELIGMAN: Good morning, everyone. It's 8:01. It's Thursday, December the 8th; is that correct? And here we are in Washington, D.C.

My name is Paul Seligman, and I'm the Director of the Office of Pharmacoepidemiology and Statistical Science, and I will be serving as the moderator today for the second day of our FDA's Part 15 hearing on communication of drug safety information.

As I indicated yesterday, the purpose of our meeting today in these two-day sessions is to get public input on the Center for Drug Evaluation and Research's current risk communication tools for health care providers, patients, and consumers.

Let me remind those of you that are here this morning that we encourage you to sign in at the front desk. If you didn't pick up a package of information yesterday, we do have them available in a red folder that contains not only an agenda, but many of the risk management tools that will be discussed today.

FDA's role at this meeting is to listen

and to ask questions and to try to garner as much input and information as we can from the panelists and organizations that will be speaking.

Individuals and organizations that are speaking at this meeting have self-invited themselves to speak. I also want to remind any of you who are not on the agenda that if you are interested in speaking, please contact Lee Lemley at the desk, and we'll try to arrange for a time for you to address the panel this afternoon.

If you don't wish to address the panel but wish to submit comments or information to the record, that's also a possibility and we would encourage you to do so.

Before I begin, I would like to just take a moment and have the other FDA members of the panel who are joining me up here today introduce themselves. Nancy, let me start with you.

DR. OSTROVE: Morning. I'm Nancy Ostrove. I'm with the Office of Planning in the Commissioner's Office.

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

DR. CUMMINS: I'm Susan Cummins. I'm the

Director of the Drug Safety Oversight Board and the Center for Drug Evaluation and Research.

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, the Office of the Commissioner.

CHAIRMAN SELIGMAN: Thank you.

And finally, before we move on to our welcoming remarks, I want to remind everyone that we are here this morning as a guest of the National Transportation Safety Board. They do not permit either food or drink within the auditorium.

Please also not that since cell phone reception is either poor to nonexistent down here, we also encourage people to turn off their cell phones or at least silence them and not to use blackberries or other wireless devices down here since they do seem to interfere and cause some feedback in the wireless system.

With that, let me move on to the agenda and introduce Dr. Scott Gottlieb, who is the Associate Commissioner for Medical and Scientific Affairs for the FDA to provide some opening and welcoming remarks.

Dr. Gottlieb.

DR. GOTTLIEB: Thanks.

I want to thank you all for coming today and extend a warm welcome to the panel. At FDA we depend on scientific gatherings like these to get important input to guide our work, and no topic is more important than how we communicate with the public and no subject can perhaps benefit more from frank and open dialogue than this one.

I also want to acknowledge the dedicated staff of FDA's Center for Drugs, especially Dr. Paul Seligman and Lee Lemley in planning today's meeting.

On behalf of the Acting Commissioner, Dr. Andrew von Eschenbach in the FDA's Commissioner's Office, I want to welcome you all here today. Across the FDA there is widespread agreement that we want to work especially hard and look for new and effective ways to improve the way we communicate information with the public. Whether it's improving our dialogue and our collaboration with physician groups or more carefully crafting the messages that we deliver to consumers or improving the predictability and consistency of our relationships with the press, we are working especially hard to improve and expand the tools and the practices to which we communicate information.

Let me take a step back first and give you

my one sentence description of FDA, my elevator speech, if you will.

Our work at the agency is complex and requires expertise and dedication that is hard to measure, but if I was asked to boil it all down into a simple phrase, I'd simply say that a lot of what we do at FDA involves helping patients manage the risks and benefits of their health care decisions.

Our job then, when you boil it down, is to help turn more information about medical products into practical knowledge that patients and doctors can use to make personal decisions about their health and health care treatments.

At FDA, we receive a lot of data about new medical products and medical products already on the marketplace, whether it's new applications for a drug or the adverse events we receive through MedWatch. With the help of our tools, with the energies of our skilled professional staff, and with the aid of the guidance we get from outside experts, we turn this raw data into useful knowledge that doctors and patients can use to help guide their decisions about how to most effectively use medical products to improve health.

That knowledge is what you read on our

labels. It is what you see in our health care advisories, and it's what we want to discuss with you here today: how we can do a better job of translating the most useful information for informing medical practice.

In short, how we can do a better job of getting this information to you when you need it and in a way that it can be more easily and more effectively integrated into the choices that patients and doctors make.

But our ability to generate and share this knowledge is only as good as the information we receive and only as useful as our ability to communicate it efficiently and effectively to the people who need it, and that is why we need the help of consumers and health care professionals. That is why we need your help here today.

It is clear to all of us that the social sciences of disseminating risk information and of measuring how consumers respond to and use this information are sciences that are being rapidly developed and expanded. If you look inside many corporations today, you'll find people expert in risk communication whose primary job it is to craft information tools that can be more effectively used by

consumers.

This wasn't always the case. Such experts didn't always exist. A large amount of the research findings has accumulated since the 1970s when risk issues started to become central themes in society. Risk communication studies first emerged in part from risk perception research that was aimed at using perceptions of risk to provide more effective information.

Gradually the field recognized that risk perception differences were more fundamental than just explaining risk estimates in a simpler way. Gradually a segment of the field moved towards adopting approaches to risk communication with dialogue, not one-way information campaigns emerged as a significant theoretical basis, as well as a method in research and safety implementation work.

At FDA, the task of measuring consumer perception and people's reaction to information and using the scientific information to more finely tune how we speak is becoming a more important part of our work. As the amount and complexity of information that we provide continues to mount, a result not only of our desire to speak more openly, but also the increasing complexity of medicine and science itself,

we know that we also need to continue to improve how we approach the social sciences of risk communication and the social sciences of measuring consumer perceptions of information.

This is true not only in how we communicate safety information about drugs, but in many parts of our work. It is true, for example, in how we measure consumer response of drug advertising to insure that there is a spare balance. It is true in how we craft public health advisories warning of a potential problem with medical devices, and it is true in how we measure how people respond to the health information included on food labels so that they can provide more appropriate guidance that makes sure we take opportunities to promote information that motivates people to adopt healthy diets, diets that can improve their lives and even help prevent the onset of certain disease.

At FDA, we are dedicating new resources and efforts to improving our scientific approaches to the regulatory work we do, to improving our hard science, if you will. Our critical path initiative, for example, is a big step forward in taking new approaches to improving the science of drug development.

We are equally committed to improving the social sciences that guide our work. They are just as important. The best regulatory science in the world can't have its full impact if we are not effectively communicating what we learned.

And so today continues an important discussion on how we improve the science of risk communication, and more than perhaps any other scientific work we engage in at FDA, making improvements here truly depends on public input. Public perceptions of risk information are inextricably linked to our ability to improve the way we speak and in the way we craft our information tools.

And so we are grateful for the opportunity to engage in this dialogue today, and we are committed to expanding on our opportunities to improve the social sciences that govern the way we inform the public of what we learned when it comes to safe and effective ways to benefit from medical products.

So thank you for coming today to join us in this dialogue, and on behalf of the entire agency, I want to welcome you to this meeting.

Thank you.

CHAIRMAN SELIGMAN: Thank you, Dr.

Gottlieb for your excellent opening remarks and for joining us yesterday on the panel.

Before beginning this morning, I just wanted to take a moment to remind the audience of the questions that were posed in the Federal Register that we're asking the panelists today to address as part of their presentations.

The first question is related to the strengths and weaknesses of the communication tools that we use here at the Center for Drug Evaluation and Research. These include patient information sheets, information sheets that are directed to health care professionals, public health advisories, press releases, safety updates that are provided through our MedWatch listserve, the use of the patient safety moves, the video broadcast, as well as our CDER Internet sites.

The second question we're asking is related to the information and data that are available about awareness, use, and perceptions of the effectiveness of the communication tools by health care professionals and by the public in general. We really want to know whether these tools provide the right kind and amount of risk and other information that these professionals need in order to make

informed decisions about whether to prescribe drugs, and that the public needs to make informed decisions about whether to use these products.

We're very interested to know and very keen to know -- and we heard a lot about this yesterday -- how accessible and understandable FDA's Internet based sources of drug information are and to what extent the CDER's patient focused safety communication tools provide useful information for people of low health literacy skills.

And finally, we're interested in learning more about mechanisms that our organization can employ to convey risk information to special populations, such as the elderly and those who don't speak English.

With that, let me just go over for a brief moment the ground rules for today's discussion. We've allocated to each registered speaker 15 minutes for their presentation. We don't have a light, nor do we have a hook, but we encourage you to stick to the 15 minutes.

If you finish prior to your allocated time, we may use some of that time for the panelists to ask questions. If not, we will reserve questions for that period of time on the agenda so designated for panel questions.

With that, let me introduce our first speaker this morning, Douglas McNair from Cerner Corporation

Mr. McNair.

MR. McNAIR: Thank you.

I'm very grateful for the chance to contribute to this discussion of risk and risk communication.

I think in follow-up to Scott's remarks about the importance of helping patients or their family members manage their health actively by providing the most useful information, the concern that we have is that by focusing on those whose health literacy is low, there is a hazard of leaving behind almost 80 percent of the population who do utilize the Web and whose health literacy is moderate to high.

Pew Research Center, for people on the press survey in September of this year, indicated that at this point there are 73 percent of the U.S. citizens who are on line, 44 percent of whom are on line two or more times each day, and almost all of those get some of their health information via the Web.

There are a series of slides that I would like to share with you that suggest increasingly

detailed information that would enable what is delivered both to consumers and to providers to be progressively more useful than that which is available currently, which, as discussed yesterday, tends to mimic or replicate what is presented in paper form.

The two questions that I'll focus my remarks on are these of the ones that the session is about: whether the risk communications that are currently in use have certain limitations and, secondarily, whether the tools, Web-based or otherwise, currently contain the right kind and amounts of information.

In the context of risk management and communication, there is this hierarchy of several different kinds of evidence. Much of what appears in labeling materials obviously is of the premarket clinical trials based sort. Somewhat less from MedWatch or other spontaneous reporting, even less from Phase IV registry information.

The content of my following comments has almost entirely to do with new capabilities that come about through the use of large data warehouses with HIPAA confidentiality protected in itemized information by which pharmacovigilance and pharmacoepidemiology can be done, but also derived

from such information, communications both to prescribers and to consumers can be implemented.

Spontaneous reports of the errors for MedWatch type have a variety of limitations that are generally recognized. They require a considerable amount of time for those who are submitting reports to prepare their submissions, those primarily prescribers who do submit reports have some amount of medical-legal skin in the game, which may inhibit certain kinds of reports or after a particular problem has received public and press visibility may actually precipitate much more perfuse reporting than had previously been done.

Insofar as health care delivery in the U.S. is progressively more and more fragmented, those kinds of adverse events that arise after a lapse of some time or may involve multiple institutions and providers tend to be under reported in the spontaneous report databases, and particularly when there are multiple concurrently active diseases. The attribution of AEs in the context of complex illness is less likely.

So those are some of the issues that we perceive in the existing spontaneous reporting system.

Much of what is available both in print

and on the Web, as was discussed yesterday, has an orientation in its language and its format to prescribers. However, with the large online community of U.S. citizens, an increasing number of them wished to have the ability to actively find and easily locate information that is quantitative

I would say that in contrast to some of the remarks yesterday about illiteracy or comprehension, if what is being delivered to people is not specific to their conditions and medication, age and gender and race and so on, then they perceive it to be not relevant, and it's not a problem necessarily of comprehension or retention. It's simply that they find it not particularly useful.

So part of our proposed solution is to increase the use of data warehouses, observational and controlled data to enable detailed, quantitative information about absolute and relative risks to be presented.

By way of illustration, the kinds of easily usable Web-based interfaces that you may wish to consider include American Heart Association, americanheart.org, cancer.org, American Cancer Society, both of which have profilers that enable consumers or providers to answer a number of filter

criteria that deliver highly specific and useful information and quantitative directions for guiding their health choices.

A pictorial representation of what I've just said in words, spontaneous reporting results not only in under reporting, but delay, the result of which is under identification of risk and not optimal mitigation of those AEs or disease.

The traditional approach is essentially that. On the inverted triangle on the left where a good bit of the burden is on manual reporting and manual case ascertainment, which the agency does, but is tremendously expensive and time consuming. By the use on the right-hand side of automated data warehouse based tools, the risk detection and ascertainment in a variety of things to quantify risk can be done at considerably less delay and expense and a greater amount of the finite resources can be spent on meaningful interventions and communication activities.

A block diagram of Cerner's approach to this includes firewall and virtual private network controlled daily feeds via the Internet to secure Cerner Data Center warehouse. A surveillance engine piece of software that looks at those AEs that are mapped to MedDRA and other terminology and is able

then when signals are detected to revise what is displayed both to members of the public, to public health and regulatory agency officials, and to prescribers.

The current status of this particular data warehouse is that it accrues somewhat more than five million in new cases per year of all patient types and venues. It has electronic medical record master person index linkage so that however many encounters, in-patient or ambulatory, there might be, it is still the same person and longitudinal studies and risk quantification can be done and analyses to identify the strength of correlations or to show causality can also be accomplished.

Data mining of this sort is nothing new. FDA has engaged in this for some years now, and particularly around the focus group pertaining to hepatotoxicity.

We look in Cerner's specific work in this area at subpopulations, particularly ones, elderly or pediatric, where the likelihood of experiencing an AE is higher than might otherwise be the case in the general population or in the population that was the subject to pivotal trials for a particular drug.

There are a variety of issues,

statistically important ones to make sure that the guidance to derive from such data warehouses is robust and reliable. The presence of missing data to the degree that it occurs in all databases is particularly important, maybe more so in safety analyses insofar as the duration of exposure or changing prescribing strengths or frequencies may have a stronger impact on the emergence or not of adverse events than in effectiveness endpoints, although this, clearly these days must be done with careful attention to confidentiality and HIPAA compliance, which is the case for Cerner's specific approach in this area.

It's also important that in order to produce reliable risk quantification and communication information that the level of detail present in such databases is sufficient to support the kinds of quantification and clear association or causality analyses.

So electronic medical record level of detail with longitudinal linkage of records and date-time stamping so that longitudinal correlations can be ascertained is very important.

Here's one of the examples of some considerable relevance in the last couple of years. We have about 40,000 cases of Vioxx exposure. The

rows are prescription, plus-minus, exposed, unexposed. The columns are whether in connection with these 18, 19 million odd cases there were or were not new instances of ischemic heart disease, MI or ACS or TIA or stroke, plus or minus in the columns.

The chi square values in orange off in the right are noteworthy and standardized relative risk, age?gender adjusted, are increased for all three and Naproxen as well as Vioxx and Celebrex compared to the baseline population in this particular data warehouse.

You can look in addition to the emergence of new cases of ischemic events also at whether the people expired, death yes or no, expiree plus-minus in the columns in this slide. We have in this collection of 38,000 Vioxx over three years, 25,000 to Celebrex over three years, and 20,000 of Naproxen, 1120 and three deaths respectively with standardized mortality ratios as shown.

The database is able to track the frequency, the strength, and the details, and able to totalized the exposure for a 24-hour interval. So we're able to see as prescribed really three prevalent doses for both Vioxx and Celebrex. There is about an eightfold difference in molar potency of these two drugs, and if we display with a probe it regression of

the incidence probability of some ischemic event on a logarithmic scale, the Y axis on this plot, versus molar potency adjusted X axis for milligrams per day exposure. The probit regression of the probability of risk of such events are very close to each other.

And there are ways familiar to statisticians for seeing whether those two curves are different. SAS and other traditional methods familiar to the FDA are ones that Cerner uses as well, and it turns out that those two curves are different at the P .003 level, a significant difference ascertained by comparing those two.

In this example, Cerner's data warehouse shows that there are significant differences in risk, and we're currently evaluating other variables, particularly age and gender as to whether Celebrex and Vioxx are really clinically significantly different.

Another relevant example, particularly in the context of Pargluva, looked at the historical use of PPAR alpha or PPAR gamma agonists, the GSK and other products, and the worsening of heart failure, same sort of 24-hour exposure on the X axis and probit regression for elderly women, diabetics taking one or the other of these thiazolidinediones and really three different levels at which this probit regression was

done. Ninety-five percent confidence intervals are the dashed lines.

Well, what if you look at those who already have some degree of heart failure and have had left ventricular ejection fraction in the 20 to 40 percent range?

At a lower dose you have from now maybe two percent level. Increase that to about five percent, and if they're taking it twice a day, you're into the ten to 20 percent range of worsening of heart failure in elderly women with existing Class II CHF.

So basically we've been in the mode of looking at these things primarily for pharmaceutical company sponsors, a variety of epidemiologically important and clinically or socially important categories of things that this data warehouse has been used for. Others like this could similarly be applied in a broader public health fashion.

The prioritization of what one ought to look at and communicate about follows a hierarchy that's generally recognized both by the FDA and by Health Canada EMEA, as well.

Cerner's own focus has primarily been devoted with the sponsors with whom we work to those things that have high priority by reason of

seriousness, previous lack of identification or not on the label, and medium priorities of which the thiazolidinedione example is one, a shifting as it were of the benefit-risk ratio for a subpopulation of patients.

The more detail that you can provide both to prescribers and to consumers that makes it specific to their particular condition, the better able you are to prevent AEs from occurring or to mitigate them if they have materialized.

So, again, the limitations of existing MedWatch and related spontaneous reporting databases are essentially these. Those limitations are substantially mitigated, we think, by using a data warehouse basic approach with very large sample sizes.

What you find in such observational databases are the heterogeneity of populations as the medications are actually used, along with all of those things that are concurrently active with them, both concomitant meds and other diseases that the patients have.

Appropriate statistical adjustments can and are being done by us and others to make sure that there's case control matching and biases are minimized, and essentially these in red are the three

ways which we feel that these kinds of tools could contribute in the future to improving the management and communication of risk.

The identification of new AEs, the ascertainment of them and quantitative evaluation or estimation of them means primarily, but perhaps not exclusively via the Web for consumers or providers to enter various features of the circumstances that pertain to this particular individual's use of a med, along with the concomitant meds that they're on, and exchanging risk information in terms of absolute percentage or two and a half fold increase in risk if you add this medication in the intended dose to your existing medication profile.

Insofar as anything that is Web based is a means by which the point and click behaviors can be captured, not only can the usability of such interfaces be measured as part of a communication evaluation program; one can also through the tracking and pattern analysis of such point and click time series determine what might ought to be added to such communication tools' Web portals.

There are some implications, we think, for any provider of such portal facilities, whether it be by an agency like FDA or by industry groups. We wish

to enable the patients primarily to explore the risk profile that's appurtenant to their own situation, find it useful, and then be better able to act upon it in their health choices.

We think it is useful also as the bottom bullet indicates to the PhRMA sponsors, manufacturers, as well as to the regulatory agencies in performing pharmacoepi. and pharmacovigilance activities in an active and proactive way.

So in much the same fashion as has been done rather effectively, we think, on American Heart Association Web site and the American Cancer Association Web site, the entry of a number of features or age-gender medications you're on enables you to then index into a quantitative expression of what the risk of selected adverse event types may be for you.

The basis on which these kinds of risk quantitative estimates can be done is really a recent phenomenon involving HIPAA compliant, large data warehouses that encompass many millions of cases per year.

To the degree that these are substantially in-patient based, there is a much lower missing data rate than is true of a clinic or doctor office kinds

of spontaneous reporting. All of these have continuity and date-time stamped information about each medication that's prescribed down to the NDC level of strength and ingredients and frequency and so on, as well as a similar detail for laboratory tests, diagnoses and the like.

There are, in addition to strengths that I've mentioned, a number of weaknesses. There could be better coverage in terms of geographic representation. We are currently at work to extend the capture of U.K. and other European data, and frankly, there could be more retail and OTC meds. covered. However, we've seen that evaluation of some very widely prescribed medication, such as over-the-counter antihistamines can be evaluated with the current data warehouse as it is.

In final summary then on the two questions that my remarks have been focused on, we think that spontaneous reports based means for deciding what to communicate or how important it is to the public are insensitive primarily or increasingly because of the multi-factorial and multi-location nature of the way that care is delivered, complicated also by the biases that come about from logistical or medical-legal and other kinds of reasons.

Do the existing tools, both printed and online, contain the right kind of information or the right amount? No, we think in summary that it is currently too course and maybe not retained or acted upon because it is not specific enough for a communication to say that some adverse event has been reported or might occur. It's too diffuse to be regarded as meaningful or relevant by most consumers or, frankly, by most prescribers.

Information, in other words, is scanty and often is delayed by many months or even years beyond when it would have been detectable and communicatable through the tools of the kinds that I've been describing.

And finally, and as was mentioned yesterday, it's primarily in its current form readable by and accessible to prescribers rather than consumers.

Thank you very much.

CHAIRMAN SELIGMAN: Thank you, Dr. McNair.

The next presenter is Dr. Cherif Bennattia from the Advanced Pharmaceutical Regulatory Compliance, LLC.

DR. BENNATTIA: Good morning. My name is Cerif Bennattia. I'm a physician, and I've been

working for about 20 years for pharmaceutical companies, and I'm right now consulting in risk management and risk communication.

I'm going to skip this one.

So this slide summarizes somehow all my presentation. I think we all agree now that communicating about risks from any sources to any audience is a challenge, and there is an urgent need to change the way safety information is communicated. That's why we're here for these two days.

Our first recommendation is to shift from the concept of information to the concept of communication and education. And we'll see how later on.

Our second recommendation is to use the same strategies and the same tools used in marketing promotion and marketing communication and promotion, and also I think it's very important to provide the right information on the benefits and the risks of treatment to health care professionals and patients to make informed decisions.

And we need to keep in mind that the health care professionals are still the most trusted source of information.

So why risk communication? I think we all

agree that there cannot be safer drugs until there are better ways to communicate and educate all of audiences about drug risk and benefits.

But communicating risk about risk is still a challenge from any source to any audience, and despite advances in information technology, and it's not going to be an easy task to do because the public is inundated by information from various sources. We all receive a lot of mail information, Internet, the media, and too much information is there, and it confuses.

And during crises, it's even worse. So the key question then is whom to trust, FDA or the regulators, pharmaceutical company, health care professionals, lawyers. I think trust and credibility are key in the risk communication is important to answer this question.

FDA provides safety information in a different format and we've seen some of it here. The problem is not publicized enough. Not all people know that it even exists.

And there was also uncertainty about what kind and how much information to communicate to patients in a form that they could understand, even with low health literacy skills.

One point that is key, I think everyone will agree that there is a gap in what the health care professional knows about risk and about safety in general and this is very important because what's important is that safety information is not always translated into practice. That's the problem. The information is out there. I'm not going to discuss further about (unintelligible) and other products that have been withdrawn from the market previously.

But the point here is that FDA said that they had to withdraw drugs from the market that would have been safe if used according to label instructions. It means the information is there. It's not used, and this is very important, and a lot of people agree on that.

We have to keep in mind that more than 60 percent of serious adverse events reported to FDA are preventable. So we should do something about it. I think we could do a lot.

Mackman (phonetic) in 1996, editor in the Lancet, said transparency in the dissemination of risk-benefit information is to make goal to empower consumers to make fully informed choices. This is very important about what drugs they take.

But I think that transparency is

important. It is not enough, and we might be overloaded by information that we cannot use. I am more supportive of the need to communicate better and educate health care professional patients maybe more to use drugs in the most appropriate and safest way.

I was very pleased to see that FDA is now using the same criteria of informed discussion to make informed decisions, but to make informed judgment, informed decision, there is a need for independent and different reliable sources information, and I think Dr. Seligman asked a question yesterday about do we need different sources. I think, yes, we need reliable sources of information because patients want to be provided with comprehensive and truthful information about their medicines, including the safety.

And in order to make these informed decisions, the patient needs to understand the risks, but also the benefits of the treatments offer to them, and they think when we talk a lot about safety to patients and where there are issues, we also forget to ask them what they think about the benefits, and we have seen some patients asking to have drugs back to the market.

The European directives and guidelines

requires the patient information with a description of all side effects listed in SPC, and they want adverse drug reactions to be conveyed using verbal descriptors.

There was some study that showed that sometimes that doesn't work very well and people don't understand really the verbal descriptors. And I was very pleased to see that the guidelines that were posted for comments up to October, last October, risk communication is a key component in the risk management.

So let's see now some of the strengths of FDA current communication. Despite what we are hearing, I think FDA is still trusted and a credible body when they talk about safety, and the information provided by FDA is reliable based on strong data from clinical trials, pharmacoepi. studies and spontaneous adverse drug reporting system.

FDA has resources and easy access to media information and communication. I think they can get on the news whenever they want and could send information largely widely to people, and this is very important.

I think all the documentation and information resources are excellent. All the document

we have seen there are excellent. The problem is not all people know that they exist. And FDA has still the power of enforcement laws.

Now I'm going to talk a little bit about some areas of improvement for FDA. I think FDA roles and responsibilities are not clear in public eyes. At least they're not clear in my eyes, and the discussion with some people yesterday seemed it's not clear for a lot of people, and someone just told me today it's not the role of FDA to communicate. Their role is to regulate.

Certainly it is to regulate, but I think some people said the role of FDA is to protect public health. So when we ask the question, under public health, do we understand regulate, inform, communicate, and even educate? That's the question I'm asking.

In a lot of people's minds approved by FDA means safe. Many physicians' minds -- I'm a physician, and I know physicians are overloaded by information. They don't have time to read. So they rely a lot on FDA, like also the public.

And also the goals and objectives in risk communications are not clear. What does FDA want to start talking about risk communication? Inform,

educate, influence and change behaviors, reassure? All of them?

I think these are questions that maybe FDA should think of.

Access with FDA information. So I'm not sure the public knows how to access FDA information and FDA tools, and even DTC companies on TV, I mean, they always refer to the prescribing physician or to the manufacturer. I'm not sure I've ever seen an ad referring to the FDA Web site.

And even when we discover the FDA Web site yesterday, I didn't want to put my comments on the slide because I had difficulties with the FDA Web site, and I thought it's me. And then yesterday I've heard all of the comments from other people, and I think everyone agrees that it's not friendly user.

And even in most of the slides yesterday people were on the CDER Web site, and not all people know CDER. I went on FDA and put a drug name. It was very difficult to find anything. I had to go through CDER and scroll down, but we discussed this yesterday.

Another, I think, problem in communication, FDA conveys almost the same information to all agencies, health care professionals, patients, media, and it might be confusing for some patients.

It might not be easy to understand, and sometimes in some alerts, all I found in FDA Web site was the "Dear Doctor" letter or the alert made by the company.

So the question for me was: do they agree totally with this? What's their position on that? So it was not very easy for me to say what's FDA's position on the problem.

Labeling. It's not the subject of today's meeting, but I think everyone agrees it's too long, too much information, difficult to understand, not easy to identify key information. It's an information tool. I don't think it's a communication tool, and my opinion is it's even legal tool made by lawyers for lawyers.

Black boxes. I think they impact efficiency, and I've been very challenged these days.

Another point is I'm not sure FDA has fallen making to evaluate response process with safety information. When FDA sends an alert to the Web site or later, I'm not sure they have a mechanism to make sure the information was there.

And I don't think FDA has the resources for ongoing public safety education. Do they need to have resources? We'll see.

I've seen some opportunities and I would

like to recommend some. I think it's a unique opportunity for FDA to obtain resources for safety education and to play a key role in public and health care professional education. I think FDA could play this role.

It's my recommendation. Maybe all people won't agree with this, but I think there's an opportunity to do this.

FDA could gain more trust and credibility by improving its communication content and tools, and we all know that trust and credibility are the foundation for an efficient risk communication.

I wish FDA could lead regulators and pharmaceutical companies' efforts worldwide to change this communication strategy, and I would love to see an initiating starting on good risk communication practices.

Some recommendation to FDA. I think there needs to have clear goals and objectives, to develop risk communication strategies and risk communication plan.

Yesterday a question was asked on what should be the priority for FDA. Where should we start? I think you should start by building a risk communication strategy and a risk communication plan,

having people brainstorming on that, and then define the priorities. I don't think we should just start with priorities. I think we should have a real risk communication strategy.

And I think risk communication is an important tool in risk management in general, and I think it should be required in risk management requirements. It means when FDA asks the risk management plan from pharmacy company, they should ask what's your risk communication plan, and I think FDA could gain from engaging partners for education association, academia, and communication professionals.

Someone said yesterday you guys need professionals. I think the FDA has a lot of very strong scientists, M.D.s, but I think you guys really need communication people, people who are professional. In my opinion, through 20 years of pharmaceutical companies, no one is born a good communicator. You have to become a good communicator, and people work on that.

And I think FDA should publicize the other sides of communications tools and market them, certainly market their tools outside, and they should recommend that DTC actual drug-patient treatment at

the Web site, too.

Another point, the pharmaceutical company marketing departments have used communication tools for a while, and billions are spent every year in promoting with very good results, and I think everyone agrees. I mean, we know how to communicate well.

I think PhRMA has developed strong expressions how to prepare, test, pilot, message strategies, develop messages that translate into practice, and we've seen this. I mean the sales show it. They know exactly how to target (unintelligible), M.D.s, pharmacies, patients, even different communities, Hispanic community, others, and they know also how to evaluate the efficiency of messages and to change. I mean the tools are there. Why can't we use the same tools to talk about safety?

And I think we should really all take advantage of this strong expertise and use the same communication strategies and tools to communicate about safety and risk.

Because also I think communication write about drug safety could also be good business for pharmaceutical companies and there was at least one who had the courage to pilot communication, risk communication, to patients, and they did a pilot, and

guess what. They had a surprise. They said it pays back. Patients who understand how to use their treatment stay on treatment and they trust it.

So even for pharmacy companies, my recommendation is to change the way they communicate and talk, try to start talking about safety.

Shift from information to communication and education is very important because we need to develop a mechanism to insure the information was received, processed, remembered, and has been translated into practice. We've seen some examples yesterday.

In my opinion, what FDA and others do today in communication is information. It's like a news channel. The same information is made available to all people, agencies, but there is no mechanism to insure that information has been received, and that's the problem.

Communication, our recommendation, it's a two-way process based on trust and credibility. So one of the key things to communicate better is to build trust and credibility, and there are mechanics to make sure the information was received, processed, understood, remembered, and has been translated into practice.

Education is one step further. It's an ongoing process and practice to insure all agencies have acquired the (unintelligible) and they know how to behave now, and the communication has been translated into practice and has induced a profound change of behavior to use medicine safe and in the most appropriate way all the time. It's like the safety belt in the car. It has to be minded.

I think this has been said many times that we should communicate in a format and vocabulary the patient could understand even with low (unintelligible). Avoid medical and technical terms when you talk to patients or consumers, and adapt the message to audiences in terms of content, but also in terms of format, but to do so you need to identify who are the different audiences and choose the right channel for the right audience, but also to pilot and test messages and communication strategies and change it.

So in conclusion, I think to be safe with drugs there are better ways to communicate and educate all audiences about risk and benefits, including health care professionals. Keep in mind that if we just do something about this 50 percent preventable adverse event we do a lot.

And if health care professionals and patients have the right information to make informed decisions, the changes will change their behaviors.

I think it's a shared responsibility. It's not just FDA's problem. I think PhRMA companies, everyone, health care professionals have all (unintelligible) to pay news communication, and I would love to see the development of this concept of good risk communication practices because I think the ultimate goal is the right product for the right patient in the right indication with the right information.

Thank you.

CHAIRMAN SELIGMAN: Thank you, Dr. Bennattia.

The next speaker is Dr. Alan Goldhammer from the Pharmaceutical Research and Manufacturers of America.

DR. GOLDHAMMER: Thank you very much, Dr. Seligman.

It is, indeed, a pleasure to be here to speak on the important topic of risk communication. PhRMA is a strong supporter of improved and effective risk communication for this one principal factor in making appropriate treatment decision.

The research enterprise results in the development of new therapeutics that provide improved positive patient health outcomes when used according to the drug label. While no drug, including those sold over the counter, is without some degree of risk, the goal of any therapeutic intervention is to maximize the treatment benefit while minimizing the risk to the patient.

We must not lose sight of the fact that the overwhelming majority of medicines are administered safely to tens of millions of American patients each day and exhibit a favorable benefit-risk profile in accordance with the treating health care provider's expectations.

FDA approves drugs based on an assessment of risk and benefit. A corollary to this statement is that drug safety information cannot be communicated in the absence of benefit. This is a key point that must not be obscured as risk communication tools are discussed.

After all, the definition of risk must extend to a patient who does not take the appropriate drug therapy or discontinues it. In such cases, an adverse health effect of some consequence is likely to ensue. These may be short-term health effects, such

as in the case of calcium channel blockers whose consequence may be ameliorated, provided the patient is appropriately treated by a physician and doesn't discontinue therapy on their own. The consequences may also be long-term, such as in the case of hormone replacement therapy, where a woman may be at an increased risk of bone fracture in the future.

PhRMA has a longstanding commitment in this area. Our involvement extends to a number of stakeholder groups shown on this slide. Some of these groups work on improved communication of benefit and risk. Others have been working and focused on personal medical records that can help in assessing whether the appropriate drugs are being given, and to prevent medication mix-ups.

We have also worked with the CERTs, the Centers for Education and Research in Therapeutics, and FDA on five workshops relating to risk and benefit assessment, risk communication, and risk management.

PhRMA has also spearheaded an effort to deliver drug labels to dispensing sites in electronic format. This is our paperless labeling project. This began six years ago, and this past spring we completed a field trial involving almost 200 pharmacies throughout the United States.

Drug labels in easy to read, accessible electronic format were delivered to pharmacies. Updates were delivered within 24 hours, and the vendors also delivered FDA alerts at the same time. This was a critical patient safety initiative as pharmacies have access to the most current prescribing information, something that's not guaranteed in the paper environment.

We hope to move this initiative forward during 2006. The appropriate information in the new drug application is synthesized into the FDA approved drug label. This provides physicians, pharmacists, and other health care providers with ready access to the important information needed to maximize medical outcomes in the patients being treated.

However, no clinical program can be large enough or lengthy enough to understand all the risks. Rare adverse events are seldom detected during the clinical development process. It's well recognized that new information on both benefit and risk will be acquired during the post market period.

For example, an oncology drug may be approved for a single indication and subsequent work demonstrates the utility for the treatment of other cancers. Similarly, the risk profile may expand as

the drug moves into widespread use.

These fundamental precepts highlight the delicate balance between the need to approve drugs in a timely manner and the need to understand drug safety in as complete a manner as possible. It is for this reason that companies maintain large pharmacovigilance and epidemiology divisions whose responsibility is the detection and validation of new safety signals.

It's appropriate for this hearing to consider how new safety information is acquired and communicated to health care providers. This slide shows the flow of information following product approval.

The process, however, is not a short one, and in some cases can span several years before a safety signal is fully understood. Communication of premature of invalidated safety observations not only has the potential for confusing health care providers, but also the unintended consequence of disrupting beneficial treatment.

Well founded clinical decisions may be compromised as the patient is moved off one therapy into a second, whose therapeutic risk-benefit profile may be less favorable.

In addition, consideration must be given

to the problems that will arise if early communication turns out not to be valid or if it's unrelated to other drugs in the same therapeutic class.

And it's instructive to look at a paper that appeared in this week's New England Journal of Medicine by Wong and colleagues, and there was an accompanying perspective by Ray. Earlier this year, FDA issued a health advisory noting that the use of atypical antipsychotic medicines in elderly patients increases mortality.

What was left unsaid was the relative side effects of conventional antipsychotics for the same indications. The Harvard researchers carried out a retrospective cohort study involving almost 23,000 patients, suggesting that conventional medicines are at least likely as those subject to the health advisory to increase death among elderly patients.

This raises significant concerns about whether such patients should automatically be switched to older drugs, as the authors noted, and highlights a major pitfall in communication of preliminary risk information outside the context of all available treatments.

The questions that FDA posed today relate to a subset of safety information available to

patients and health care providers. This slide, while not all inclusive, highlights some of the major sources of information.

Despite the availability of such information, however, and educational efforts, there's a growing apprehension about the safety of drugs.

PhRMA will offer some general comments before we get into addressing each of the six specific questions and focus most of our comments on the availability of information over the Internet. The information sites that FDA posted in the Federal Register notice presume that there's ready access to the Internet, which may not always be the case.

In addition, the sources of information are spread out over a number of different URLs and are not commonly linked. The more complex the Internet site is in terms of organization, the more frustration the user is likely to experience.

And finally, there should be a common template for the presentation of information. Right now there are consumer information sheets, patient information sheets, health care professional information sheets, each having a different type of format and information content.

The first question that FDA posed: one

key problem is the access to various Web links, and I'll discuss this in more detail in the response to Question No. 4.

Associated with this question, however, is what types of studies FDA has done with various stakeholders to gauge the awareness of the availability of information. Has FDA mounted any significant public awareness campaigns advising consumers and health care practitioners of the availability of the information? Does the FDA have statistics on the number of Web accesses? How long are users staying on a particular site?

Some of this information is presented in technical terms, and if the viewer is on the site for less than one minute, it's not likely they would gain any useful information. We have some information from our own clinicalstudyresults.org Web site which posts summaries of unpublished clinical studies, and we've found that the majority of people that go to the site are on the site for less than two minutes. This is not a sufficient time to read even a brief summary of a clinical study.

In addition, some tools appear to be redundant or sometimes combined. It's uncertain whether this is confusing. PhRMA questions whether

they might be combined into a single common format. Looking at the example FDA cites for health care professional information on fluoxetine, it immediately starts with an FDA alert. This was already displayed on the first fluoxetine page and may appear redundant such that the health care professional did not scroll down and read the remainder of the information on the page.

This was the second FDA question. PhRMA was unaware of any comprehensive studies that have been done regarding these Internet sites. An assessment of the sites will necessarily be complicated by the difference in content and perspective audience.

For example, CDER educational campaigns are focused on classes of drugs and may cover dramatically different types of issues from those sites that deal with a specific drug. The health care practitioner also has different needs than that of the patient.

This was Question No. 3 that the FDA posed.

As stated earlier, evaluating drugs on the basis of risk alone is unwise and potentially injurious as the patient may not receive the medicine

that is best suited to their condition. For the most part, risk is evaluated on a population basis and may not be relevant to the individual.

One can look at case histories of a number of drugs withdrawn from the market over the past 15 years. In all cases, many more patients were successfully treated than were harmed. While the promise of pharmacogenomics offers hope for a better understanding of drug safety, we're not at that point yet.

And finally, the tools that have been noted by FDA require validation, a very important fact.

The majority of PhRMA's comments concern Question No. 4, and that's the accessibility and understandability of the Internet based sources of information.

Our principal criticism of these tools relates to the relative inaccessibility of the information. There's no single entry portal. There's very little information, as already noted this morning, on the FDA home page that offers any indication about these sources of information, and one must go to the CDER site to access anything meaningful.

The difficulty here is that there are multiple links inferring significant information content, which may not always be the case. For example, the consumer education information link leads only to three sublinks that really don't deal with benefit-risk communication. The safety information for specific drugs link does pull up an alphabetical listing of a subset of drugs. Within each link is variable information.

As FDA notes, the information could be in the form of a patient information sheet, a consumer information sheet, or a drug information page. Perhaps most problematic from the PhRMA point of view is that some of these pages don't even have the FDA approved drug label.

Since the drug label should be the health care provider's first source of information, this is clearly a major shortcoming. The CDER page is also confusing in that two other drug links, or two other links, Drugs at FDA and the Drug Information Pathfinder, provide certain information of use to health care providers and possibly patients as well.

Drugs at FDA contains the drug label, approval information, and certain risk information that may or may not be in the drug label, but one

needs to click down several screens to get this information.

The Drug Information Pathfinder leads one to a Web page with a large number of links, some of which are not terribly useful. For example, the category drug safety has only a link to medication guides and not any of the other links noted in the announcement for this meeting.

Under drug approvals, there's a link for the consumer information sheets, but not the patient information sheets, despite the fact that FDA states they are phasing out the former. In FDA's defense, clicking on the consumer information sheet link brings one back to the general index of specific drugs that was already mentioned.

FDA has worked very hard with the National Library of Medicine to establish Daily Med, and there is at least one label up there right now. This will be a Web site that will have all of the drug labels in electronic format.

However, the site is not expected to be fully populated for at least a year, as FDA will be receiving electronic drug labels in annual reports. The site notes that other information may be available, but does not specify the type and quantity.

This was Question 5 posed by the FDA.

As I noted earlier, discussing risk in the absence of benefit may alarm the patient, leading to confusion about available therapeutic choices and potentially discontinuing therapy if already on the drug in question prior to talking to a health care professional.

This does not serve the public terribly well. It is unclear whether the presentation of FDA material meets the utility criteria for persons having lo health literacy skills.

While not the subject of this meeting, PhRMA notes that this is the principal function of the consumer medicine information, or otherwise known as CMI, leaflets that are provided to patients when they pick up their prescriptions at the pharmacy.

Question No. 6 deals with communicating information to special populations, that is, the elderly and non-English speaking.

Over 170 languages are spoken in the United States. Of this surprisingly large number, Spanish is spoken by 28 million Americans, followed by lesser numbers who speak Chinese, French, German, Tagalog, Vietnamese, Italian, Korean, and Russian.

What's not clear from these U.S. census is

what the level of English comprehension is among these groups. Certainly if that level is low, the current FDA efforts, which are primarily in English, will not have much impact. While a case might be made for the development of materials in Spanish, the large number of drug related information already on the FDA Web site raises severe concerns about the expenditure of resources to providing such material in that language.

Elderly patients, on the other hand, have special concerns. Many of them are on multiple medications raising issues of compliance, that is, taking the right drug at the right time, as well as the possibility of drug-drug interactions.

These tools, subjects of this hearing, do not adequately address these needs. It's further unclear what the level of access to Internet based materials are for these special populations.

PhRMA supports -- and I'd like to go over some of our recommendations here -- we support the FDA communications efforts. However, much more needs to be done in terms of evaluating the effectiveness and impact of these Internet based tools. What is the comprehension and use of the tools? This certainly needs to be assessed.

Collectively, we all have a stake in

assuring that the patient benefits from a prescription drug treatment regimen. We must help the patient make the right decision about using a medicine and enhance and empower the physician-patient assessment of the benefits and risks in the context of individual patient needs and preference.

FDA should consider how disparate patient and health care provider information should be presented on the Internet. The current Web site is in bad need of overhaul so that the information is in one place and easy to access. Patients and health care providers should not have to go back and forth between multiple Web pages in search of information. We suggest a single Web portal that's searchable by drug, though it might also be useful to create a separate section on classes of drugs that raise certain issues. There should be a hierarchy of information that begins with the FDA approved drug label and clear notice being given to new safety information if that information has not yet been validated, and as we note here, perhaps the portal could be daily met.

There is an ongoing and marked need for better patient outreach so that patients have a better understanding and expectations of the drug they are being prescribed. This communication may be initially

provided by the prescribing physician, but it should also be supplemented by patient friendly information.

PhRMA earlier this year proposed to the CERTs a workshop on patient focused benefit-risk communication. That proposed workshop will involve a variety of stakeholders, patients, doctors, pharmacists, the FDA, communications experts, and behavioral psychologists to better understand the tools, roles, and messages in communicating benefit and risk to patients. This should be viewed as an important first step and not a final resolution of the issue as there is much that all stakeholders can do.

The workshop was accepted by the CERTs and is currently in the planning stage.

And finally, one small or, as I note in parentheses here, a very big step, we all have to work to insure every patient has a realistic expectation about the medicine they are prescribed.

CHAIRMAN SELIGMAN: Thank you, Dr. Goldhammer.

Our next presenter is Dr. John Wolleben from Pfizer.

Dr. Wolleben.

DR. WOLLEBEN: Good morning. My name is Dr. John Wolleben. I'm Senior Vice President for

Safety and Risk Management at Pfizer.

I'd like to thank the panel for letting me speak this morning, and even before I get into this, I just apologize for my somewhat annoying cough that you're going to hear every now and then. I'd like to let you know it's part of a cold. It has nothing to do with ACE inhibitors or anything like that.

The medicine safety is an obligation widely shared at Pfizer, and we take our commitment to delivering safe and effective medicines very seriously. Safety issues are a collaborative responsibility at Pfizer. The global organization that I head is dedicated to collecting, assessing, and reporting safety issues to facilitate the decisions surrounding pharmaceutical safety matters and assure compliance with the various reporting responsibilities around the world.

The safety and risk management group at Pfizer reports directly to Pfizer's Chief Medical Officer and has approximately 600 professionals in a central global organization who work with the thousands of individuals in the countries who are the people who directly collect the safety information.

Our team collects, assesses and reports on about a quarter of a million adverse event reports

annually that come from either clinical trials or commercial activities. Our team also proactively develops risk analyses, performs epidemiology studies, creates risk management plans for our major products, and communicates in a number of ways the benefits and risks as our medicines.

By way of this introduction I am simply trying to say that we have a strong commitment to safety and a strong commitment to communication of issues related to safety, to both the regulators and the stakeholders and patients who we support.

Nonetheless, and as has been noted before, we know that the communication of risk in medicine is far from perfect. This is something that we need to all get better at, the FDA, industry, physicians, and other health care professionals, patient groups, and the media.

So we commend FDA for its efforts in general to improve medicine safety and specifically for holding this public hearing on communicating risk. It demonstrates the agency's responsiveness to public input and commitment to improving its public interfaces.

Promoting better health is a Pfizer priority. So we share FDA's desire to effectively

communicate medicine risks, as well as benefits in a way that advances patient well-being. Today's focus is on FDA tools for communicating pharmaceutical risk. Since Pfizer does not have direct involvement in the production of these FDA vehicles, we will avoid commenting on the specific aspects of them, and as others have done so, we actually support most of the comments that have already been made.

However, we would like to offer some general principles that we feel are the fundamental underpinnings of any risk communication strategies that the FDA pursues. These principles have been alluded to also by others in other ways in their presentations.

The first fundamental principle has to do with the maintenance of the benefit-risk perspective. As FDA evaluates risk communication tools, we urge you to consider that any communication it provides on risk be in the context of benefits. The agency cannot effectively inform, educate or guide on safety issues without providing this broader perspective.

Public communications that are one sided that focus only on risk or, for that matter, only on benefit, are not in the public interest.

We note that all examination vehicles are

under examination today primarily focus on risk. We believe, therefore, that they may not be achieving what is in the true interest of the public, namely, enhancing an informed benefit risk decision.

Medicine safety is not defined by potential or real risk. Medicine safety is best understood as the balance of risk within the context of benefits. This balance is at the core of what FDA does when it's deciding whether to approve new drugs or indications. The benefit-risk balance is also the framework in which physicians decide to prescribe and patients decide whether to take medication.

Since the benefit-risk balance for a drug is different for different patients, it is very important that doctors and their patients are aware of at least the major possible tradeoffs. Therefore, a first guiding principle is that every communication to the public by FDA should contain a balance of benefit and risk information reminding the reader of the benefits of the drug as well as what may be known about its potential risks.

We know, for example, that the media tend to focus primarily on risks in their reports, often giving unbalanced view of therapies. If public communications only communicate risk without a

balanced presentation of benefits, those communications have the potential of unreasonably amplifying risk and creating unintended consequences, perhaps unnecessarily frightening many people away from taking much needed medicines that are safer than doing more harm than good.

So we strongly encourage FDA to minimize unnecessarily frightening people away from needed medicines and insure that its risk communication vehicles take into account and present information on both benefit and risks.

We believe that a well designed communication system should allow for the distribution of safety and risk benefit information in such a way that a metered response from the patient-physician community can be achieved depending upon the nature of the specific risk-benefit information that is communicated. One size does not fit all for risk communications.

The second fundamental principle that we believe needs to be emphasized is empowering the physician-patient relationship. A second guiding principle for FDA to consider is insuring that its risk communication vehicles respect, reinforce, and empower the doctor-patient relationship, and is not a

substitute for it.

Since there are so many variables that affect whether an individual can tolerate and effectively use a modern medicine, an uninhibited dialogue between the health care providers and patients who may decide to use medicines to treat illnesses is essential. It is important to remember that supplementary risk information that FDA provides on medicine will be only one of many inputs a physician will rely on in treating patients. Other information likely used in describing decisions would be the medical history and situation of the individual patient, the information contained on the drug label, the physician's experience with the specific drug, alternative treatment options available, and the risk tolerance of the patient, among others.

Consequently, it is critical that the FDA insures that implementation of FDA tools respect physicians' prescribing discretions. In order to maximize the effectiveness of FDA risk communication tools for physicians and other health care providers, it is essential that these tools provide clear, accurate, useful, and actionable information that physicians in discussions with patients can use as an input in their prescribing decisions.

We encourage FDA to continue to work with physician groups on the usefulness of current tools directed at health care providers and have providers think that they can be improved. We remind everyone that when a physician shows up or when a patient shows up in a physician's office, that patient is unique and is treated as an individual and not as a population.

The next principle that we believe should be an underpinning of any communication has to do with enhancing the audience and public comprehension, and actually this was addressed very nicely yesterday in a few of the presentations.

A third area of consideration is insuring that FDA's tools communicate in a manner that the intended audience truly understands. FDA certainly recognizes that individuals have varying degrees of health literacy and perceive risks and benefits differently. So its communication tools should strive to reflect this diversity.

Literature on communicating risks to the public indicates that many persons are illiterate and cannot understand some of the basic mathematics used in risk concepts. There is still uncertainty about how individuals personally characterize risks, how best to communicate risk to the public, and whether

and how persons understanding risk concepts and communications.

In fact, we do not yet know what people want to know, in what format they want to know it. In May of 2004, Pfizer made a presentation to the FDA about its clear health communications initiative. The clear health communication program aims to reach as broad a consumer audience as possible with information people can understand and act upon in both print and Web based materials.

We are reaching out to all consumers who can benefit from Pfizer products and services by promoting better health outcomes through improved medication compliance. This program provides Pfizer personnel a step-by-step approach to shaping materials that maximize understanding of the benefits and risks of our medicines.

For print documents, for example, we have established principles for clear communication with a clearly defined process of achieving each principle. Those principles include focusing the content of the needs on the audience, explaining the purpose of the content to the audience, involving the reader in the document, making it each to read, making it look easy to read, selecting visuals that clarify and motivate,

and writing content at a sixth grade reading level.

Pfizer makes these principles available to the public through its health literacy Web site at www.pfizerhealthliteracy.com, and for those who are familiar, Pfizer health literacy is spelled as one word in Internet language, no dots or dashes.

The last principle that I'd like to make sure we emphasize is a willingness to collaborate. Given the importance of risk communications and the potential for giving confusing and possibly harmful information to the public, we urge the FDA to empirically study the real impact of its tools on patients and physicians. FDA should seek the advice and counsel of experts in risk communication, including those in the pharmaceutical industry, researchers in cognitive psychology, and practicing physicians.

We also recommend that FDA regularly monitor patient and physician behavior in response to risk communications, and then modify its communication tools accordingly.

You have heard from PhRMA about the industry's willingness to partner with FDA, academia and others on risk communication. Pfizer has been and continues to be an active partner with others to

improve risk communications globally, working with the ICH, PhRMA, EFPIA, et cetera.

We would like to reaffirm our willingness to partner with FDA to find solutions that enhance risk comprehension and patient safety.

So in conclusion, the principles that we believe should underpin any action are very simple. Risk cannot be presented without understanding it in the context of benefit. The patient-physician relationship is premier and should be encouraged and supported. The tools must be comprehensive and comprehensible, and therefore, they need to be tested, and finally, we look to collaborate with the Agency on any opportunity we can with them.

Thank you very much.

CHAIRMAN SELIGMAN: Thank you, Dr. Wolleben.

Our final speaker on this panel is Dr. Stephen Goldman from Stephen Goldman Consulting Services.

DR. GOLDMAN: As mentioned, I'm Dr. Steve Goldman, and as Cherif had talked about his 20 years in industry, I am first and foremost a clinician, and during my career I've been a full-time academic doc, full-time regulator including several years as the

MedWatch Medical Director, a couple of years in industry as Director of Pharmicoepi for one of the pharmaceutical companies, and then I was a full-time consultant in safety and risk management, risk communication for industry, including the device industry, government, and health professional associations.

I mention that background for two years, so that you'll know the vantage point that I've got, and the second point that I'll make is when I was at MedWatch and some of the work I do now, my concern is one thing, and that's public health. And any time you put out risk information, whether it's a label, notification of any type, it's the man or woman sitting in their office trying to decide how to use that information with the individual patients Dr. Wolleben talked about; that's the bottom line on all of this.

It's the bet possible information to be utilized in treating patients, individual

I always like to start with a quote that will establish the mood. So I figured I'm on Capitol Hill. Why not go with one of our Presidents I'll show you in a minute?

I'm going to be addressing four questions,

and the ones that I'll run through very briefly are the Internet, the strength and weaknesses of the communication tools, the information, awareness we've talked about, and whether it's the right kind of information being provided.

And this is what I thought would set the mood. Our greatest President, Abraham Lincoln made the point early in the Civil War that we cannot escape history, and Dr. Wolfe talked about this yesterday in the Santayana quote, but there's positives and negatives of history. We don't want to throw out things that we've learned that work simply because we've forgotten that they worked.

By the same token, we cannot forget what hasn't worked and try and utilize that information.

In terms of accessibility, the documents are up there, and we heard some nice presentations yesterday, but if you don't know they're up there, they're useless, and this is one of the things that MedWatch sought to do. Dee Kennedy and I were there, and certainly I presume they're continuing this with the partners program.

That's a group of about 165 organizations that are notified directly when things come up on the MedWatch Web site. We always knew it was working when

I was at MedWatch when I received four notifications from all of the organizations I was a member of after we went it out.

So that's clearly an information extender. Now, the FDA also has, I believe, up to 20 free listserves, and many of us are subscribers to that. Sometimes you get the same notice from more than one. There are all terrific if you know they're available, and if they don't vanish into the white noise of all the things you're receiving every day because we plow through hundreds of E-mails, and that's one of the problems you run into with even terrific information sources, is they get lost in the morass of information that we do get.

Much of what I'm going to be describing today is actually based on a study I did last year addressing several of these questions, and that's the reference to that.

These are the questions I posed as part of my research, is label changes in health professional notification are clearly the tools being utilized. The question is, number one, are they effective, and the second part is if we're going to say they're effective, what's the standard we're using for effectiveness, which really has not been brought up

over the last couple of days.

Secondly, the interventions to improve medication use, do they really result in modifying behavior? Well, I'm a card carrying shrink. I'm a neuropsychiatrist. I'd better believe in changing behavior. Otherwise my field doesn't exist.

And if these fields of communication don't exist in changed behavior, then why even utilize them?

Thirdly, educational efforts. We always assume that education leads to changes, but to they really? Do they really make a difference when we train particularly health professionals?

One of the first things I did when I put together my research, which is based on several years of this, is making the point that all risks are not the same, and there were four essential, significant categories that I've put together on the notification we've seen and the things we see with medical product use.

In the case of drug-drug interactions and two of the classic examples are terfenadine and cisapride; promfenac, which Dr. Wolfe mentioned yesterday was an example of off-label use, a drug being prescribed for longer than the period it was supposed to be prescribed for. Troglitazone, also

mentioned yesterday, that was a monitoring program. You had to monitor the liver function test when you were on the product, and acitretin, an example that was done in the Netherlands, as teratogenicity.

These risks are not the same. Therefore, the tools utilized, therefore the behaviors you're looking at are not the same, and Dr. Wolleben talked about one size not fitting all. I presume you were reporting my article because I'll show you because that was one of the conclusions I came to.

All right. Cisapride. Now, what happened to Cisapride? I'm not going to run through all of the different examples. I wanted to show this slide for a reason. Take a look at the numbers. There's three separate studies, including two different countries, by the way, and the third using computerized techniques.

After notification, co-prescription of contraindicated meds was three percent, the same statistic for all three. Now, you look at that. That means 97 percent of the prescriptions did not have contraindicated meds prescribed with them.

So you might look at that and say, "Gee, 97 percent were not co-prescribed. Maybe it was an effective notification program."

But how effective is effective enough? If you want no co-prescriptions, this is not effective.

When one looked at the notification program, one group of researchers said that the notification program was almost a complete failure because the standard of care that was desired was not achieved.

But then a second group of researchers looked at the actual notification, and they looked at the way it was worded, and they looked at the information that was provided, and what's really striking with our second group, with Weatherby and colleagues was that when you look at what was actually written in the professional letter that we denoted specifically which drugs were contraindicated with Cisapride, that was much more effective. When you talk about a general drug class, that was contraindicated.

Why is that important? Because you can put out two letters. You can get completely different results based on what the letter contains and how things are worded, and I think that's very important in terms of that.

We've see studies replicating this. The first, at the top of the slide, is from the same

article from Weatherby, and they felt that the key features of a successful notification were being specific, being brief, good publicity, prominence of message, does not depend on secondary information, which is very interesting because we're talking about a lot of place where there is secondary information, and personal discussion, and I'll talk more about that when we talk about acetretin.

There has been a brand new study that just came out from Mazor and colleagues, and they looked at the content, organization and formatting of "Dear Doctor" letters, and look what they found. Well, they had docs, actual practicing docs look at these letters, and they talked about areas that were deficient, and see if the same themes emerge: clarity, readability.

The proportion of perceived relevant information to the supporting information. That's fascinating. Perceived importance of the information, and easy discernability was felt to be critical. And it was a clearly stated preference, the letter with formatting that highlights key information. Very important to look at that.

Now, there's a second kind of format which I'm delighted to say the FDA has gone back to. I was

involved with this notification. This was on the low molecular weight heparins and the heparinoids.

You may recall that there were several reports coming in unfortunately about epidural spinal hematomas with the use of the low molecular weight heparins when people are having spinal epidural anesthesia or lumbar punctures, and some people having long-term or permanent paralysis.

There was a public health advisory -- there's a list -- at the end of '97. Two months later there was an advisory committee. The transcript went up, but we continued to get a lot of calls from the health care community.

So a task force was put together, and which I was honored to serve, and we looked at and put together questions that clinicians wanted to know about these products. We spent practically months on this getting questions that came into MedWatch. We had treating docs at the FDA also involved with these specialties, and we put out Qs and As talking about the common clinical aspects of the cases, the signs and symptoms of spinal epidural hematoma that came from the reports, the factors to consider when you performed the procedures in which patients were at risk, and where to find further information.

We put this out. I can't tell you the number of phone calls we received from MedWatch. Two things they said to me. "This is great." Secondly, "why aren't you doing this more often?"

And I think this is important because the FDA, although it does not regulate the practice of medicine in pharmacy, this is not regulation of medicine in pharmacy. This is providing good clinical data to be used in the clinical community in association with patients, again, for the benefit-risk association with it.

I'm delighted to see that the FDA is using the Q&A format more and more, and these are two examples. When the COX-2 selective and nonselective, nonsteroidal anti-inflammatory drugs announcement came out in April, I thought this information was great. I really thought that what was put together by the agency with companies was excellent, and you can see there was a public health advisory, there was a separate drug information page, and then Qs and As that were product specific, talked about the perceived risk-benefit profiles, talked about the repressive labeling changes, including a box warning, and the related issues associated with decisions made by the Advisory Committee.

So I certainly support the idea of using this. As you can see, two months later, very similarly with the nonsteroidals in general, the NSAIDs, there was a prescription about a request letter for changes, the labeling template to be used, the medication guide which used, once again, a Q&A format.

Why is it so important? It's easy to ready, and it's not just for doctors, pharmacists and dentists. Consumers find Qs and As are easier because they address issues that you've got that are very germane.

As a matter of fact, I'll be honest with you. I often go to the Qs and As first in terms of the things that I'm looking for, and I can even go to some of the other supplemental things.

The idea of personal contact, this is a terrific case study that came from the Netherlands, and this is with isotretinoin. What happened was that as one of the retinoids, they have a very long half-life, and the Netherlands had to notify women of child bearing potential that instead of a two-month post treatment contraceptive period, because of the long half-life of the parent compound, you had to go to two years. So that's a major notification to be made.

They use -- there was no Internet at the time. Believe it or not, folks, there used to not be an Internet, and they used radio, TV, and the media, and even though there were a lot of approaches being utilized, they were not that successful, particularly with consumers.

Why? Well, for example, 35 percent of people were never contacted by their health professional. Those people who read the newspaper ad, well, three-fifths of them couldn't recall what the message said. When you looked at the radio and TV ad, a third couldn't recall the message, and maybe the worst statistic of all, nine percent of all women at risk use no contraception with a known teratogen.

So the effect was seen as moderate. The recall of the notice as poor. Overall, it was felt that this notification program failed because there was insufficient personal communication with those at risk.

I really want to reiterate this because we talk about all of the tools we've got. If we leave out the human factor, we are missing one of the most important aspects of benefit-risk communications to patients.

A multi-faceted approach, another terrific

case study. This one comes from Australia, and what happened was that flucloxacillin was found to be associated with adverse hepatic reactions, and what the government of Australia wanted to do, along with the manufacturers of the products, was to explain to people when to use flucloxacillin, not to use it for superficial skin wounds, but to use it for serious skin infections.

They tried several different methods by which to notify, and what they found was it was a combination of several different things: journal articles, notifications from the national dispensary, things that were put in directly to docs and pharmacists, changes in the ads that the company ran in terms of utilizing the product. They were all put into the mix, and lo and behold, they were able to achieve the desired result, which was decreased utilization of this medication for patients in which the benefit might be outweighed by the risk as opposed to other patients with severe infections where the benefit would outweigh that in terms of that.

So the point to be made here is using a lot of different things, coordinating them, but not presuming that one is the reason why there was a change, it's a concatenation of events.

Now, how we communicate risk. I think this was touched on before. This makes the point that there were a lot of social influences on how people respond to information provided by physicians. You cannot make the point about trust too often. Trust is easily lost and hard to regain.

Secondly, the relevance of the information to someone's life, the relationship with the other risks they understand, concordance with their previous knowledge, and the difficult and significant choices and decisions that are made. So that when you want to improve risk communication, you must build trust, and you must be aware of patients' access to other and in many cases conflicting source of risk information.

You know, the Web is a marvelous thing, but there's a lot of direct (phonetic) on the Web because there's nobody monitoring what goes up on Web sites, except for government Web sites and others or company Web sites.

And you know, we've had this at the agency when I was there where someone put out a spurious announcement that was completely wrong, and we had to spend a lot of time telling people the information was incorrect.

Other things, and this came from a

terrific series of articles in British Medical Journal. This is one of my favorites. How difficult it is to communicate risk and probabilities. This is one of my favorites. You would think the innocuous statement, and you hear the statement every day. You turn on the weather report. You know, Friday we're tracking a snow storm from New Jersey where I live, and they tell there's a 30 percent chance that it's going to rain tomorrow. That seemingly innocuous statement, this is the different ways this can be interpreted. It's going to rain in 30 percent of the area covered by the broadcast, which I found fascinating because I don't know what the area is covered by any broadcast. It's going to rain 30 percent of the time tomorrow so we go to like 5:10 and then 7:30 it would start to rain again, and my personal favorite: it's going to rain on 30 percent of days like tomorrow. I have no idea what they did to come up with that.

But the point is that an innocuous probability, yeah, it's going to rain; you know, you're not going to die because it's going to rain. Translate that to explain to a patient what the five-year survival is on the neoplastic agent (unintelligible), and what they hear, what you thought

they heard as opposed to what they actually did hear.

So what have we learned? What are the lessons learned? When you're going to choose a communication method, you must also look at the perceived risk because the behaviors associated with east-west differs. So maybe the communications.

And, again, as I said, last year in print, all risks are not the same. One size of risk notification tool may not fit all.

Secondly, multiple modes of risk communication and maximum publicity may well heighten the effectiveness of the notification program. If you're going to assess effectiveness, you must state what the goals are because if you're going to say there will be no, quote, prescription, almost nothing is going to achieve that for the most part.

As I pointed out, there have been some successful program notifications, but the product still came off the market, and that's a shame in terms of things that might still be utilized by patients.

Medical products differ at perceived benefit-risk based on factors such as the disease entity in the population treated, availability of the products, and versatility. Therefore, you cannot use a cookie cutter approach. That's why each individual

product carries a different societal perception of risk. It carried a different patient population being treated. You cannot fit this into a formula and spit out a result at the end. That's not how you practice medicine. That's not how you do public health.

Understanding how health professionals use communication information is very important. The different information sources. We're all using brand new techniques. I'm still learning on them, and, again, I say this from my fellow practicing docs, pharmacists, dentists, and others. People are overloaded. It's not a question of too little information. It's a question of too much information and too little time.

We've got to acknowledge that to hone down to what is the message we want people to get, and we have to think about that when we notify about risk.

I fully believe that risk information intended for health professionals must be clinically oriented and relevant to patient care as greatly as possible. Otherwise they're not going to read it. If it's not related to patient care, why would they be reading it?

I advocate for Qs and As. I think that's a great way of getting information from both health

professionals and consumers, and it should be devised to address the leading concerns at issue for both patients and physicians and other health professionals.

Therefore, you may want to draft different Qs and As for consumers versus health professionals.

To optimize risk and patient effectiveness, you must be aware of the social and societal factors. Psychological factors have impacted perception. Clarity presentation, minimization of ambiguity. I'm not saying don't use scientific terms, but try and use terms, but try and use terms that are more easily understood.

Deserve trust. We've all talked about this, and you must evaluate the sources of who's providing the risk information because as Edward R. Murrow said, "The speed of communications is wondrous to behold. It's also true speed multiplies the distribution of information we know to be untrue."

Health professional education. I'm a great believer in drug safety risk management education that is not product specific. The general principles of how you recognize, manage and report medical product induced disease, this is critical. People should have this in the back of their mind as a

differential diagnosis. Occam's Razor, common things heard common.

Adverse drug events are common, and they cause significant morbidity and unfortunately mortality. You must have in your mind the differential diagnosis to recognize it, and I always tell people when I do lectures or grand rounds somebody somewhere has to be the first person to recognize a previously unrecognized serious adverse event with that product out on the market.

We must enhance the knowledge of pharmacotherapy and the impact individual patient factors have on pharmacotherapy. The education effort must be at all levels, medical school, dental schools, nursing schools, pharmacy schools, training programs, and post graduate education. I believe it should be delivered in a clinical care setting to make it clear it's clinically relevant. They must be ongoing. One shot programs do not work, period. This must be an ongoing program.

Take a look at Frank May's academic detailing work, some of the beautiful studies he's done in Australia. Those are ongoing programs. The same thing with the Rhode Island adverse drug reaction reporting program the FDA had in the '80s. It worked.

We don't have to reinvent the wheel. We know these programs work. What do we have to do? We have to fund them, and there has to be a commitment to funding them, and there must be a commitment to keeping them ongoing as training programs.

So to answer the questions that I had asked at the beginning of my study and the questions being asked here: do the risk communications modalities used result in desired outcomes?

Frankly, I think, yes, they do, but not in all circumstances, not every time, and unfortunately, not always to a great extent, but we've got new techniques. We've got new methods. We need to look at these. We need to test them. We need to tell them the specific risks that we know about.

We also need hopefully to tailor them to prevent both preventable adverse reactions, also picking up new adverse reactions, and minimize the possibility of medication errors.

I served on the task force in 1999, the task force of the Commissioner. We made the point that this is not just the FDA's responsibility. It's FDA, it's health professionals, it's the regulated industry, patients, health care delivery systems, professional societies, other federal groups. This is

shared by all. It's not just the FDA's.

And I believe when you ask the question about where the FDA risk communication tools fit in, I fully believe that the FDA tools need to be seen as part of an overall risk minimization effort that incorporates the other methods, such as clinically based teaching, consumer education that may well employ the FDA provider information through all the different mechanisms we've mentioned.

And I will end with Clarence Darrow who said, "History repeats itself. That's one of the things that's wrong with history."

I think we should look at history repeating itself so that we can learn what we've learned in the past that works, and we can learn what didn't work so that we don't repeat it in the future.

Thank you.

CHAIRMAN SELIGMAN: Thank you, Dr. Goldman.

Let me start with a question for all the members of the panel. We've heard lots about the importance of strategic planning and about principles for good risk communication, about issues related to partnering and leveraging. I'd like to challenge the panel and ask them what they believe the role of the

FDA should be in the realm of risk communication and how you would distinguish it from the role that sponsors play.

We heard about, you know, the Pfizer program on clear health communication. We know that there are a lot of private vendors of information out there. There are lots of associations, some of them cited that have profilers, such as the Heart Association, Cancer Association, many patient specific groups, and I'd like to hear from the panel what they think the role the FDA should be playing in this realm of communicating both to health care providers and patients that would distinguish itself from the organizations that I've just mentioned.

Anyone want to start? Do you want to go first?

DR. GOLDMAN: Well, I think I made it clear in my talk what I felt the FDA's role was. The FDA is a public health agency, a trusted public health agency, and that is a unique position to be in, and one of the things that we did with the heparinoids, low molecular weight heparins was utilize that pulpit to put out good clinical information that clinicians needed to be able to make decisions with their patients based on the information we had.

I think that's a unique opportunity and responsibility that the agency has, in combination with, of course, the sponsor of the product with whom you work in terms of that.

You know, again, you run up against the fact that you do not regulate the practice of medicine or pharmacy, and there are things that are talked about when it does push up against the envelope. Providing good clinical information does not do that. It does not cross that line.

So I would see the agency's role as, number one, a public health advocate. The MedWatch program exists to provide information on medical product safety on not just drugs, but biologics, devices, dietary supplements, and in some cases veterinary medicines or vaccines. That's a unique responsibility. I think it does belong to the agency in the role it has as a government regulatory and public health agency.

CHAIRMAN SELIGMAN: How would you distinguish that from the role that other organization play?

DR. GOLDMAN: That's an interesting question. Other organizations, for example, let's say the American Psychiatric Association -- I'm a

member -- they put out treatment guidelines. The agency doesn't do that. They are more specifically concerned with one specialty. There's really no over arching. I guess AMA would be, but not every physician is a member of AMA.

The agency sees all the data. Health professional organizations do not. They funnel information into the agency, and I think that the FDA is rather unique, frankly, compared to some of the other regulatory agencies worldwide in being rather transparent with information. There's a lot of information that goes up on the FDA Web site you don't see on other governmental Web sites.

So I think that one of the things that we tried to do with the MedWatch program, with the partners program, was utilize the health professional organizations as disseminators of information, as people who could give us feedback as to how the information was being perceived, and also, frankly, fostering adverse event reporting and monitoring through the health professional organizations.

It was very clearly a partnership as it was with PhRMA in terms of getting information in. So that I think Dr. Wolleben and certain Paul talked about putting together situations where you're

collaborating on matters of public health because everyone does have a different role.

MR. GOLDHAMMER: Yeah, I guess just to follow on, FDA is both a public health agency and as part of that, you know, there's the communication role that you have, and I think that, you know, the level of respect and trust plays into that.

But then also the regulatory part of it as well, and I think as Dr. Goldman noted, you see all of the data. So you're going to be identifying things that come down and come into you. The question is: how is that communicated?

Now, part of the communication is borne by the sponsor. The other part, I think is borne by the agency, and both of those roles are important. I think the more critical factor, and it's one that we tried to stress in our comments, although maybe it wasn't stressed carefully enough, is that there's a partnership among all of us that if the goal is public health and getting these issues out so that the medical community and the patient community can be alerted to it and then take the appropriate steps, you know, there's a whole series of issues that have to be addressed as part of that, and that goes to, you know, data analysis, data validation and so forth, and then

communication.

I mean, I can't stress this largely enough, and I've had conversations with Dr. Ostrove on this. We've got to be able to do a better job. I don't think that collectively all of us are doing as good a job as we could be doing.

MR. WOLLEBEN: I agree with what Alan is saying. The bottom line of this whole thing is if it's good for patients and physicians, it's good for the industry, and it's good for the FDA, and we should be working harder to collectively figure out the right way to do that.

Now, I fully recognize the fact that FDA is a regulator and regulates the industry, and I understand that relationship, but when it comes to the communication of these risks and issues, I think there's a lot more that we could collectively do together.

And even on working on the tools that you're working on, I think there's expertise that exists within the companies that could greatly help you advance those tools to the point where they could be more effective.

I mentioned in my talk that I think that the ultimate goal here is to try to get the tools

designed in such a way that you get a metered response. Not all issues require -- we know how to turn off the use of drugs. I think we know how to do that. The question is how do you turn them on and off at the right rate.

And that's something that perhaps a lot of work would have to go into to figure out how to get done, but I don't think the agency could do that alone. There's resources elsewhere.

MR. BENNATTIA: I agree with all that has been said. I think the role of FDA with all of this is a partnership. It's a win-win relationship,b ut they see a little bit different role of FDA in the fact that FDA should be somehow coordinating all of the risk communication activities.

It is the expectation from the public that FDA is somehow the gatekeeper, and I think the goal really should be the most trusted body. The problem is that FDA is a little bit, I think, behind pharmaceutical companies in terms of being reactive, in terms of organization, and they should try to catch up on this communication tool and be more reactive.

MR. McNAIR: I think that FDA inasmuch as it sees everything has a special and perhaps a unique role in identifying new safety signals, particularly

with the co-morbid illness and polypharmacy. It is unlikely that individual companies of any sort would pick up on new signals in the way that FDA is particularly well positioned to do.

Secondarily, I believe that there are some special or unique insights within divisions of CDER and notably, but not exclusively, the Oncology Division has done a rather good job in looking at the risk-benefit ratio as it relates to the desire on some patients' part to extend their life versus preserve life, however long it might be, with the desirable level of quality.

So the points that had been made by several of the speakers, I think, have very insightful and good exponents within FDA and particularly Oncology Division is notable in that respect.

CHAIRMAN SELIGMAN: Thank you.

Other members of the panel? Questions? Yes, Dr. Trontell.

DR. TRONTELL: I'd just like to follow on to your responses to Dr. Seligman's question. I think we all agree that cooperation and collective use of our resources is important.

Can I press you, if possible, to be a little more specific? Because I've heard actually

several different and potentially large responsibilities for the agency coordinating all of risk communication, being the definitive scientific source, work with the professional societies.

The risk in a partnership with roles and responsibilities aren't clearly defined is you may have some inefficiencies of duplication or worse, as we've heard, people may be too much information or potentially conflicting information.

Can I just ask you to quickly expand, if you can, on more specifics of what FDA might actually do?

MR. WOLLEBEN: Well, I was specifically referring to the development of tools. I think that if there is the right partnership on the development of tools we will both get a benefit out of it and that the tools could be used basically by either piece of either the FDA or the same principles could be used by the pharmaceutical companies.

Now, there are obviously different roles in the execution of the tools. I mean, this gets back to you are the regulators and we are the regulatees; is that right? And we understand the difference between that .

But I think that in the development of the

tools, if there were perhaps a task force, we haven't talked about this with our PhRMA colleagues, but if there were perhaps a task force of experts from FDA and other PhRMA companies, there could be something there that would be very good.

DR. GOLDMAN: If I may, I always had this, and I always want to make the point that I feel it acutely now because I'm neither in PhRMA nor am I a regulator any longer. There's a lot of expertise outside of companies and the agency, and frankly, they're not being utilized enough. I'll be honest. ICH is strictly industry and the regulators, with no other input. I don't think that's as helpful as it might be in terms of that. Maybe it sounds self-serving as a consultant, but there's plenty of us out there who do this, and we do a lot of this, and we do it on both sides of it.

Secondly, and the point that you're making, is it is hard to tease out who's the clearing house for information as being pointed out. One of the things that I thought was being fostered by putting together a NEBASH (phonetic) program and things when I was at the agency in the '90s is that when you have a situation, let's say, where you have to notify, let's say, on a box warning or a

withdrawal, it is coordinated with the company. You do take a look at the material so that it is the same message being given.

I got that impression, for example, at the COX-2s. As I mentioned, the information that was given was very valuable information. It was not simply that something was coming off the market. It was why. What was the benefit-risk assessment on that? What was the royalty advisory committee? Why one product versus another?

I think that kind of thing done in partnership with the regulated industry is a model that you might utilize because the whole purpose of that is getting the best information out that can be utilized from by practitioners and by the public.

Concerning the media, I can't miss a chance to mention this, that I tend to agree that some of the information portrayed is always about the risk, but that's what people want to hear about in terms of that. It is very hard to put out a message about relative benefit-risk from a regulatory agency when they're not the ones who are -- as I say, promote the product, and that may not be their role in terms of that.

It is a hard balance to strike as to what

the benefit risk of the individual product is, and it does rest ultimately with the clinician and the patient making decisions based on that. So I'm not sure in relation to my PhRMA colleagues and what alan was saying and what John Wolleben was saying. This still is a differentiation between the FDA and the regulated industry as to that kind of role.

MR. GOLDHAMMER: I think though, Dr. Trontell, there's another thing that we can't lose sight of, and that's what in the patient's best interest, and FDA is part, I think of every stakeholder group that I had up on one of my slides, and all of those groups are working towards improved drug safety, drug benefit in some way or another.

And one of the things, SOS Rx, and I don't know if Rebecca Burkholder -- I was not here yesterday -- I don't know if she mentioned that, but one of --

CHAIRMAN SELIGMAN: Yes, she did.

MR. GOLDHAMMER: You know, something as simple as a personal medication record. You know, not rocket science, and yet we've spent a lot of time. I went back to PhRMA and I said, "Look. We've got this patient prescription assistance program. We've enrolled over a million people. Why couldn't we send out a patient medication record, template or form when

the contact goes out?"

Because these are largely elderly, indigent people who probably aren't even keeping records of this kind and yet we know from what happened in Louisiana because of the hurricanes, when people are displaced, they go into the tent, see the doctor. What medicines are you on? Well, I don't know. Pink pill, red pill. Sometime simple.

But if we can maybe coalesce as part of a larger stakeholder and I guess, you know, I agree with Steve. You know, it's not just PhRMA. It's not just FDA. There are lots of good people out there that could also contribute to this, but to identify what do the patients need out of this, and then I think we'll do the right thing.

CHAIRMAN SELIGMAN: Dr. Ostrove.

DR. OSTROVE: Maybe it's because the breadth of this issue is so wide that, you know, the thoughts in my head kind of keep bouncing around from place to place, or it may just be that it's kind of empty in there, but nonetheless, there are two things that I heard from my perspective coming out of what you've been saying. One is the issue of communicating benefits, as well as risks. I heard that from, I think, three of you.

And the other is kind of an inconsistency, at least from what I was hearing, between what you were saying about whether you can take kind of a common template approach. I believe, Dr. Goldhammer, I heard that from you, or whether, you know, we're on the "well, everybody is unique" and one size doesn't fit all and you can't take a cookie cutter approach.

In both of those instances, you know, one of my questions is for you to consider and perhaps you can talk about it more now and, if not, please consider in terms of comments to the docket. Where are the data? What are the data? Where's the research, the kind that backs up these different perspectives?

If we need to communicate benefits, do we know how to do that in a way that you'll get that dreaded word "balance," in these kinds of documents. That's one thing.

And secondly, in terms of the, you know, one size fits all or not, as the case may be, Dr. Goldman, you talked about you like a question and answer approach. I like a question and answer approach, too, but I haven't been able to find a whole lot of data that really supports that.

You know, as we're fond of telling people,

FDA is a science directed, science focused agency. Getting people internally to also kind of come together on something, it helps a lot to have the data behind that.

Now, I know that there's data out there about risk perception, and I know that there's data about risk communication in general, but that's in general. To the extent that you can offer, you know, kind of recommendations for us that are based on research in this particular area -- and I heard you saying we need to evaluate -- the industry is out there communicating. What kind of information can they give back to use -- I know Pfizer is doing some of this -- you know, that they can make public in terms of how consumers perceive your clear health communication stuff, the new brief summary, for instance that you're using, you know, as what I would perceive to be, I guess, kind of a cookie cutter approach?

You know, all of that -- I realize I've given you a very large things to respond to -- but I think that that's kind of what certainly I'm looking for and I would find very helpful.

MR. WOLLEBEN: My comment about the cookie cutter really had to do not with the fact about all

communications, but there's really levels of communications that are required in different circumstances and that, you know, a press release, for example, isn't the right thing to use in all circumstances. That's what I was referring to about one size does not fit all.

We'd be happy to work with you on exchanging information that we might have on the effectiveness of these communications. I suspect that the information that Pfizer has right now doesn't directly address what FDA is trying to do, but perhaps the people that we have that have worked on what we have been trying to do have expertise in the area that could help you identify how the data can be obtained to accomplish what you're trying to do.

And this gets back to my suggestion that the collaboration on some type of a task force or something like that.

You know, the Pfizer programs are not really designed to do what you're trying to do. We're trying to get people to understand what our drugs do and get them to see physicians, which is very different, a little bit different than what seems to be your objective right now.

MR. McNAIR: And likewise, Cerner would

be delighted to work with the agency related to the observational data for any number of the pharmaceutical products that are out there. The current visibility of the material that I had discussed earlier this morning is with a subset of PhRMA sponsors, but not yet with FDA.

DR. GOLDMAN: I was the one who talked about the cookie cutter approach and also about one site fits all. So let me further explain what I mean.

I have not seen, frankly, a stratification as I've done of the different types of risks. They are not the same, and we do have data from other countries, other examples that I gave in terms of that. You've got a new program, for example, with Isorette and Owen (phonetic) in the United States. It's a different program than you would use for a different type of risk. You know, preventing the results of teratogenicity is not the same as getting people to draw LFTs before they start somewhere on a product. They're completely different behaviors.

So there is material; there is information we have on that. The cookie cutter approach I was also referring to is I don't believe in a concept that benefit-risk could be fed into a magic formula and then you can spit out at the end whether a product

stays on the market or it doesn't.

There were products that stay on the market with significant risks because society has determined along with the medical community, the consumer community, and the agencies that that product stays on the market because the benefit outweighs its risks. There are parts that have come off the market for adverse events that may not even be as serious in some cases because there were other available alternatives for that treatment. There other things that people had in terms of that.

That's the aspect that I'm talking about in terms of benefit-risk. That's why we don't use ratio anymore. It's a benefit-risk profile, a benefit-risk balance because you cannot quantify to the extent that has been suggested over the years because each case is different, and that's the reference I was making in terms of that.

And, again, that's getting back to what Alan was saying and what John was saying, is the products are unique. You know, even drugs within the same drug class can be unique, as we've seen. So that I think we need to get away from that idea, and we talk about personalizing. As we're mentioning, if we know which techniques work and which circumstances, we

can better tailor our methods of communication based on the particular risk that is presented by the particular product that we're looking at.

MR. GOLDHAMMER: Yeah, and just to amplify on that, and, I think, address your other question, I think I was the one that may have talked about templates, whether that was the right term I used or I may have used another word in my presentation; I think I was focusing that as if there is a standard format, the format ought to be consistent whether it's oriented toward the patient or the physician because, you know, patients may be physicians and physicians may be patients or physicians are probably always going to be patients at some point in time, so that they know where to look. Where's the information?

It's not unlike what the agency went through when they were working on redesigning the drug label, the content and format of the drug label, which I think we hope will come out soon. I know I've got my fingers crossed as well.

That's part of it. I think the second one related to research needs. When we talked to CERTs, we said, yes, we would make some funds available to do some research. We're still committed to doing that.

There's -- and I say this with a great

deal of trepidation and with the caveat this is not a PhRMA position; may be, but it's not right now -- we're going to be sitting down to talk about what the PDUFA program should look like as we reauthorize it. We heard at the public hearing about four weeks ago a lot of people talking about drug safety. Drug safety needs to be part of PDUFA.

Well, part of that is risk-benefit communication. Maybe there's some things that we can build into a PDUFA program. It's not a PhRMA position right now, but maybe there are some things that we can talk about when we have those discussions next year because we understand agency resources are constrained with you. They're also constrained with us. We're not an inexhaustible font of resources to do everything, but I think collectively maybe there's some things that we can do that will benefit this whole area.

MR. WOLLEBEN: Can I just follow on? We've been thinking about this, and when we were thinking about this particular meeting, one of the thoughts that went through our head was that in the last reauthorization of PDUFA the concepts of risk management were imbedded in the program, and to some extent we have not fully obtained the benefits of what

we have put into that last reauthorization, and quite frankly, what we're talking about here is an element of risk management.

And it may very well be that something along the lines of PDUFA is a way to move this ahead where we could collectively understand what it is we want to do and have common goals and seek those goals.

I really do see this as an extension of the concepts of risk management which we have not really fully capitalized on.

Basically it comes down to transparency. What we're trying to do is get transparency in the medical community about what our risks are, what our benefits are, what our problems, what our unknowns are so that people can make those decisions in the face of unknown information in some cases.

CHAIRMAN SELIGMAN: We'll go a little bit over. I wanted to give the other panelists an opportunity to ask their questions. Terry.

MS. TOIGO: Nancy covered my questions, but, Dr. Goldhammer, I'd like you to comment on the patient medication profiles, sending it out to your patient assistants program people.

The Office of Women's Health about four or five years ago started the Take Time to Care campaign,

and their first campaign was working with partners to develop the patient medication profile that was extensively used. There was a partnership with the chain drug stores.

So before you embark on that, you can learn from our experiences, and I'd be glad to share those with you.

I think the forms also got sent out with tax returns. So there was a very wide campaign, and they put a lot of time into focus testing it and developing the information.

CHAIRMAN SELIGMAN: Thank you.

DR. CUMMINS: I just wanted to hear from each of you. We've heard a lot of comments about areas where we might improve what we're doing in terms of risk communication, and I'd like to hear from each of you how you might prioritize the work and what might be our first -- what we should tackle first, second, third.

CHAIRMAN SELIGMAN: We can start with first actually.

MR. GOLDHAMMER: I think the first thing to do is you really need to revamp the Internet site. I mean, there's a wealth of information up there, but when I was preparing my talk and I was going back and

forth between, you know, typing and looking at the Internet site, it is terribly frustrating, and I think probably it -- and I know that the people who manage your Web, they can count hits and they can also see how long people are on, and this gets back to some of the data that we've generated, and I know GSK with their drug registry that they've generated, too. People don't stay on these sites for a long period of time.

And the information needs to be crisp. It needs to be understandable, but it needs to be in a format that they're going to stay there. If they get frustrated, they're going off to Amazon to buy books, and they're not looking, you know, to find out about the medication they're on.

CHAIRMAN SELIGMAN: Others that wish to comment?

MR. WOLLEBEN: Yes. Following the concept that Dr. Ostrove mentioned, this is a big thing. I mean, there's a lot in here. I would like to offer a suggestion that the first thing that should be done is to break this big thing down into the pieces of what is it that you're really trying to do. All right?

And then once you have those pieces, then identify how you can move each of those buckets

because it is so bad that to try to approach the whole thing as one problem, which it isn't, it's many different problems. You're never going to be able to do it, and of course, when you break it down into a subset of problems, then you have to figure out, you know, which are the priority components that you're trying to go after because the solutions may be different for different subsets.

MR. BENNATTIA: I favor with what John said. I think the Web site is important, especially what you do on the Web site, but I think you guys really need to step back a little bit and define what do you want to achieve in terms of risk communication. What are your goals and objectives? What does risk communication mean really for FDA? What's your role?

And starting from that, really work with professional agencies, with other partners, maybe PhRMA companies to define, to have your own risk communication strategies and risk communication plan. There you will have the priorities that will come in that plan.

But if you don't define your goals and objectives in risk communication, it will be difficult. You might rush on the Web and all the other things, and you have to step back. It might

take time, but you have to step back and look at what do you want to achieve.

CHAIRMAN SELIGMAN: Dr. Trontell had one more question.

DR. GOLDMAN: Did you want responses from us?

CHAIRMAN SELIGMAN: Sure. If you have something unique to say that hasn't been said, sure.

DR. GOLDMAN: Yeah. You have to improve the relationship with the health professional organizations because they're the end users, and if you want a -- as Dr. Ostrove points out, I fully believe in the Qs and As. I think there is data. I'd like more data.

Nancy, you did focus groups for the labeling. That was very helpful in terms of the formatting. Ask docs, pharmacists, nurses, dentists what they want to see because they're the ones who are using the material just as consumers are, and they've got to be in the mix.

And unfortunately they're often not to the extent that would be most desirable.

CHAIRMAN SELIGMAN: thank you.

DR. TRONTELL: Several of you talked about the importance of communicating not only risks, but

benefits, and I wanted to ask particularly those of you with industry experience or consulting for industry can you tell us what we can learn from industry's experience in communicating benefits, and how might we learn it, you know, in terms of what's publicly available or published so that some of those principles could be extended to risk communication in the overall communication of how to use drugs appropriately.

MR. GOLDHAMMER: The rule of thumb by people that have experience in public affairs is that when you frighten people, you need to extend then ten times the level of effort to get them back so that they're comfortable with whatever you've frightened them about, and I think that that's kind of key here, and there are numerous examples.

We did a workshop with one of the divisions last week on developing new approaches to treatment of menopause symptoms, and everybody knows the story of the Women's Health Initiative. Big things in the paper, lots of people getting off therapy because they were frightened about what the consequences were.

We never had much follow-up at all about some of the other things that were in that study, if

anything, and what's happening now is that you've got a lot of women that are going and getting bone density scans because they're been off therapy, and their bone density scans are coming back very, very poor.

One example I alluded to that in my comment, and that's one of the real difficulties here, and I know that's beyond your control because that was somebody else publishing a study beyond the FDA's. But you need to look at that when you're examining risks and you've got to look at the issue that I think a lot of us had mentioned, is that therapy is -- the responses in virtually every case are individual responses.

Drug label looks at group responses, and that's as it should. The doctors, however, are treating individual patients, and that's very hard to communicate, but it's a step that needs to be done.

CHAIRMAN SELIGMAN: Go ahead.

MR. BENNATTIA: I think talking about risk and even benefits we should think about perception and the perceived risks and benefits, and there's a lot of work outside, I mean, that had been done on perception and on risk communication outside of the drug area, and people have even defined what they called the fear factors.

I'm going to give a couple of examples. I mean, we accept more risk from a product that we know, and there are products that are still on the market that are, in my opinion, quite dangerous that are widely used because we've known them for decades.

If you take the new drugs, the new therapies for migraines, I mean, most of the people who just have a headache from time to time will not accept to take the risk of taking a new drug because of some of the side effects. If people really have a real migraine and just one that are just two or three days, they will accept to take this product even with a safety profile. That's why I mean risk communication is in my opinion just a part of risk management.

I mean, regulators and PhRMA companies do risk management at the level of population. The physician does it at the level of one patient, and the patient has also to do his own risk management while taking drugs.

So, I mean, there is a lot of work out there. There is not that much in the risk communication or in the medical area and drugs, but outside of this area, there's a lot of work that has been done talking about the benefits and risk, and you

could see the nuclear program for energy and how it has been successful in some areas in Europe and was completely done in the U.S. after the Three Mile Island crisis.

So there are areas and a lot of people have been working in this area for a while and they could give you some names or references later on.

CHAIRMAN SELIGMAN: thank you. Dr. Goldman, make this the last comment. Okay?

DR. GOLDMAN: Okay. Very briefly I was going to say that's what we tried with the announcement on the heparinoids, the low molecular weight heparins. We didn't want people not to use them. We wanted people to know how to use them more safely, and I think that's the point that we're getting at.

The second aspect, anyone who has ever treated Stevens Johnson Syndrome, I've treated one in my career. I never wanted to see it again, and one of the problems you run into is with some of the adverse events you know that there's a problem. You could recognize it.

I still would advocate for a clinical teacher how to recognize and how to treat adverse events because they do differ in terms of

irreversibility. That's also an aspect about treating about the benefit-risk balance.

CHAIRMAN SELIGMAN: thank you for your presentations as well as your response to our questions.

We'll reconvene in 15 minutes, at 10:40 for the next panel.

Thank you.

(Whereupon, the foregoing matter went off the record at 10:25 and went back on the record at 10:44 a.m.)

CHAIRMAN SELIGMAN: While you all are taking your seats, let me just announce one brief change in the agenda. At the request of members of the listening audience, I'm going to take probably about ten to 15 minutes at the end of the session designated as expert panel questions and open up the microphones on the floor for anyone who wishes to make a statement for the record.

I know that some of you sat here patiently now for two days, and I do want to afford the opportunity for individuals who may not be able to stay for this afternoon to say something this morning. If it turns out you are going to stay this afternoon, we will also have some time as well in the afternoon

for remarks as well, but, as I said, at the end of our questioning probably around noon, I will open up the microphones for that purpose.

Let's then turn to the next panel. Welcome to all of you, and ask Janice Dunsavage from the Institute for Safe Medication Practices to come forward.

MS. DUNSAVAGE: Thank you.

My name is Janice Dunsavage. I am actually a practicing pharmacist and Director of Pharmacy in a multi-hospital system in Pennsylvania. I also sit on the Board of Trustees for the Institute for Safe Medication Practices, which is an all voluntary board, and I'm here today representing ISMP.

ISMP is the nation's only nonprofit organization devoted entirely to medication error prevention and safe medication use. We are known and respected worldwide as the premier resource for impartial, timely and accurate medication safety information.

The institute represents more than 30 years of experience in helping practitioners keep patients safe, and our efforts have been built on a nonpunitive approach and a systems based solutions. We have a direct connection and a trusted relationship

with front line practitioners of all denominations, which sets us apart from other patient safety organizations.

One cornerstone of ISMP's efforts is a continuous voluntary and confidential practitioner error reporting program looking at errors that occur across the country, understanding their causes and sharing lessons learned with the entire health care community.

The National Medication Errors Reporting Program operated by the United States Pharmacopeia in conjunction with ISMP receives error reports from health care professionals, and ISMP independently reviews these errors and submits all information to the pharmaceutical companies that were involved and the FDA.

Our other programs include a number of newsletters. We have an acute care and ambulatory, a nursing and a consumer newsletter, and we also have 16 columns in professional journals and other newsletters.

Overall we estimate that our articles reach about 3.5 million readers.

We'd be happy to include selected FDA drug safety alerts in any of our various information

formats.

To accomplish ISMP's ambitious mission of understanding and preventing medication errors, ISMP continuously collaborates with legislative, regulatory, and accrediting agencies, as well as health care institutions, health care practitioners, as well as employer and insurer groups, and the pharmaceutical industry.

In regard to risk management, ISMP believes that medication safety needs to become not just a priority in health care, but an entrenched value associated with every health care priority and linked to every activity. It needs to become an enduring constant that is never compromised.

Although much has been done since the last IOM report, more is needed, especially with the FDA, to have a more prominent and accountable role. ISMP applauds the FDA and the stated goal of seeking stakeholders for collaboration and implementation of additional risk communication tools and encourages the agency to work more closely with organizations such as ISMP to raise awareness among practitioners and the general public about medication errors and adverse drug events.

The institute already collaborates with

the FDA by being a MedWatch partner and regularly providing information to the FDA that we get the right error reporting programs.

We are also about to embark upon an educational campaign with the FDA to eliminate the use of error prone medical abbreviations and dose designations, but more can be done. ISMP is uniquely positioned to provide the FDA with a forum for reaching health care professionals with risk management information.

For instance, the FDA currently produces only one regular column on safety in drug topics what targets pharmacists. In the past the FDA has provided a regular feature article in ISMP's acute care newsletter, and we invite the agency to do so again.

The biweekly ISMP acute care newsletter is the nation's only publication reaching almost every U.S. hospital with vital and potentially life saving information. A lot of this is because the buying groups actually purchase this newsletter for the hospitals, and currently it estimates that it reaches about 600,000 health care professionals from a wide variety of disciplines.

In my own organization we make the newsletter fully available to all of our staff,

including physicians, nurses, pharmacists, et cetera. And interestingly, from the pharmacy staff, I can tell you that on an ongoing basis, as front line practitioners are practicing, they almost always have the FDA Web site up and the ISMP Web site up, looking at information as their day goes on.

ISMP could also assist the agency in posting more current information about medication errors in the CDER section of the FDA Web site. Only a limited list of articles that's currently offered and could be expanded considerably.

The institute already does something similar with the FDA Center for Devices and Radiologic Health. Each month the FDA provides Web videos based on information published in the ISMP Med Safety Alert Newsletter. We'd be happy to have a similar arrangement with CDER where copies of the ISMP drug safety articles or links to our articles can be posted on this site.

The ISMP could also post more FDA generated information on the ISMP Web site. We currently offer a link to the FDA patient safety videos, and we have a section for FDA safety, medication safety alerts. Additional FDA resources and tools could be added as well. The ISMP Web site

is where I became familiar with personally with the FDA safety videos and since then we have used them extensively in our organization to educate and train our staff.

Another way that ISMP and FDA could work together to improve risk management is by raising greater awareness of the reporting methods, including promoting air reporting to the USP ISMP medication error reporting program in addition to MedWatch.

There's precedent for this suggestion. Different models of risk management are being developed in other countries where regulatory authorities depend on and promote other reporting programs. For instance, in Canada and Spain, ISMP's affiliate organizations have received funding from the National Health Ministries to carry out these functions.

We'd like to thank the FDA for the opportunity to provide input on the management communication and how ISMP could further partner with the agency to raise awareness of medication errors and prevention strategies.

CHAIRMAN SELIGMAN: Thank you for your comments.

Our next speaker is Dr. Joe Cranston from

the American Medical Association.

DR. CRANSTON: Good morning. My name is Joseph Cranston. I'm a pharmacologist by training. I currently serve as the director of science research and technology at the American Medical Association, and I'm speaking on behalf of the AMA at this Part 15 hearing.

The focus of my comments today will be on the communication of drug safety information that is risk communication to physicians. The AMA shares a common goal with the FDA and other stakeholders that there's a need to optimize this balance of drug therapy.

In approving the safe use of prescription drug products after they are marketed is a primary means to achieve this goal.

In June 2005, the AMA's house of delegates, which is our policy making body adopted the recommendations of our Council on Scientific Affairs report entitled "Enhanced Physician Access to Food and Drug Administration Data" that addresses post marketing drug safety issues, key recommendations from that report are s follows. One, the FDA should issue a final rule as soon as possible, implementing modifications to the format and content of

professional labeling that is the package insert with the goal of making the information more useful and more user friendly to physicians.

Two, the FDA should collaborate with physician organizations to develop better risk communication vehicles and approaches.

Three, the FDA should apply new tools to gather data after drugs are approved for marketing, including broader use of targeted post approval studies, institution of active and sentinel event surveillance, and data mining of available drug utilization databases.

And, fourth, there must be adequate funding of FDA to implement improved post marketing prescription drug surveillance process.

For the remainder of today's presentation, I will discuss the AMA's views on improving risk communication about marketing prescription drugs to physicians. Most of what I will say is a reaffirmation of previous comments that the AMA has provided on risk communication to the FDA, the Senate Committee on Health Education, Labor and Pensions, and the Institute of Medicine's Committee on the Assessment of the United States Drug Safety System.

However, I will also comment on some of

the risk communication tools that are of particular interest to the FDA as listed in the Federal Register notice announcing this meeting.

While technically outside of the scope of today's hearing, the FDA approved professional labeling, or the package insert, must be discussed because this is the primary mechanism by which physicians obtain safety information about a prescription drug product.

The AMA strongly agrees with the FDA that the package insert updated from time to time to incorporate information from post marketing surveillance should be the routine risk minimization plan for the fast majority of drug and biologic products.

The information provided in the package insert, along with other information about the products, such as published clinical trials, should remain the standard method of providing benefit and risk information to physicians about the use of a drug for biological products.

However, as previously communicated to the FDA, the AMA believes that the current package insert for prescription drugs is a barrier to effective risk communication. As one of the results of our nation's

medical liability crisis, the package insert has become a complex legal document to protect the manufacturer rather than a useful resource for busy practicing physicians.

In December 2000, the FDA issued a proposed rule to modify the format and content of the package insert, with the goal of making the information more useful and user friendly for physicians. The AMA has supported this effort, especially the proposed highlights of prescribing information.

The AMA urges the FDA to issue a final rule implementing these changes to the package insert as soon as possible.

Furthermore, there is need for a readily available electronic database of the most up to date prescription drug labeling of all products in lieu of the hard copy PDR that is both cumbersome and dated for certain products.

In that regard, the AMA commends the FDA for its recent announcement that it will now require manufacturers to submit drug product labels electronically, and that it will create an electronic data base of today's package inserts for all drug products.

As post marketing surveillance uncovers important new safety information about a prescription drug or biological product, there must be effective mechanisms to insure that physicians are aware of this new safety information.

This is especially important when a new and serious adverse event can be prevented or minimized by modifications and prescribing behavior. Under these circumstances, physicians need to be more than just aware of the problem. They need to put this new safety information into action and prescribe the drug appropriately to prevent the adverse event from occurring.

There is evidence that traditional "Dear Doctor" letters have been relatively ineffective as a means to communicate new risk information about marketed drugs to physicians. Thus, more innovative and effective approaches to inform and educate physicians about risk need to be developed.

In its Federal Register notice for this meeting, the FDA requests feedback on various risk communication tools that the agency has developed. I think it is fair to say that FDA talk papers, public health advisories, press releases, MedWatch listserve safety updates, and patient safety news videos are all

methods that can provide important, timely, and accurate information about new risks of drug products.

However, one must either proactively seek out this information by routinely accessing the FDA's Web site or by participating in various CDER listserves that E-mail all types of new information, including non-urgent information to users on a frequent, that is, almost daily, basis.

While we do not have objective data, the AMA believes that most busy practicing physicians will lack the time to actively seek out new drug safety information from the FDA's multiple sources. What is required are innovative mechanisms to both filter, that is, prioritize, the FDA's valuable information and more effectively deliver it to physicians so they'll be aware of it and act accordingly.

The AMA believes that the FDA, the pharmaceutical industry, and physician organizations, and I want to emphasize especially medical specialty societies, none of which have spoken at this meeting today, must collaborate and identify innovative ways to communicate new risk information about drugs and biologic products to physicians so that they will be aware of it, remember it, and act on it in prescribing drug.

In prior comments to the agency, the AMA presented a number of potential ways to accomplish this goal. Many of these options could be implemented immediately, and they are as follows.

One, the FDA, the pharmaceutical industry and physician organizations should undertake a major CME initiative on risk communication. Physicians need to be aware of labor and changes that identify serious adverse events, and that in some cases these serious adverse events can be minimized by modifications in prescribing.

The AMA's recommendations that the FDA publish its final rule on the package insert and create a computerized database of up to date package inserts as discussed earlier should be implemented as part of this education initiative.

Two, the FDA in collaboration with physician organizations should work with major medical journals and medical society and specialty society Web site editors to identify standard places for the dissemination of important new risk information about drugs and biological products for the particular physician population.

Three, "Dear Doctor" letters should be disseminated by mechanisms in addition to hard copy

mail. Alternative mechanisms could include publication in medical journals, placement on medical society Web sites, transmission to individual physicians by Blast Fact, Blast E-mail, and direct downloads to PDAs.

Unlike letters, electronic transmission is inexpensive, timely, and repeatable. Thus, important risk information can be reinforced by more than one transmission.

Fourth, the content and format of "Dear Doctor" letters should be changed to emphasize the need for action by the prescribing physician. For example, the "Dear Doctor" could contain a bold faced opening paragraph that emphasizes the possible severe outcome to patients from a new adverse event; that the adverse event is probably preventable if the drug is used appropriately, and what necessary steps the physician must take to prescribe the drug appropriately.

Fifth, pharmaceutical companies under appropriate FDA oversight should be obligated to train and send their sales forces to physicians to educate them on important new risk information about company products. The company should provide incentives to sales representatives to do this because the highest

priority of any pharmaceutical company should be to prevent harm to patients who use their products.

The effectiveness of the 90,000 pharmaceutical sales representatives in the United States in promoting the benefits of their company's products is well documented, and they should have similar success in educating physicians about important new safety problems associated with their product.

Sixth, and this one may not be implementable immediately, but it's very important. New information technology, such as electronic prescribing, offer enormous opportunities to communicate important risk information about drug and biological products. The prescribing systems with well designed decision support programs potentially could communicate important new risk information to physicians at the point of prescribing. That is the time when the information is most needed.

As these new information technologies have become integrated into physician practice, the FDA, the pharmaceutical industry, and physician organization should work with database providers and software vendors to incorporate the appropriate risk information into these electronic systems.

Again, the AMA encourages the FDA and the pharmaceutical industry to work with physician organizations to optimize physician education about the risk of drug and biological products through identification and implementation of effective methods of risk communication.

Finally, I would like to comment on the FDA's proposed health care information sheets as a risk communication tool. As previously stated in our August 2005 letter to FDA on its Drug Watch draft guidance, the AMA does not support the development of health care professional information sheets because it will result in redundant and perhaps confusing information for physicians who rely primarily on the package insert.

Instead the AMA recommends that the FDA invest its resources into developing a high quality Drug Watch Web page for emerging drug safety information that would include the following information for a drug product that appears on the Web page.

One, the FDA alert describing the emerging safety concern;

Two, a brief summary of the available evidence that warranted inclusion of the drug product

on Drug Watch;

Three, advice but not mandates for physicians on potential changes for prescribing of the product when warranted;

Four, a disclaimer that this is preliminary information and no final regulatory action has been taken;

And, fifth, linkage only to the professional label, that is, the package insert.

As discussed earlier, the final rule for the revised package insert with a highlights prescribing information section should also be among the agency's highest priorities. We can give Drug Watch citation with the information I just listed above to the package insert. It will be more useful and more user friendly to physicians as opposed to creating a whole new database of health professional information sheets.

This concludes my formal presentation. I'd be happy to answer any questions.

CHAIRMAN SELIGMAN: Thank you, Dr. Cranston.

Our next speaker is Susan Winckler from the American Pharmacist Association.

MS. WINCKLER: Good morning. Thank you

for the opportunity to present the views of the American Pharmacist Association.

As background, APA represents 53,000 pharmacists in all practice settings, whether that would be the community hospital, long-term care, Hospice, wherever those pharmacists might practice.

Insuring the public's health and safety, especially with respect to medication use, is the pharmacist's and APHA's highest priority.

At this meeting, the panel is charged with examining Food and Drug Administration's current risk communication strategies for human drugs. The safety of prescription and over-the-counter drugs is obviously of vital importance to pharmacists as we are committed to helping patients manage the risks and optimize their medication use. We appreciate the opportunity to appear this morning and provide the pharmacist's perspective on the agency's risk communication tools.

My comments will focus on two of the questions posed in the announcement of this meeting, Questions 2 and 4. I will focus on pharmacists' awareness, use, and perception of current risk communication tools and the accessibility and usability of safety information on the FDA Web site.

Let me first express our support for the agency's efforts. We appreciate the agency's commitment to improved drug safety through the implementation of communication strategies to inform pharmacists, other health care providers, and consumers of potential safety concerns with medications. Providing accurate and up-to-date information is critical to pharmacists' ability to work with prescribers and patients to insure the selection of the most appropriate and safest medication therapy to be in a patient-specific health care needs.

Before I move to talking specifically about the communication tools, I also want to comment a bit about this safety discussion that has been occurring over the last two days. As we talk about the risks and safe use of medications, it's very clear to understand there's unintended side effects, adverse events, and other things that we want to protect against.

We should also remember that it is a safety issue when medications that should be used in a certain population are not being used in that population for whatever reason, but particularly if they're not being used in that population because of

an overemphasis or an inappropriate emphasis on the risk communication for that patient. So we must always keep in mind that we have to share information that's very important to share, risk information, but keeping in mind also that the medication will not yield benefit for anyone if there aren't any patients using it appropriately.

My first comments will touch on the risk communication tools that are available. The announcement for this meeting identified the nine types of tools currently used by the agency to communicate risk information, and they're listed on the slide here.

There are also a number of additional risk communication tools, which although they're outside the scope of this hearing, they are valuable to health care professionals in understanding medications and knowing more about the risk. Those include product labeling, patient package inserts, medication guides, consumer medication information, "Dear Health Care Professional" letters, and the agency's Drug Watch Web site.

This is a long and impressive list, but having so many different tools to communicate drug risk information can be problematic. The increasing

number of tools may lead to a situation where the quantity of communication vehicles diminishes the quality and usefulness of those tools.

By my count there are at least 15 different communication vehicles for the agency to choose from, a significant number. While we understand the need for multiple communication vehicles, for example, simply changing the labeling is not a very time effective way to get information to health care professionals or patients. We have to question whether the vast number of communication tools is necessary. It may be a situation where, frankly, we have too much of a good thing.

With so many communication vehicles for the agency to choose from, it's increasingly difficult for health care providers and consumers to determine where to find appropriate information. For example, should a pharmacist look for a public health advisory, a talk paper or a press release to find the latest safety information on a medication?

Because the FDA can choose to release new risk information in any of these formats, it's challenging for pharmacists to identify the appropriate tool that may contain this information. If a pharmacist regularly reviews FDA press releases

or monitors the agency Web site for public health advisories, they may miss important safety information if it was released as a talk paper instead.

The situation is further complicated by the apparent lack of uniformity or lack of system for selecting what communication vehicle to use in certain situations. There are numerous tools to select from, but it is unclear how the agency decides what tool to use when communicating new risk information.

Is the agency's decision to communicate information in one vehicle indicative of the seriousness or level of potential risk posed by a medication or is the vehicle selected based on the type of information being presented.

We conducted a quick review of several of the tools used by the agency and found examples of the agencies selecting different tools to communicate information that seemed to be quite similar. For example, the FDA recently issued a press release to announce updated labeling for the contraceptive patch to alert providers and patients to potential risks associated with exposure to higher levels of estrogen.

About the same time, the agency used a public health advisory to announce forthcoming

labeling updates for long acting bronchodilators to alert providers of the potential for an increased chance of a severe asthma episode.

In both cases the FDA was communicating a potential for increased risk associated with the use of these medications, but the agency chose to communicate that information using two different risk communication tools.

Our review also found that some of the communication vehicles are used by the agency for for a wide variety of purposes. A press release, for example, is used for purposes ranging from announcing updated labeling for the contraceptive patch and problems with glucose meters to announcing new agency staff appointments, reports on agency activities, and general agency news.

While all of this information is important, using one type of communication vehicle to communicate a wide variety of information may have the unintended effect of diluting the safety information. Simply put, the number of communication vehicles and the lack of a uniform system to communicate risk information is confusing to providers. There are too many communication tools for pharmacists, other health care providers and consumers to track. Many are also

unaware of all of the different tools used by the agency, do not understand the difference between them, and as I'll discuss later, are unaware of where to find this information.

All of these factors can be significant barriers to widespread use of the communication tools and the important risk information that they contain.

The second area I will address is the accessibility and usability of the agency's Internet based sources of drug information. This is an important area for examination as the majority of the risk communication vehicles under discussion today are Internet based communications distributed through the agency's Web site.

Because the tools are primarily Internet based, it adds a new dynamic to the question of providers' and consumers' awareness and use of risk communication information. Pharmacists and others seeking FDA drug safety information often actively search for the information on the FDA Web site or sign up for one of the agency's E-mail listserves. While the Web site and the listserves are both valuable methods of communication, they may not bee the most effective means of communication as currently designed.

Pharmacists who visit the FDA Web site seeking information are faced with one significant barrier. They must know where to find the information. Unfortunately, this may be easier said than done. I am personally a frequent user of the agency's Web site and consider myself to be fairly familiar with the information that's available.

When preparing for this presentation, however, I reflected on the reality that I have to admit having difficulty finding some information. I also searched for examples of the agency's risk communication tools that were mentioned in the announcement. For a few of the tools, I could not find examples on the Web site without using the links that were in the Federal Register announcement.

Part of the difficulty in locating risk communication information is the lack of one central depository for medication safety information on the Web site. Although the main CDER page contains a prominent drug safety section, it contains limited information. A link announcing the agency's initiative, a link to patient information sheets, and a link to general educational information for consumers.

While some of the patient information

sheets themselves have links to additional risk communication tools, it's not true for all of those sheets. Many of the communication vehicles are currently housed on different areas of the Web site, requiring providers and consumers to actively search for the information.

As the level of difficulty in finding the information increases, the less likely individuals are to search for this information. Therefore, usage will decrease.

The second option I mentioned, signing up for agency listserves, removes some of the need for pharmacists and others to actively search for information, but poses its own dilemmas. The listserve delivers information directly to the individual. However, there are challenges with listserves and information overload. In every pharmacy practice setting time is at a premium and the need for quick access to the news pharmacists need when we need it is vital.

Listserves are a good mechanism for communicating timely information to pharmacists, but they can lose some of their effectiveness if providers are inundated with them. In a single day within the last few weeks, I have received three E-mail

announcements from FDA on drug safety issues. Two were from the MedWatch listserve, one announcing labeling updates, the other with news of a suspension of manufacturing of specific product.

The third communication originated from the CDER new listserve and contained information on alerts, the MedWatch safety program, and multiple new drug approvals. While all of this information is valuable, the quantity and frequency of the E-mails can be overwhelming.

One way to address this is to also consider how practitioners may use such information in their practice site. Many health care professionals are not as connected to E-mail as those of us in the business and professional regulatory world are. They're not as connected to their blackberries as probably everyone else in this room is.

One suggestion for how to help with the volume of E-mail that we want to send to health care professionals is perhaps to collect that and send on a daily basis the information that the agency wishes to communicate, and then the provider knows each day what information has been sent from the agency in what format and for what purposes.

We've identified some challenges to the

widespread use of risk information distributed by the agency, the number of communications tools, the lack of a standard system for communicating risk information, and the level of difficulty for providers and to consumers to locate the information on the Web site.

But these barriers are not insurmountable. They may be overcome. A few simple changes could improve the quality of risk communications and increase providers' and consumers' use of this information.

The first step to improving risk communication tools should be a review of all existing tools. This review should go beyond what the agency is hoping to accomplish at this meeting. The review should focus on streamlining and consolidating risk communication tools with the intent of identifying those tools that may be eliminated. This could include tools that are similar in purpose, content, and distribution as other tools; could include communication vehicles that are used for a wide variety of purposes other than communicating risk information.

By identifying tools that duplicate one another or are inappropriate for communicating drug

safety information, the agency could reduce the total number of drug safety communication vehicles. Fewer vehicles will allow pharmacists and other providers to concentrate their focus on the remaining communication tools and reduce the potential for information overload.

The second principle is the need to address risk communication in a systems based approach. We recommend developing a standardized process to communicate risk information to health care providers and consumers. The process should include criteria to determine when drug safety information should be communicated, to whom it should be communicated, and how. What communication tool would be used?

This initiative would help avoid the situation we have today where tool selection at least appears to be somewhat random. A risk communication system would also help eliminate confusion among providers and increase providers' familiarity with the communication vehicles in use.

I'd also like to support the comments of Dr. Cranston about the need to change the format of some of these risk communication tools so that it's very clear to the provider what action is necessary

and what information they need to know.

Our third recommendation is to house all information in one central location on the agency's Web site. The current drug safety section on CDER's home page could serve as the central location if it is expanded to include all risk management communications.

Simply creating one central drug safety section, however, is not enough. The public must be aware of the location of this new drug safety information, and providers and consumers must be able to locate it easily.

We recommend that the agency place a prominent drug safety information link on the front page of the FDA's Web site.

Finally, we recommend that the agency work with APHA and other stakeholders to continue to explore ways to minimize the pharmacist's role in communicating risk information to consumers. Pharmacists are not only the medication experts on the health care team. They are also the last health care professional to interact with patients before they receive a medication and begin to use it.

This places pharmacists in the ideal position to work closely with patients and help them

make the best and safest use of those medications. Such efforts will help insure that valuable risk management information is communicated not only to pharmacists and prescribers, but also to the ultimate user, the patient.

Thank you.

CHAIRMAN SELIGMAN: Thank you for your comments.

Our final panelist, Tom Lawlor from the National Association of Chain Drug Stores, as well as Walgreen Retail Pharmacies.

MR. LAWLOR: Good morning. Members of the FDA, my name is Tom Lawlor. I am a registered pharmacist, and my current position is Director of Quality Assurance for the Walgreen Company.

I have been with Walgreens for 28 years and have had the opportunity to hold many different pharmacy positions throughout my career. Thank you very much and thanks to the National Association of Chain Drug Stores for the opportunity to address this hearing.

Today at Walgreens we operate over 5,000 pharmacies across the United States. We operate retail pharmacies in 45 states and in Puerto Rico, making us one of the nation's largest retail pharmacy

chains serving over four million customers and filling almost 1.5 million prescriptions every day.

I am here today to discuss the views of the chain pharmacy industry regarding the effectiveness of the FDA's current risk communications strategies for patients and health care professionals. Walgreens is one of the nation's top employers of pharmacists, and our pharmacists interact with millions of patients every day.

Pharmacists, as Susan just said, are a primary source of information, both oral and written, about prescription medications. Our role in assuring the appropriate use of medications will be increasing dramatically, given that Medicare will start covering prescription drugs for our seniors in jut a few short weeks.

This milestone will mean more prescription drug utilization and better health care compliance from millions more patients. We believe that the information patients receive about their medications, whether it is from Walgreens, the drug manufacturers, or the FDA, should be balanced in terms of presenting the risks as well as the benefits of prescription drugs.

Patients should not be unnecessarily

frightened about their prescription drugs lest they fail to comply with their medication regimen.

Alternatively, patients need to understand the risks associated with taking medication in such a way that they can make informed decisions about starting a drug or continuing on a drug once they have started. Obviously, information concerning risks could affect the patient's decision to even fill and use or continue to use any drug product.

We are proud of the patient information programs that we have at Walgreens. We are pharmacy driven company that is run by pharmacists and providing the highest quality pharmacy service for our customers is very important to us. Our pharmacists comply with a variety of state laws that require that an offer to counsel was extended to the patient, and we take seriously our responsibility to do so if the patient wants to be counseled.

In fact, our company policy is to extend an offer to counsel to every patient every time. Along with the offer of verbal counseling each patient receives a patient information leaflet, a patient education monograph, if you will, about each of their medications that meets the current FDA guidelines for the provision of useful prescription medicine

information.

These are commonly known in the industry and at the FDA as consumer medicine information, or CMI. We work with a large and respected international drug and patient drug information publisher, Walter Sclure Health (phonetic), who is our vendor that produces the content of our consumer medication leaflets.

Our pharmacists then print these monographs electronically in store and provide them with each prescription dispensed for the consumer to use at home as a reference or for the pharmacist to use in store as a support tool when counseling patients.

Walgreen pharmacists receive important updates on vital patient safety trends via E-mail communication from our corporate office through monitoring CDER's FDA MedWatch listings through local monthly peer review meetings on pharmacy practice, from the Clinical Services Department of our Walgreen Health Services Division, and finally through company sponsored pharmacy continuing education programs.

We try to address good pharmacy practice for all of our patients, and to that end, currently print our prescription label directions in 14

different languages, depending upon patient need and request.

Our patient information leaflet, our CMI, is currently available in both English and Spanish, again, based upon patient need and request.

Our pharmacists also distribute a mandatory medication guide to patients if the FDA requires that these be distributed with certain prescription drugs. As you know, the agency has recently required that these med. guides be distributed with all anti-depressant medications and all nonsteroidal anti-inflammatory drugs, or NSAIDs, which includes the Cox-2 inhibitors, the subject of two recent large market withdrawals.

These two very popular classes of drugs, antidepressants and NSAIDs for which millions of prescriptions are dispensed each year, account for over 500 separate and individual drug products.

We hope to have the FDA's approval shortly to be able to print these mandatory and beneficial medication guides electronically for our patients.

As an aside, we are concerned that there does not appear to be an FDA led effort to encourage the makers of the dozens of NSAID medications, including the COX-2s, both brand and generic

manufacturers, to use a universal medication guide that could be distributed through a single entity.

This type of program is critical to reduce duplicative efforts and help assure that pharmacists have these guides available in their pharmacies to distribute to patients, thus insuring compliance with the FDA and its approved patient information policies.

While I know that this hearing is not supposed to focus on mandatory medication guides or voluntarily provided consumer medication information, I think this background is necessary to help answer the questions posed today by FDA about the effectiveness of current risk management communication strategies and approaches to the same.

The fact that the agency is not considering these med. guides and CMI within the context of this hearing, frankly, is concerning. It suggests that the agency may lack a coordinated plan for the development and implementation of a risk communication strategy and may be unnecessarily and dangerously duplicating private sector efforts that provide consumer oriented and health professional information.

Everyone's goal in the practice of the profession of pharmacy is to help the patient and

improve their quality of life. However, we are concerned that the preponderance of paper that patients receive with their prescription medications from pharmacies, which is being driven by FDA guidance for CMI and mandates for medication guides, is not serving its intended purpose of risk-benefit communication because it is excessive.

We have been from consumer focus groups that this may be creating a situation where the patient will simply not know what to do with the paper information they are receiving, thus defeating the purpose of trying to inform and help the patient.

Similarly, if the amount of risk information being presented is such that its balances emphasize primarily the risks, without equal time for the benefit, which is the very reason the patient went to their doctor for help in the first place, patient compliance and, therefore, improved health, may not happen, and this then will lead to increased health care costs.

Are we forgetting that the scope of this entire communication effort is to help patients and caregivers management their health care and reduce overall costs.

You should know that to meet the current

action plan for the provision of useful prescription medicine information, simply referred to as the Keystone criteria, the pharmacist generally has to print two to three eight and a half by 11 inch sheets of paper to give to the patient.

If the patient is also receiving a mandatory medication guide with their prescription, each of which averages three pages in length, but which could be up to 12 pages long, that would mean at least five sheets of patient risk-benefit information dispensed with one prescription.

Admittedly this is all part of the effort to respond to public pressures to provide additional information on certain medications that have been associated with high profile risk incidences and which is all supposed to benefit patients and their health care management. Very little information exists in the literature regarding effectiveness of these types of risk benefit communication tools. We all may feel better that we are covering our bases, so to speak, by giving patients all this paper.

However, if it does little to reduce adverse events, or worse, if the volume of paper reduces compliance because patients do not read the information and, as stated earlier, they have told us

they do not, and because they don't read the voluminous paper, they don't know how to take their drugs appropriately or, conversely, they read the information and don't take the drug because they become frightened of the risks, we are defeating our intended purpose and sadly doing no good for patients at all.

The agency's decision to create their own patient information sheets is particularly concerning to us because these initiatives can duplicate private sector efforts. It is not clear why the agency would produce a patient information sheet for every drug when the private sector is already producing high quality, Keystone compliant information that balances the risk with the benefit of taking medications.

There is also no clear relationship between these PIS documents and the mandatory medication guides that are currently being distributed by pharmacies for antidepressants and shortly will be distributed for NSAIDs.

We are concerned that these PI sheets will emphasize risk information rather than create a balanced picture of how the patient should use the medicine in accordance with the prescriber's directions to improve whatever condition it is that

they went to their doctor for. FDA has stated that these PI sheets will include information from the Drug Watch Web site, and that includes recent emergent drug safety information.

Patients may not know how to distinguish between the emerging safety information as compared to the risk information that is well established. This may reduce compliance with medications of patients cannot adequately independently determine whether or if the emergent safety information might apply to their own medical situation.

The private sector has demonstrated a much better ability to update information in a more timely fashion than the FDA. We are concerned that the PIS leaflets will not be made current quick enough to reflect the latest contemporary knowledge about the drug.

Retail pharmacy also believes that these PI sheets should meet the current action plan for the provision of useful prescription medicine information, that is, FDA's PI sheets should be held to meeting the same Keystone criteria for patient information to which the private sector is held.

Patients that may go to the FDA Web site to obtain these PI sheets should have the benefit of

being provided with the same level and scope of risk and benefit information had they obtained the information sheet from their retail pharmacist. All of us today really do have to stop and remember what got us to this point, namely, that the patient chose to go to their doctor for a reason, and that the patient's doctor, based on education, overall knowledge of and acquaintance with the patient, the patient's condition, and the patient's medical history deemed that a prescription drug would help them. Again, benefit versus risk.

And then the doctor wrote that prescription for the benefit of their patient. Pharmacy and pharmacists need to further that relationship through counseling, education, providing answers and guidance to help and inform that patient.

Risk information, including side effects, adverse event scenarios, contraindications and precautions, are most assuredly vital to this process, but need to be communicated in their proper context, namely, in order to help, not intimidate patients.

Retail pharmacy believes that the agency should, as a long-term goal for risk management communication -- and I truly believe the right term is "risk management communication," not simply "risk

communication" -- seek to incorporate all information into a single communications document that is of sufficient length, content, context, and literacy level so that it will be read and conveys all of the information necessary for the patient, including any information required as part of the mandatory medication guide.

We all need to listen to what our patients are telling us will help them to better themselves health-wise. It surely will help us all if we do.

Thank you very much for this opportunity. We look forward to answering any questions you may have.

CHAIRMAN SELIGMAN: Thank you for you comments.

Let me start. I want to try to focus for a moment on communication with health professionals since we have the health professional side of the risk communication world represented at the table.

And we certainly clearly hear the message regarding the proliferation of tools, preponderance of paper, lack of plan for -- lots of P words -- but I guess I was interested particularly in your presentation, Dr. Cranston, and clearly took to heart the message about the need to streamline and

prioritize and make clear the avenues by which information is transmitted and communicated.

And in that vein I wanted to ask the panelists at large about the role for other means of communication beyond just the use of paper and whether there might be other means effectively communicating the benefits and risks of information that emerges about products once they are marketed, such as the use of professional conferences or what the pharmacists-physician interaction might be that might serve to either improve or leverage the information.

I know that the ISMP presentation in many ways sort of touches upon that, and that clearly is an organization that sort of reaches out to communicate using a variety of means.

And again, I just want to ask the panel to reflect whether there might be if, indeed, we are able to achieve the goal of simplifying the written materials that are available to health care providers, whether there should be an emphasis or focus on other means of effective communication of emerging information.

DR. CRANSTON: I guess in an ideal world, you know, everybody would have an electronic health record. We'd be doing all of the prescribing and the

message could be very succinct and get to the doctor or the pharmacist right there at the point of care.

We're not there. So that's obvious. I really believe that your first step irrespective of the labeling rule, which I still think is a high priority, but I really think your first step needs to -- and Dr. Goldman had it right on the last panel -- is to reengage the medical specialty societies with the agency.

About -- I don't know -- seven, eight years ago, the Office of Health Affairs was disbanded. I don't know whether it was that useful. Maybe you folks felt it wasn't and it cost too much to run, but at least you got them there, and I think, you know, most physicians belong to their medical specialty, and that's where they go to learn about, you know, practice guidelines or, you know, what the current educational stuff is. Those are the organizations that run meetings unlike the AMAs, which is primarily a business meeting, you know, not really scientific meetings.

And I think that, you know, it would be helpful if they could be included to include the industry as well because, you know, there may be dollars there that could help get this thing going,

but I do think that, you know, if you can engage the medical specialties and get them on board with their membership that this is important, and I think there are good examples out there with drugs like Cisapride and others that have come off the market that, you know, we could at least get the ball rolling. I mean, that's what I think really needs to happen.

We first made some of these suggestions in 2002. We subsequently made them in 2003, and I think in 2004 as well, and nothing has really happened, and so, you know, physicians need the information filtered to them, I think, to some extent, and it also has to be reinforced, and I know the idea of using the detailed folks is probably pretty controversial, but if you go back to the original work that Dave Warren and others, you know, they're really successful at promoting products and getting physicians to use them.

And counter-detailing has been the one method shown to counteract that, but we can't afford to do that in this case. So, you know, it requires a culture shift in the way the industry thinks and the way you may want to enforce things, but that might work, too.

MS. WINCKLER: If I may chime in here, too, I want to agree and say that, yes, there would be

a benefit in some type of interactive outreach. One of the things we've learned in helping pharmacists prepare for the Medicare drug benefit is you can put a whole lot of things on paper, but until the health care professionals have the ability and the opportunity to read that and react to it and then ask questions that are generated by it, you don't really get the penetration and the understanding.

So I think an interactive, whether that's appearing at professional meetings or Webcasts or some other opportunity for direct interaction between agency officials and practitioners would be very helpful.

And I'd suggest it would be helpful in two arenas. The first arena is just in communicating a baseline of how the FDA operates and comes up with these recommendations in an understanding of the risk communication tools and why they're used so that people understand when they get an announcement what that means, what it's based on. What's the process behind that?

And then second area would be when it's specific risk information about a product and helping to explain and better understand why we need a medication guide for NSAIDs.

Understanding the why will go a long way in making sure that that information actually gets from the box in the pharmacy where they're trying to keep track of all that paper to the patient because it's not only the cue that it prints out with the label or they have a reminder in their computer system.

It's a clinical understanding that, yes, there is this risk that we want to communicate, and we're going to use this specific vehicle. So both the structure side of the FDA and why things are being communicated in a certain way, as well as the specific information would be helpful.

MR. LAWLOR: I'll just add to both Joe and Susan's comments that a collaborative effort for communication in the beginning of the process would do a lot. You know, if you got pharmacy involved, if you got all of the health care providers involved up front so that neither organization has to try to undo something or react to something after it is all said and done would go a long way.

CHAIRMAN SELIGMAN: Any other comments, questions? Nancy.

DR. OSTROVE: I just have a couple of questions for Mr. Lawlor, and again, this doesn't need

a whole lot.

You said that the patients tell you that they don't read the information, and I was wondering. The work that you've done, is it qualitative? Is it quantitative? Is it available to the public? Is it something that you could put on the docket?

MR. LAWLOR: I actually have a DVD with me if you want it.

DR. OSTROVE: Oh, fantastic.

MR. LAWLOR: It's both qualitative and quantitative, Doctor, and really we did seven focus groups, none of which started out to be a discussion about paper information. It was labeled literally label changes that we internally were going to do, and we wanted to see if people liked it or didn't like it.

And it led to a discussion of the preponderance of paper that patients were receiving. So we just took snippets of their comments from that, but I do have the DVD with me, and I'll be glad to leave it.

DR. OSTROVE: Right. Also, did you get in -- I mean, if you did -- get into any discussions of the other kinds of tools that we're specifically focusing on today in terms of their -- I mean, do you have any sense of these extent to which they go to the

Internet and what sources they use when they're looking for information about the medicines that they're taking?

MR. LAWLOR: We had several different groups. We had caregivers. We had young mothers. We had, you know, middle aged family parents. We had some seniors.

There wasn't a whole lot of -- there was maybe 30 percent of the population that were involved in these seven groups used the Internet for health information. The rest of them mainly wanted to make sure that they got the right medication in their bottle. That's about all that they really looked at the monograph that we give them.

But they didn't get into, you know, "I use this rather than the paper, you know.

DR. OSTROVE: Well, thank you.

I mean, again, to the extent that you -- the more detail that you have, the better. So certainly the DVD and the snippets would be very useful, but if your group would be willing to share kind of the details of that, I think that would be very helpful for us.

MR. LAWLOR: Absolutely. In fact, before I came out, our media group said that whatever NACDS

wanted, whatever the FDA wanted, we'd be more than happy to work with either organization to get. Really what we're interested in is patient safety and getting the right product to the right patient for the right reason. You know, I can't say it any more simply than that.

So, yeah, we'd be very happy to work with you, with NACDS, through NACDS to accomplish that.

DR. OSTROVE: Right. Thank you.

DR. TRONTELL: I want to thank you all for your remarks. You're a very appealing panel representing a lot of pharmacy and pharmaceutical groups.

I think we've heard that there's a large array of materials that FDA makes available. So clearly, on that long list that Dr. Winckler displayed, could I ask you to suggest what you believe your constituencies might prefer if we were to approach consolidation?

I think we've heard the PI. Others have said, you know, Keystone compliant materials. Could you volunteer your top one or two that might be a good model for us?

MS. WINCKLER: Can I volunteer the top to not use to communicate drug safety information? It

worked from the other way around.

I think the idea of the news release is the first one that we can take out. Let's separate out things that are designated as news releases, as things that are agency operational and not used for drug safety information. As we look at the longer listing and where we want to go, I was struck by Dr. Cranston's comment about the health care professional information sheet or, yes, the health care professional information sheet and the product labeling and the confusion that you may create between the two.

It's an interesting idea that perhaps you don't want both, although I'm not sure we're ready to jump on that because I think there is some benefit in having a concise piece of information that's readily available for health care professionals to use. So let's seep that and perhaps improve it so that it more clearly says, "What is that action item for the physician?" and then has the availability of the full product insert to provide that extensive information.

I personally am not sure of the difference between the talk papers and the public health advisories, and maybe we just don't need to have different names for those types of things, but if we

perhaps focused it on the audiences who we're targeting at the information at the right level, is it a patient piece and a health care professional piece? And those are the two things that we need.

And then with the backup from a comprehensive document like the labeling.

MS. DUNSAVAGE: Just a comment. I also think it does matter on who the audience is, and if you look at the ISMP perspective, one of the reasons we developed the nursing newsletter is that the acute care newsletter was used pretty extensively by pharmacists originally, and certainly in our organization as well as physicians, but nurses commented back that they don't have time to read all of that, and they wanted bullet points.

So in our nursing newsletter, what we do is very little snippets that they can use that are very practical in their daily performance of duties. So I think, again, it depends on the audience and what we're looking for.

DR. CRANSTON: I guess from my perspective most of my comments really were addressing information that a physician really needs to know about, keep it in his head or her head, and if this is a preventable, then change something to prevent it.

And so why I don't object to any of the information you have on your Web site, I use it all the time. I think it's fine. I can navigate, but I have the time to do it. I mean, I'm a policy wonk.

But I don't know of the best way to get that information to physicians, and I suspect you may not either because you've been dealing with this now for quite a while, and that's why I feel, you know, you really need to engage the medical specialty societies which have the bulk of their members, you know, and that's where they look. And if you can work with them to tailor the message and perhaps reinforce it and determine which mechanisms work best for that particular group of physicians, you know, I'd like to say E-mail would work great, but I know a large percent of AMA members either don't use it or won't let us send them E-mail messages. So it's really difficult.

With regard to the health professional information sheets, I think if you read the comments we made on Drug Watch and also if you read the testimony that's in the transcript, some of the elements of that would, in fact, be on the Drug Watch Web page.

Now, I know that's in trouble in and of

itself and I've decided to keep the comments in here because we did support to it. It's not so much opposition to some of the information. It's opposition to the creation at least of a footnote of that guidance, staff guidance, you know, is a whole new database of health professional information sheets, which would be mind boggling, I think, for physicians.

DR. CUMMINS: If I could just follow up on that, you gave a list of health professional information sheet content that actually follows almost exactly what we're doing right now, and I wondered if you had looked at those sheets and could say whether that seemed to fit the model you laid out. It does provide an alert information that summarizes the data that's the basis of the information. It provides recommendations about how that emerging information can be folded into practice. It has a disclaimer, and it also links to the current CPI.

So is that what you have in mind? Are there ways you might suggest we could improve it? Are there elements of these sheets that have been issued to date that you find unuseful or misleading?

It would be really helpful to hear about that.

DR. CRANSTON: And I think -- and this is mainly, you know, due to a fairly small, you know, staff analysis -- again, I think they may be a little long. We are concerned about the recommendation sections in that there seems to be more of in some cases almost like a mandate as to advice, and I know that's a fine balance, but we're concerned that this may be emerging information and, you're telling physicians to do something, and if they don't do it, you know, and a bad outcome occurs, then they're dead in the water in terms of a lawsuit and so forth.

I think my main point is that the Drug Watch citation -- if Drug Watch ever comes to be, I would expect it to have relatively few drugs on it at any given time, and it would seem to me, you know, that the information that I laid out, which you're right; a lot of that isn't what you know is the health professional information sheet would appear on the site with the product at the time of the citation of the introduction of the problem to the public domain.

No other drug would have such a health professional information sheet. So it might be limited at any given point in time to -- I don't know -- ten or 12 drugs, and the link would be then to the professional labeling.

In other words, the way you read that guidance document is you're going to create a database of health professional information sheets from which you link from the Drug Watch Web page to these, and I think that is the major point of objection, that, you know, why do that when, you know, it has been 15 years sine Dr. Ostrove started the focus group and things on the PI.

You know, it would seem to me that that should be the area to really focus on getting labeling, which physicians are familiar with what you use to some extent, and particularly if you can have a highlight section for quick ready reference. That's where the focus should be, getting all of that changed, and if you, in fact, end up having a Drug Watch Web page, then you can incorporate some of this information that you're now calling a part of the health professional information sheets right out to the Web page with a citation, enough information so that the physician knows that there is an emerging problem, what the evidence is support that and what they might consider doing until the resolution of this is complete.

MS. TOIGO: Each of the panel members appears to have experience using our Web site, and

we've heard a lot about the things that don't work. Is there any example you can give us of some things we might have done recently where you say, "Gee, they got it right," or, "I don't have any other questions, or you know because you didn't get a lot of questions from your members or your writers that are taking that information and compiling it for your newsletters, didn't have a lot of questions, but based on the information they had, they could use it?

Are there any specific examples?

MS. DUNSAVAGE: I think the information on the Cox-2s was excellent. I think it was to the point. I think we needed it quickly. I think a lot of times with some of the things that came out of the FDA, it's not timely enough, but I think it was. I think we got the information that we needed, and again, exactly what you say. We boiled it down, put it out in our newsletter the way we wanted to get it out to our physicians, and I know we reached them very quickly.

MR. LAWLOR: I would agree with Janice's statement. The COX-2 information came out fast, and it was accurate, and we were able to paraphrase a lot of it quickly to get information out to, you know, in our case a lot of pharmacists, and they were able to

translate it to a lot of patients quickly.

DR. CRANSTON: I mean, I'd be happy to describe, you know, what I do. I mean, everything when I go to work, one of the first thing I do is I go onto your home page, not the CDER page, the home page, look in the middle for, you know, any important new news, whether that's news or a talk paper or whatever.

But you know, from the perspective of someone who's interested in policy issues, I mean, I love your site. You know, like you can go there and look at the history of the drug from the time it was originally approved and all of the different changes. Sometimes you might need that kind of information.

That's wonderful. For a physician? Come on. They're not going to do -- I mean, I think they would have an awful lot of trouble navigating your site. It's designed -- it really is designed for the most part, I think, for policy folks and perhaps, you know, some consumers are successful in using it.

I mean, I don't know. I don't deal that much with consumer issues, but from a physician's perspective, I just don't see it. I think there has to be other ways.

MS. TOIGO: Thank you.

CHAIRMAN SELIGMAN: With that then let me

thank the members of our panel and conclude this session. I do, however, want as I indicated before we began to allow some time for any members of the audience who wish to make a statement at this time. I would ask that you try to please limit your comments to about three minutes if possible. And please identify yourself and your affiliation.

DR. GOLDSTEIN: My name is Gustov Goldstein. I'm a practicing psychiatrist.

CHAIRMAN SELIGMAN: We're not picking up the feed on that floor mic. So just give us a second. Do you want to try again? Hold on. No, I don't hear the one, two, three.

Actually, do you know something? If you like maybe you want to sit here at the table. Let's see if that microphone is working.

Again, anyone who wishes -- just push the button. There we go. Perfect. Again, please introduce yourself.

MR. GOLDSTEIN: I'm Gustov Goldstein, a practicing psychiatrist in Rockville, Maryland, with no other affiliations.

Let met start by saying that this is basically this idea of the focus group is one of the greatest. However, I criticize the implementation,

the fact that by the length and the way it was designed, very few practicing doctors could afford to lose a day to attend any of these meetings, and I'm very grateful for your modification of the format on the fly.

I will try to be a little politically correct, but I'm not usually successful. I understand that in this matter of medications and the public, there are three forces that are absolutely different in their objectives.

One is the pharmaceutical industry whose bottom line, whether we like it or not, is to make money.

The second one is the FDA, whose bottom line, whether we like it or not, is to protect and to comply with every single regulation that ny politicians and lawyers might have prefabricated.

And on the third poll is the dichotomy of the people in the trenches that is composed by pharmacies, doctors and patients that deal on an everyday basis with having to prescribe and provide medication to a patient that is suffering hopefully to alleviate him and without hurting him.

I heard today the word "transparency," and it would be fantastic, but unfortunately, we ended up

with a PDR which is more lawyer-like than scientific-like at any chance. I don't remember the last time I even look at the PDR for anything relevant.

The same with your Web site, by the way. It's so complicated that by the time I have five minutes to check if a particular drug has any particular side effect that I need to know, the patient is gone, and I'm with my next patient. So forget it.

So based upon this, I just suggest that there is such a thing as too much information. I suggest that we all, physicians and patients, are not sophisticated enough to understand the tools of risk and statistics and percentages and twofolds, et cetera, et cetera, and I propose to tone it down to our level, keeping the science for the scientists, but understanding that when you have 15 minutes or one hour in my case to see a patient, you cannot navigate your 19 kinds of publications before you get to a relevant matter.

So with this in mind, I suggest for the meetings that they are broken in chance of perhaps one hour with public participation. That would allow people to walk in and out and still we heard without having to spend the whole day here.

For the patients to use what it works. We know that the bouncing ball, the little whatever, Pac Man of Zoloft worked. People in the private industry knows how to get to the patients, and their message was successful in selling the drugs to the point that for us physicians to be abreast, to be up to date, because when a client comes to me saying, "I want this," or, "I don't want that because it has this or that side effect," we cannot say, "Huh? What is this?"

So that is effective for the patients. The other thing that is effective with patients is really personal communications. For any of my patients, it's more important about what the uncle said about something than what FDA has in their Web site. We need to reach those people.

And the private industry have done it already. Why reinvent the wheel?

Regard changes to physicians, detailing is the single most important way of communication. They know it. PhRMA knows it. That's why they spend big bucks on that. We like it; we don't like it. It's real. Let's use it.

Other than that, the only other way I get my information on many of my colleagues is through the

professional associations. I don't read your communiques. I don't read your Web sites. I go to annual meetings. I meet with other colleagues, and through the professional associations is that I get what I hope is the best available data.

So contacting those professional associations and communicating with them for their distribution to their members is absolutely essential.

And finally, again, borrowing from the private industry, the PDR as I said is useless, but they've got other tools nowadays that are very useful. One of them, and just one of them, is Hippocrates. Hippocrates is a PDR-like database that provides useful information for medication that provides weekly updates, sometimes more often than weekly updates, and that also provides a section of handouts to patients.

So if we could somehow take that example and use the horse's mouth, FDA with the whole official information to do something that's user friendly as Hippocrates is, including with handouts, then perhaps the PDR would com back to live.

Finally, for governmental and policy and lawyers, I understand the FDA has to have a place where all the information, all the percentages, all the twofolders are recorded, but that's not for us.

It should be there.

So what I propose in that respect is to create an FDA site which is a la Hippocrates for most of us, with a link for those who want full information afterwards.

My last comment that I would be really opposed to FDA creating standards of practice like when you said a patient should be seen every two weeks or every week for 35 minutes. I think that the standards of practice are better issued by the practitioners and those are the different medical associations.

thank you very much.

CHAIRMAN SELIGMAN: Thank you for your comments.

Is there anyone else who wishes to make a comment at this time?

(No response.)

CHAIRMAN SELIGMAN: If not, then we will adjourn until one o'clock.

Thank you.

(Whereupon, at 12:06 p.m., the meeting was recessed for lunch, to reconvene at 1:00 p.m., the same day.)

AFTERNOON SESSION

(1:06 p.m.)

CHAIRMAN SELIGMAN: Welcome back to FDA's Part 15 hearing on drug safety-risk communication.

Without further ado, let's begin this afternoon session by introducing Dr. Nicholas Ratto from First DataBank.

DR. RATTO: Thank you.

These comments are going to be placed into the public record after this meeting.

My name is Nick Ratto, and I hold a Doctor of Pharmacy degree and clinical residency certificate. My initial training was in pharmacy practice, was with the VA system providing direct patient care services as member of the medical and surgical care teams and also working in clinics in which we had prescriptive authority and counseled patients on a regular basis and interacted with providing drug information to the professionals.

The reason I mention this is that I'm here not as a manager at First DataBank so much as a pharmacist, a practicing clinical pharmacist.

I have been at First DataBank for nine years, and first database is actually a significant provider of medication information, CMI, if you will;

also a wide variety of clinical information to everyone from the government on down through hospital chains, retail pharmacies, PBMs, et cetera, consumer Web sites.

And my group is responsible for the authorship and updating of the private sector CMI that we maintain.

I would like to thank FDA for convening this meeting and for allowing me the opportunity to comment. The agency is to be commended for its intention to increase transparency and also assess the process of disseminating emerging drug safety information to professionals and consumers, and specifically to Dr. Seligman and Dr. Trontell. I think they've demonstrated a definite commitment to the process of CMI review and all the issues that have occurred over the last several years in conjunction with NCPIE. I'm also a board member of the NCPIE organization.

My comments will be directed at the MedWatch monthly professional labeling updates and also the patient information sheets. And, again, I'm speaking primarily as a clinical pharmacist concerning about promoting quality care for patients.

The MedWatch monthly labeling changes are

generally useful documents. However, a loophole does exist in the system which can result in the omission of important safety data, specifically data which changes within professional labeling sections other than the typical safety section, such as the box warning for contraindications, warnings, et cetera, adverse reaction section, is not notated by the MedWatch system.

An example of this is the labeling for the professional labeling for metaclopromide or Rezulin. Well, after MedWatch was established in 1996, a labeling change occurred within the indication section of the Rezulin labeling, and the bolded statement was inserted which reads, "The use of Rezulin tablets is recommended for adults only. Therapy should not exceed 12 weeks in duration."

Now, this specific information did not appear in the MedWatch flagged sections. If you're familiar with MedWatch, it highlights specific areas where changes occurred within the labeling. This was not flagged, and I believe that's because there was not a review of the indications or the dosing and administration section.

In the process of reviewing changes, but just as a highlight, obviously this is a safety

related issue and should be considered for review in the MedWatch process.

Now I'm going to switch gears and discuss the FDA patient information sheets pertaining to purpose, content, consumer interpretation, and risk communication, and I'm not -- from the standpoint of definition, you've heard the term CMI already, and that has been referring to the private sector consumer information.

I'm more inclined to say that CMI, which is consumer medication information, really applies to the private sector information medication guides and the patient information sheets sine they're all consumer medication information.

But be that as it may, I particularly wish to encourage not only FDA but also consumer advocates to carefully consider this following information, and I'll include my contact information on the public record for any questions.

Private sector health care data, including CMI, has been portrayed sometimes in an unfavorable light, and it is time for a fresh look at the CMI for the sake of improving consumer safety and quality of life.

I was pleased to note that without my

prior knowledge, other than having looked at the NCPIE information Dr. Bowman presented yesterday, I had no knowledge of the other speakers' information, and I'm pleased to see, again, there's probably a half dozen of them have reinforced to one degree or another the information I'm about to present.

FDA approved and authored patient education, whether it be medication guides or PIS, the patient information sheets, communicates risk information effectively to those with a high degree of medical literacy.

However, the sizable consumer population that to one degree or another is not medically literate is very likely to misinterpret risk information as presented. This is a serious quality of life issue, as such misinterpretation of the information by a patient frequently results in lack of adherence to the medication regimen or not taking the medication.

For example, and I'm about to discuss the Salmeterol PIS, but before I do that, I think I want to emphasize one point. Medical literacy has nothing to do with education level or intelligence. You can have a Ph.D. in chemistry that is medically to one degree or another illiterate or at least less than

fully literate.

So we're not just talking about people that have a very low education level or, you know, that sort of thing. We're talking about large percentages of population that can cross many different socioeconomic and ethnic levels.

Now, back to the specific PIS that I wanted to use as an example. There was a recently created patient information sheet for Salmeterol, which is a long acting bronchodilator for people with asthma that relieves their wheezing. This sheet begins with the following bolded information, and I quote: "FDA alert. In some patients with asthma, medications called long acting beta agonists may increase the chance of death from asthma problems."

A couple of paragraphs later, "because these agents, such as Serevent, may increase the chance of asthma death in some people, the following recommendations are made."

Now, if I'm a patient, I think anyone could probably logically walk through this and say, "Why take this medication if it can do more harm than good?" There has been no indication within this information of key information such as how often this is occurring or any other details. It's basically

just saying if you have asthma and you use your asthma medicine, in some people with asthma they will basically -- this medication may kill them.

Now, this is supposed to be emerging safety information, and there's a disclaimer that's included to indicate that it is emergent, newly emerging information.

However, I would take issue with the fact that it's actually useful partly because of the grade level, but party because I really -- as a health care professional, I can understand what they're trying to get at, but I don't think a patient necessarily would, and I quote: "this information reflects FDA's current analysis of data available to FDA concerning this drug. FDA intends to update this sheet when additional information or analyses become available."

I think you would agree that there is probably a sizable number of people in the population that would not necessarily understand that this is preliminary data, and that's the double edge sword here. You do want to communicate risk information. You want to get the word out early so to speak, but you also do not want to present this as gospel, and typically what's read on Web sites related to the FDA could easily be taken as definitive information, and I

don't see that this disclaimer properly addresses the fact that this information is, in fact, preliminary and that people would really understand what that means the way it's described here.

Salmeterol nonadherence could result in a decreased quality of life due to poor asthma control and needlessly restrictive physical activity because of that poor asthma control. Salmeterol can significantly decrease the number of asthmatic episodes. It has been used for several years in many patients and has been very effective, and there is a paradoxical drug related wheezing effect that does occur, and this is probably something that is related -- that has been known for a while now, and this probably could be something that's similar to this report in terms of its etiology.

But this is an uncommon occurrence. No one debates the point that communication of risk information to consumers is important. However, all too often, as in this case, FDA approved or authored medication information is written by professionals who have not effectively placed the drug risks into proper perspective for those with to one degree or another limited medical literacy, including little or no attempt to present the drug benefit or quality of

life information.

Now, at this point I think it's important to define what benefit is, at least in my view of it as a clinical pharmacist. Benefit in FDA terms in the past from various documents essentially in terms of medication information anyway has focused primarily on how to get the most benefit out of the drug meaning do you take it with food; do you not. Do you take it at bedtime, that sort of thing?

And to me that's fairly low level benefit or shall I say it's sort of the rudimentary issue of benefit, but there's a much greater issue that needs to be discussed in terms of quality of life, and that would be what is the benefit of the drug for you in terms of your overall disease and quality of life.

So, for example, with the statin drugs for cholesterol, I've heard other speakers here, and I've read information that says benefit is communicated everywhere. Benefit is communicated, you know, all over the direct to consumer advertising and all of that sort of thing.

And, again, I'm not here by any means to be a representative of the pharmaceutical industry. We're an independent organization, and I'm speaking on behalf of patient care. I don't think that saying

that a medication will help control your cholesterol is necessarily benefit information, at least not complete.

What's more complete and what we state in our information is that by decreasing cholesterol levels, that you can help prevent heart attacks, strokes, and other, you know, serious diseases. And I think that is more of an incentive to patients to understand as they're making an informed choice in weighing risks and benefits. That helps them definitely get more information related to the drug's actual effect as opposed to some laboratory effect perhaps.

Another factor to consider that has been alluded to by a couple of other speakers is that no one tracks the morbidity and mortality consequences of noncompliance or nonadherence with drug regimens due to excessive fears because the patients are to some degree or another medically -- they're not fully literate, and these spheres can be generated by poorly communicated information.

But be assured that harm does occur. If patient are not taking their medication for a prescribed condition, assuming it was prescribed properly, then if they stop taking it because of

exaggerated fears or poorly interpreted information, then harm certainly could occur.

I think the old saying is relevant. Frequently it's not what you say, but how you say it. So what might be a more effective way to communicate he Salmeterol bronchospasm risk?

Here are excerpts from one of our monographs as an example, certainly not the only example, but an example of a more useful approach to communicating risk information in a proper perspective.

Now, again, I'll remind you of what was said on the FDA alert. In some patients with asthma, medications called long acting beta agonists may increase the chance of death from asthma problems. Now, what we've done to incorporate that basic information, which by the way is related to information showing that some patients when they're using their inhaler have unexplained severe cases of wheezing that can lead to death, and that, again, has been to one degree or another for perhaps different reasons has occurred in the past and has already been noted, but now has been highlighted with this new information, which is important to be highlighted.

However, what's lost in that is that the

number of overall episodes is decreased, and certainly not every patient by any means, since it's uncommon, experiences this particular problem. So the large majority do have significant relief of their asthma symptoms if it's prescribed properly.

So our statement is rare, parenthetically possibly fatal, asthma type breathing problems have occurred with the use of products containing Salmeterol. Do not stop your medications for asthma or other breathing problems without doctor approval since your condition will worsen if you suddenly stop your treatment. Consult your doctor or pharmacist for more details.

Now, we go on in our how to use the medication section to discuss a number of issues related to how to monitor, if you're using your quick relief inhaler, which asthmatics automatically should have had prescribed well before they receive Salmeterol. We discuss how many inhalers they should be using per month before they get concerned that they are using too much.

We also indicate that using your quick relief inhalers more often than the scheduled amount may be a sign of worsening asthma in that it's serious, and that if symptoms do not improve or if

they worsen after using the medication, call your doctor immediately.

So the key points here, we've noted the rare incidence of the effects in order to help put this in perspective. The importance of continuing therapy - and this drug, by the way, again, having already been on the market for several years.

The importance of continuing therapy until you discuss the issue with your physician or pharmacist is also emphasized. Practical advice to mitigate risk is given in terms of proper dosing and how to recognize and immediately report worsening asthma or severe wheezing because that can be either drug induced or it can be disease induced. They may not be well controlled, but they need evaluation quickly.

And the benefit is inferred by saying do not stop the medicine or your conditions will worsen, and of course, we're assuming that they're not having a wheezing episode. We're trying to deal with the fact that some patients may just read the information, become frightened and then just stop their medicine.

Dr. Day yesterday gave medication guides a good rating for communicating numbers of side effects or whatever side effects they were addressing, and I

think this information complements what she said, and I think that she may very well be correct about that.

In reading them, there's clearly risk information communicated in the med. guides, but what the patient does with the information is what I'm trying to emphasize, i.e., if the risk is communicated without the proper perspective, then the medication may go unused. The patient may stop their medicine.

The antidepressant drug class recently received a labeling change regarding increased risk of suicidality in teenagers and possibly adults using the drugs. As an example, First DataBank responded to this risk information with the following update to our CMI, and again, I would expect that other private sector information would be similar in many ways.

While antidepressants -- this is in the warning section of our particular consumer information -- while antidepressants can provide great benefits, a small percentage of people taking these medications for various psychiatric conditions have had a worsening of depression or other symptoms, including suicidal thoughts or attempts. However, depression itself can sometimes lead to suicidal thoughts and attempts as well in both children and adults. Therefore, when medications to treat depression or

other psychiatric conditions, parentheses, antidepressants are used, the benefits and risks must be discussed with the doctor.

And then we follow with a statement that says, "Tell your doctor immediately if you notice the following conditions," and we note more than a half dozen of the cardinal symptoms that might occur that would trigger concern, such as panic attacks or trouble sleeping, impulsive actions.

Watch for these symptoms especially at a time of antidepressant dose change or when an antidepressant medication is being started. Close quote.

This information provides the risk and benefit data in perspective. In contrast, FDA's response to this issue was a multi-page medication guide which is almost completely devoted to this uncommon suicidality issue, to the exclusion of other adverse effects and to the exclusion of the proven benefits of the drug.

Again, I'm not saying ignore risk information, but it has to be put in perspective.

Further, a director within the CDER division stated during a meeting that I attended that while First DataBank -- the text may be true, FDA

would never state that type of information, and he was referring to the fact that the drugs can provide great benefits.

Now, it has been well proven for decades that antidepressants treat depression. The reason I bring up that quote is that it indicates that at least with some people in the agency there is a definite level of aversion to benefit information that is a bit stunning.

It's not difficult to imagine the amount of fright that can be generated in a parent after reading this medication guide with no other information, looking at three pages, all related to the suicide issues which, again, are uncommon. It doesn't mean that they're not important, but they're the total focus of this, and perhaps as you might imagine, leading to them feeling as though they would not want their child to take the medication.

So, therefore, you have in some cases untreated depression, assuming that the patient should have been treated in the first place. You have untreated depression and potentially suicide from untreated depression.

However, no one ever tracks that information, or at least not typically. So I'm just

trying to make the point that because it's not tracked, it doesn't mean it's not occurring. As was said in previous lectures, there is the issue of information that -- there is the double edged sword here. You can communicate risk information and you can also cause harm as well as good, depending on how you do it.

Antidepressants likely were overused in adolescents, but let's not swing the pendulum completely to the other extreme.

The other thing we do with our data that can be helpful in risk communication is provide prodromal symptoms as emphasized. In other words, the early symptoms of whatever condition is arising, we try to focus on those, and also alternate treatments.

There was some discussion this morning and actually yesterday as well about the Women's Health Initiative and hormone replacement therapy. In our monographs, we indicate, as were discussed in the fact that there are issues related to risks for hormone replacement therapy. The fact that there's other possible treatments for osteoporosis that could be discussed with your physician or pharmacist, and we give a couple of examples.

The bisphosphonate group with fosamax and

reloxifene or Evista in order to give the patient some other information to help make an informed decision knowing all of the benefits and all of the risks that are important.

I think just to reemphasize, we must make the paradigm shift to address the general population and avoid the understandable but problematic view that everyone thinks like we do as professionals, and so patients are going to look at information and misinterpret it when it's presented out of perspective or just as basic medical statements, such as I quoted in that PIS for Salmeterol.

Now, related to the PIS, what is the purpose of it? The PIS was supposedly for emerging safety information and critical drug information. In fact, there were statements made that it was not supposed to stand alone, not be a complete CMI document, and the PIS was intended only for those selected drugs.

However, the agency now has revised this plan, as was noted by other speakers, and at least on paper has intended to produce a PIS for all drugs, despite the existence of a complete CMI database among a few different companies that already exist, in other words, reinvent the wheel.

CHAIRMAN SELIGMAN: Mr. Ratto, if you could take a minute to conclude your remarks, please.

DR. RATTO: Okay. What standards for patient education content and format will the PIS meter exceed? The FDA has not been -- the standards have not been applied for medication guides or PIS that are applied to the private sector, and that's the Keystone guidelines or the action plan, and they should be applied to all equally.

What resources are available to FDA to order to produce a PIS for all drugs, any surplus resources must be relatively scarce, and at this point there are some problems related to the professional labeling, let alone attempting to start a new effort in the consumer arena, and one example is the hypotension effect that has occurred with Viagram and nitrate heart medications.

The professional labels were looked at for nine different nitrate products about a year after the initial report of the fatalities and problems with people having hypotensive episodes, and three of those labels on the professional side had no information whatsoever about that particular warning, whereas, three had the outdated relative contraindication and three more had the correct absolute contraindication.

So if this type of situation exists with professional labeling, it's difficult to envision the agency assuming a new resource intensive role in authoring and maintaining PIS.

Also, how will the usefulness of the PIS be assessed and validated? Currently the FDA is planning to formally assess private sector CMI in 2007, but no FDA authored or approved CMI has ever been systematically assessed versus standards or validated for usefulness in consumer testing, and we feel that it should be assessed objectively with the same criteria applied to the private sector.

From a consumer patient care perspective, it's logical and responsible to propose that FDA use resources they might use on creating PISes instead for CMI consumer testing in cooperation with NCPIE, who they have commissioned actually to work on the CMI project so that the information can be improved.

This is despite flaws in the 2001 survey that's been quoted. The private sector has been working diligently with NCPIE objectively assessing and enhancing CMI. So why reinvent the wheel? Why not work together with the FDA in the consumer's best interest by reviewing the data as it exists?

FDB, First DataBank, and other NCPIE

stakeholders stand ready and able to work constructively with the agency for the optimum benefit of the consumer.

thank you.

CHAIRMAN SELIGMAN: Thank you, Dr. Ratto.

The next speaker is Wendy Jezarian from Time.

MS. JEZARIAN: Good afternoon. Thank you for having me here. My name is Wendy Jezarian, and I'm from Time, Inc., and I'll be taking you through portions of a research study that we conducted last fall with Harris Interactive.

Our study was conducted on line in late September, early October of 2004, and the study was adjusted for the act that it was conducted on line and is representative of the U.S. adult population.

In this study, caregivers were defined as someone involved in the care of an ongoing medical condition of a family member or friend. Of our total sample of over 3,500 respondents, 19 percent of the population characterized themselves as caregivers.

This is a brief profile of caregivers. As you can see, they are more likely to be female and also to be a sufferer of some illness themselves.

In addition, more of them are taking

medications and are taking a higher median number of prescription medications. We've postulated that one of the reasons for this trend is that caregivers are under greater amounts of stress due to their caregiving, and this takes a toll on their own health.

We found that caregivers are most likely to be caring for a family member, their spouse or partner in 44 percent of the cases, and almost a quarter are caring for an elderly parent while one in five are caring for a child.

Our study found that caregivers are overseeing a variety of illnesses, almost all of which require long-term treatment and management and which may include a regimen of prescription medications. Four of the top five conditions seen here, hypertension, diabetes, cholesterol disorder, and heart disease, are related to metabolic syndrome and are on the rise in the U.S. due to lifestyle factors.

Here are the three main ways in which we found that caregivers assist patients with their medical conditions, and I'm going to go in more depth about each of these in the next few slides.

First, let's look at different ways that caregivers intervene with the patient's doctor. Nearly nine out of ten caregivers go with the patient

to see the doctor, and between 65 and 70 percent encourage the patient to continue with the prescribed treatment and/or talk to a doctor about their condition. Sixty-three percent make the doctor's appointments for the patient.

So we see that caregivers are influencing the patient's actions and are a key to compliance. Therefore, the caregiver needs to hear and understand the benefits and risks of treatment options since treatment appears to be a joint effort in many cases.

Now, let's examine how the 92 percent of caregivers help with the patient's medications. Nearly 85 percent help the patient by picking up the prescription for them. About six out of ten help the patient remember to take their medications and/or help administer them.

These numbers are important because they illustrate that the caregiver is interacting with the pharmacist, is helping to administer medications and can be a key to compliance. Therefore, in addition to the sufferer, the caregiver needs to be made aware of dosage information, side effects and risks, and possible drug interactions.

As you recall, earlier I stated that 74 percent of total caregivers said they looked for

information about the patient's medical condition, and this slide looks at the information sources that they used.

On the next slide, we'll look at information sources they used to learn about prescription medications. Here we see that health care providers are the primary source of information about the condition, at 86 percent. After health care providers, we see about four in ten turning to the Internet and direct marketing, nearly one third turning to magazines.

These types of media suggest caregivers are proactive searching for detailed information from sources that can educate them and are turning to written forms which could be passed along to their patient.

We then looked to see if these sources differed from the sources used by recent sufferers to learn about their condition, and we defined recent sufferers as those who have been doctor diagnosed within the last two years.

We found caregivers to be significantly more likely to use proactive sources of information, such as health care providers, direct marketing, and pharmaceutical company Web sites.

We also found that they were significantly less likely to use a passive medium, such as television, as an information source.

This chart shows us the information sources used by caregivers to learn about prescription medications, comparing caregivers to the general population. Caregivers are more likely to use the majority of these information sources, significantly so for health care providers, direct marketing, the Internet, newspapers, pharmaceutical company Web sites, and medical books and journals.

You'll notice that the media types that are used as a source of information on prescription medications are similar to the sources that caregivers use to learn about the patient's conditions, sources where they can be proactive and get detailed information, and again, they're less likely to turn to TV as a source.

Also noteworthy, other friends and relatives are important sources of information, building on the idea that the circle of people around the sufferer are influential and should be informed and communicated to.

In response to seeing information on a condition or treatment option, caregivers are likely

to take action. In fact, they're just as likely to take action for a family member or friend as for themselves, and of particular importance is talking to a health care professional and looking for more information.

In summary, our study found that caregivers are very involved in the care and treatment of their patient and, therefore, should be well informed of the risks and benefits of treatments and medications.

Also, in addition to consulting with their health care provider, caregivers are likely to turn to proactive written sources of information on their patients' conditions, as well as on prescription medications.

And caregivers are likely to take action as a result of communications regarding conditions and medications, including increasing compliance and seeking out more information.

Thank you for your time.

CHAIRMAN SELIGMAN: Thank you.

Our next presenter is John Kamp from the Coalition for Healthcare Communication.

MR. KAMP: Thank you very much.

Just quickly, the Coalition for Healthcare

Communication is a coalition of trade associations and professional communication companies that support drug, device, and other companies in their professional communication. We're not speaking today for any of those specific companies or representing PhRMA as an institution or any of the PhRMA companies.

Just sort of quickly, my major points are we'll talk about the need for new policy; some of the limits I think that we all are beginning to understand from the two days of discussions; the need that I don't think surprises you now after two days about a clear distinction between professional and consumer communication; some ideas about some of the court requirements that we might all face; and a thought that hasn't been discussed before about the protection of the FDA jurisdiction in this area.

The existing policy problems, this has been a fascinating discussion for the last two days, and I thank you for our opportunity to participate in this dialogue. I want to put sort of a finer point about what we've been talking about and what we're really talking about, and part of it is my point of view because I happen to have gone to law school, even though I try not to think like a lawyer all the time.

But there's really two different basic

questions going on here, and the first one is fairly simple, but still hard to execute, and that is the general question that we were asking most of yesterday about how do you do what we're doing now better, you're actually at the end of the first panel this morning.

What's the role in all of this though is another question, and I raise all of this because I think that the second question, what's the role of the FDA particularly in consumer facing communication about risk and other information may be a new question and may have some legal aspects to it.

Essentially let's think about the question about whether or not the FDA wants to get in the business of doing consumer labeling as the gold standard and the legal standard that virtually every other organization that does consumer facing communication about drugs has to follow, particularly the regulated industry.

That is a fairly new idea. It's not a new idea for the FDA to participate, to collaborate with NCPIE, all the other organizations, and it's not a new idea for the FDA to supervise the communication of direct to consumer advertising by the companies, but the idea that the FDA essentially take on the sort of

super labeling notion for consumer facing communication is a new idea, I think. It's an idea that I fear that PhRMA lawyers might like too well.

And one of the discussions that I think several people had over the last couple of days is that one of the problems with professional labeling is that it serves the legal community inside of PhRMA companies perhaps too much, and in serving that master, it doesn't serve the prescribers very well in doing so.

And I fear that a similar thing might happen if there is a gold standard by the FDA that everyone has to follow, and so I think the suggestion that I have is that you think about whether or not you really want to go there or if the existing process where you collaborate rather than create the gold standard, if the existing process if broken or you want to go and take on what I call the new responsibility.

If you do that, I have a few notes from the trenches about that for some things for you to think about. Consumers are complicated. You know, some folks think that consumer communication is not rocket science and we can all do it, but I think what we found out for the last two days is that it's a lot

harder than we thought.

In fact, I think consumer communication may be harder than rocket science. It may be harder than medicine. I suggest that you may want to avoid some of the mistakes that the PhRMA companies have done in consumer communication over the last 15 years since the explosion of DTC advertising.

Think about the PhRMA principles, PhRMA as a self-regulatory volunteer process has essentially developed some new principles about DTC that the companies are all agreeing on, and one of the first things that they're agreeing on in DTC advertising is to focus again on the prescribers and make sure that the prescribers get it first before they start rolling out DTC.

They're also taking very seriously the notion of risk communication and the discussion of risk communications in ways that clearly can be understood by consumers instead of putting them all in the end in the mouse type or in the real fast type, with maybe distracting things going on.

They also sort of got it, and they're no longer going to put ED ads. during family time. Don't upset the consumer unnecessarily. Don't create a situation for yourself that you have to go back and

fix.

I think these are some things that even the FDA might have -- there might be some parallels on.

I want to use an example of one of the ads, what I think of as the post-PhRMA guideline ads, but the PhRMA guidelines really don't go into official effect until January, but just use one ad as an example of the kind of things that the PhRMA companies are now doing in their consumer facing communication that I think are helping them communicate more effectively.

The troperads (phonetic) -- and we're going to look at one of them in just a moment -- there's a lot of focus on disease education. There's a lot of focus on compliance by the patient. The messages about benefits and risk are really very clear -- and then the thing that I think is very hard for us, and I'm a former government enforcement person -- I think it's hard for the government to do, engaging creative.

The reason for the new approach, why in hypertension area do we have to look at this differently, Astra Zenica in this case? The high rates of noncompliance. They jeopardize the patient's

health. They make it more and more likely that very expensive treatment for complication is going to come later.

We heard some of the statistics yesterday. The statistics sort of range across the basis, but it's really appalling to think about of the people who are treated for hypertension, somewhere between 30 to 60 percent of them are not compliant with the drug regimen. This is a huge number of people.

We're not talking about the people who are not yet even diagnosed, less treated. We're talking about the people who are being treated. There's clearly a problem here. Consumers aren't getting it.

And it's interesting in the research that was done on this. Not surprisingly, here the patients that are taking these drugs who have been diagnosed with hypertension who are taking the drugs sort of know that it's a bad thing not to be compliant, but they think that it's bad thing for other people. It's sort of like the early days of safety belts. All of us thought it was a good idea to wear them, but when it came to whether we need to wear them, they weren't so sure. These very patients were the focus of the ads.

So what did drug companies do in all of

this? They've essentially first researched the audience, and the research of the audience for these people, what did they find out? Consumers respect the doctors. The patient, and what the company found here is that the model for this is the consumer-patient dialogue.

They also found out that consumers really want to understand the risk information, the compliance information, but it must be very clear, and it must not be complicated.

Also, it must be reassuring, not frightening. Several other people have talked about that today and yesterday. One of the suggestions today, I think, by Dr. Goldhammer at PhRMA was that if you frighten someone, you've got a much larger barrier to get past to get them then to understand more about what's going on and then particularly to be compliant.

And then I think, you know, it's intuitive, but also supported by the research, the physicians, whatever the communication is must support the physician's discussions. Physicians themselves like the kind of compliance messaging that we're talking about here, and they like DTC campaigns that support their messages, particularly on compliance contraindication side effects and warnings.

So let's take a look at it. Can we run the ad right now? We'll just take one example of sort of how it works.

(A video was played.)

MR. KAMP: This is the kind of communication that I think works. In fact, I want that doc. I think his raised eyebrow said more than any of the contents said, and if he raised his eyebrow at me, I'm going to take my drug.

The next thing that's going to happen with this series of ads is to measure the results. There's now in the field some measurement about what's going on here. There's some measurement about most importantly whether the patients really understand the message, the black box warning kind of message, whether patients intend to discuss it more directly with their doctor at their next visit, whether they intend to adhere to the drug regimen, whether they really understand the value of compliance after seeing one of those ads.

Actually they're going to do some tracking study on this message understanding, and then more important going directly to the question that Dr. Smith asked yesterday, one of the things they're going to be doing is looking to see about the behavior

change. Do the patients actually make a change based on this ad?

So, you know, again, it's just an example or the kind of thing that has to be done to do good, clear patient communication. It's the warnings. It's the encouragement about compliance. It's the benefit and risk information that's in this clear, realistic, and fair, serious matter. It's about the availability in this case they're working on their patient assistance program, but it also entertains and engages the patient in ways that I think at least when I was a government employee trying to communicate with the press and the Congress and the public, engaging the consumer or the audience member was not something that we were particularly good at.

With all of that aside, meanwhile let me give, you know, some of our free advice about some of this. I think that there is clear guidance that's possible from the FDA that can help us all get where we need to go.

More objective, predictable standards by the FDA, maybe even a clarification about this notion of whether the FDA, in effect, wants to take on this role of being the creator of the gold standard in consumer communication or wants the rest of us to do

it as well as possible with the FDA giving very clear oversight.

Some value of consistency from the FDA, of course, would be useful. Respecting the differences we heard from virtually all of the witnesses yesterday about the difference between professional and consumer communication.

I have to use this forum to talk again about brief summary form. I think it's time for the FDA in the context of DTC advertising, which is not really the central focus of this, but we're talking about essentially the same kind of information on the patient package insert and elsewhere; we have to issue, I think, the final guidance. We have to have that guidance give us the ability to do clear, uncomplicated messages and in a format that work.

And it's time. I notice that Bob Temple is not here today. Bob Temple was the first one who used what I thought was a fabulous analogy in 1995. He said at that time at a DTC hearing that the brief summary has no friends, and it's like the Holy Roman Empire. It's not holy; it's not Roman; it's not an empire. It's not brief nor a summary.

I think it's time for us, all of us, just to blow away and sort of get on with it and get to a

different stage.

This is some suggestions from us that if you do make some very clear policy choices essentially to take on officially this role to create an official, gold standard labeling for consumer communication; if you do that because of court requirements, there are some things that need to be done.

And the first one, of course, is a public record. The FDA, if it does decide to do some things in there and, in fact, has limits on the commercial speech of other players, even the PhRMA companies, it must articulate the need for the new rules. It must have evidence that the new policies or rules work. It must have considered other alternatives, and it must use marketing limits by drug companies or others. It must use those only as a last resort because nothing else would actually enable the agency to insure that the safety information was understood.

I also suggested that I think that there are some very interesting ideas that came out of the last hearing, and they've been being kicked around, and there are some things that I think we ought to keep on the table and think about more seriously.

Peter Pitts on November 2nd in this room suggested that maybe we ought to be looking at the

idea of a permanent advisory committee in the communication area or maybe another way of doing the same thing would be to have an advisory committee person in the other advisories, perhaps especially in the new drug approvals, who was a communications expert, and that the agency start developing a set of social science, behavioral science standards that people can know and understand just as it does in the medical area.

If it's going to go there, if it's going to take charge of these behavioral science issues, it should put behavioral sciences in the places where these decisions are made.

Again, a good, simple rule: high profile enforcement when those rules are broken. It's good for all of us, and use a public process.

I also want to put on the table something nobody else has put on the table, but I think we all have to fully understand right now. In these areas, and it's not just the marketing jurisdiction; it's sort of the whole labeling jurisdiction. It's the reputation and the important understanding of the agency as the gold standard in this area. The agency's jurisdiction must be protected. It must be protected not just for the sake of the agency, not

just for the sake of the regulated industry. It must be protected because the American public, citizens, patients need it.

We must resist the incursions on the agency's jurisdiction in these very important communication areas by state laws, Attorney General enforcement, state cases, state legislatures. We must resist the private actions, plaintiff's cases on failure to warn and false advertising kind of theories. I think we must resist and work much more carefully even with our own sort of inside the house, the HHS IG and the Department of Justice as they develop their own theories about what's legal and what's legal by the regulated entity under the False Claims Act and anti-kickback statutes.

So the summary sort of quickly. I think we all need clear objectives about what the FDA is up to, what it wants to do. If it wants to go in new areas, it must proceed carefully.

I think we must separate the consumer and professional warnings and risk communication. We must follow the court mandates for due process, open record, and other kinds of things, and for all of our sakes, especially for the sake of the patients in America, we must resist the attacks on the

jurisdiction of the FDA.

Thank you very much.

CHAIRMAN SELIGMAN: Thank you for your comments.

The next speaker is Dr. Susan Kleimann from the Center for Plain Language.

DR. KLEIMANN: Good afternoon. Thank you very much for this opportunity.

I must admit, however, that I do not come to speak before you as a person who is a medical expert. I come to speak before you as a person who is a part of the communication field that is interested in plain communication.

The Center for Plain Language is only a recent coming together of people, of government employees, of academics, and of private sector consultants who really do wholeheartedly believe that plain language, clear communication, and clarity is a civil right that we owe to every single one of our civilians in the United States.

Now, that is going to make me sound like a very strong advocate, and I am, but I do want to be clear that I'm advocating on the part of clear communication.

For my own background, I do have a Ph.D.

in composition and rhetoric, and in my business, when I'm not wearing the hat of Director of the Center for -- I can't even remember the name of our center --

CHAIRMAN SELIGMAN: Plain Language.

DR. KLEIMANN: -- Plain Language -- thank you very much, that I am president of Kleimann Communication Group and have over 30 years of experience in working primarily with government clients, such as VBA, the IRS, recently with the FDC on privacy notices, and with HUD on the good faith estimate.

So I've been doing a lot of work in this, and I hope that you will appreciate the kind of very narrow focus that I want to bring today.

I want to be able to focus primarily -- I'm not a mechanical engineer either. So I apologize. I want to focus really very narrowly today on the Adderall patient information sheet, and obviously I want to talk about what is clarity and how do you know when you have clarity.

As a very simple definition, I think that we can say that consumers find the -- clarity is when consumers can find the answers to their questions very easily. As Dr. Ratto said, you know, we're not talking about people who necessarily have a high level

of education or have a high level of intelligence, nor are we talking about the opposite when we're talking about clarity.

What we're talking about is people who have questions. That's how we read. If you look at all of the reading research, what you're going to see again and again is that when a consumer goes into a document, they're really looking for only one thing: the answers to their questions, not questions that are necessarily in there, but the questions that brought them to the document.

If they can find the answers to their questions, they're very happy readers and we have clarity. And if they can't find the answer to their questions, they're going to do a couple of things that are really quite unfortunate, especially when we're dealing with health information, which is they're going to one stop reading or, secondly, they're just not going to understand what they read and perhaps misinterpret and misindicate upon the information and their misinterpretation.

So how do we do this? How do we find out what consumers want to know about a particular product, about a drug, about any of the myriad of things that we want to give them information about?

One is we have to figure out what those questions are. So in preparation for today I did a very, very quick survey asking my own staff. Gee, if you were going to go look for information about a drug, any drug, what are the questions that you would want to have answered?

First question, nine out of ten people, are there any side effects?

Secondly, will the drug react or interact with other medications or vitamins I'm taking?

How long has this drug been on the market?

What do I do if I turn out to be allergic to this drug? A very high percentage of people are interested in that, perhaps our sample.

Where can I find the information about how or whether this drug was tested?

Now, I'm not trying to claim that these are all the right answers. Consumers are complicated, but the point is that we really do need to know what those answers are or what those questions are.

Clarity for the consumer is going to be when we answer those questions, the questions that they have. So what's on the information sheet when we go out to the FDA?

Well, first, there's the usual FDA

information. I was on the Web site. Dr. Anetta Cheek, my colleague, spoke yesterday about the Web site. So I'll refer you back to her comments about that.

There is an FDA alert. There's a warning about abuse, and then there are a series of questions and answers. What is Adderall Rx? Who should not take Adderall? What are the risks? Are there any interactions? And how do I take Adderall?

So how did we really do? Well, the first question my staff had is are there any side effects, and it seems to me that the FDA alert and "are there any interactions," both of those are going to get to the consumer or allow the consumer pretty easily to get in and get answers to their questions.

What about the second one? Will the drug interact with other medications or vitamins that I'm taking? Again, we have are there any interactions.

I will point out that all of the Qs and As are on page 2, however, when you print this out. So you have to delve a little bit into it, but you can get to it.

What about how long has the drug been on the market? Not so sure about that.

What do I do if I turn out to be allergic?

We certainly have interactions again.

And where can I find out if the drug has been tested? I would assume that we would find that under what is Adderall XR or who should not take Adderall or what are the risks. It's someplace in there. I can't go directly to it.

Now, again, I'm not trying to say this in a way of saying that that particular patient information sheet is disorganized. My point is merely to illustrate that when you are going to organize information, you want to organize the information around the questions that the consumer has. A sample of ten is insufficient to really predict what the basic questions should be, nor am I presuming that FDA hasn't gone about and done this at some level, but it's really that the consumer's questions need to be able to drive the organization.

So if we can assume we can get to that and we can assume that we can make those questions prominent, we're at least part of the way along the road to clarity. What's our next step?

Let's look at the language of the Adderall alert, and from now on I'm just going to focus on the little alert.

"Health Canada has suspended marketing of

Adderall XR products from the Canadian market due to concern about reports of sudden unexplained death (SUD) in children taking Adderall and Adderall XR. SUD has been associated with amphetamine abuse and reported in children with underlying cardiac abnormalities taking recommended doses of amphetamines, including Adderall and Adderall XR. In addition, a very small number of cases of SUD have been reported in children without cardiac abnormalities taking Adderall. At this time FDA cannot conclude that recommended doses of Adderall can cause SUD, but is continuing to carefully evaluate these data."

I believe this is totally intended to communicate to consumers. Let's go back and think about the situation under which this came: a lot of media coverage.

You're going to have the anxiety of people going to this because, "oh, my God, my child is taking Adderall," and, again, if we think that we have a very large range of reading levels of people's medical literacy, is this going to address what their needs are?

I would argue probably not. Doing a Flesch-Kincaid, we have a reading grade level of 16.7.

Maybe we all have that, but I don't know about the general population. I think we can assume that most people will not have a reading level of 16.7.

I think we can also assume that reading levels are kind of false measures. There's much in the newspaper about children who graduate from high school, which would put them at a 12th grade reading level, and who actually can't function at that level. So let's not assume that just because they're a college graduate they're going to have a reading level of 12.

Even if I take out the word Adderall because readability formulas are based on some combination of how big are the words and how many words did you put into a sentence and how many sentences do you have in the paragraph. It's a very simplistic way of calculating how difficult something is to read.

But even if I took out the word "Adderall," it still stayed at 16.7. So this is a fairly complex little passage that's giving an alert about a drug that's been covered in the media. Again, I think we have a problem.

But what I want to be clear about is that readability is a function of so much more than simply

how big are the words and how many words do we put into a sentence and what is the sentence length. So let's see what could we do with a rewrite.

In the rewrite that I'm going to be showing you in a moment, it reduces the reading grade level to 13.3. Well, guess what, folks. That's not much better. But is it easier to read? And I'm going to leave part of that to your decision to make.

I also, before I show it to you to protect myself, I don't want to presume that this is a perfect rewrite. I'm pretty sure it's not. There may be some technical inaccuracies in it. I do believe that when we're talking about readability and clear communication, technical accuracy is paramount. So I apologize again for my lack of knowledge if I have perhaps not quite gotten the details right.

"Status. Health Canada no longer allows marketing in Canada of Adderall XR products. Reason. Some children taking Adderall XR have died suddenly and without apparent cause. A sudden unexplained death (SUD) has occurred with three types of medical conditions: (1) in children with an abuse of amphetamines; (2) in children with underlying cardiac abnormalities and who are taking recommended doses of Adderall and Adderall XR; and (3) in a very small

number of children without underlying cardiac abnormalities.

"The future. FDA is looking at these data, but cannot conclude that recommended doses of Adderall can cause SUD. FDA will update this information when we learn more."

It's not perfect, but I will argue that it is clearer. Now, why is it clearer? And, again, this is going to speak to readability.

What would you rather I do? Should I leave this up so you can follow along with the changes or put my list of changes?

Response?

PARTICIPANTS: Changes.

DR. KLEIMANN: Okay. What did we do? First we set up a predictable structure, a structure that followed status, reason, the future. Not the best words, absolutely not the best words.

Even as I was coming over, you know, it could say "What? Why? What's next?" We could make those words work better.

But what it does is it gives for an alert a cognitive map for the reader. It allows the reader, a consumer who comes to this, to be able to have a predictable structure if all of them would be

structured in this way.

In addition, it categorizes the information according to consumer questions. We all grew up with newspaper articles. Who, what, where, when, why? Maybe those are not the right questions here, but they're still the basic information that we are going to want.

What's going on? Why is it happening? And what's going to happen next? Those seem to me to be very basic questions, and if we can group that information for a reader, anticipating what the reader's question is and then labeling it so that the reader can find the answer to his or her question more quickly, we have done a service around clarity and around readability.

We simplify words. Let's see. I have to find what the original was. Where the original is talking about "has suspended marketing," well, it's not that those are hard words, but it's a little bit more direct to say it no longer allows marketing, and again, I'm not trying to claim that I've got this precise, but I want you to see the gist, the illustration of the direction these types of alerts could move in.

It breaks up long sentences. The first

sentence in the original, "Health Canada has suspended marketing of Adderall XR products from the Canadian market due to concern about reports of sudden unexplained death (SUD) in children taking Adderall and Adderall XR." That doesn't trip off the tongue.

And if it is not quite accurate, it is still closer to being controllable if we are saying simply Health Canada no longer allows marketing in Canada of Adderall XR products.

The other thing that I did in breaking that sentence is that we separated what the status was or what was going on from the reason.

It isn't that "because" is a terrible joiner. It isn't that what comes after it was a terrible sentence or clause. It's that together it was very long, and we can simply split it apart and then identify what the different functions of those two sentences become, one status, what's going on, and secondly, cause or reason.

We defined unknown words. I consider myself relatively educated, and there's something about the phrase "sudden unexplained death" followed by an acronym that dehumanizes this. There's a way that that -- there's something about that phrase, even if it's a valid phrase, that just speaks of jargon.

Now, what we did in the rewrite was say children have died suddenly and without apparent cause. Again, I'm not claiming that that's the best or most solicitous, but it is also much clearer, that it's children have died of X. Then due to concerns about reports of sudden unexplained death in children.

Let's be more direct. Let's be more focused. More direct. That's it.

We broke out the key three pieces of information using numbers, one, two, three, who was being affected, children with an abuse of amphetamines, children with underlying cardiac abnormalities, and a very small number of children, they who do not have underlying cardiac abnormalities. It breaks it out. It's visual. They can see it. There are three instances. You're in one of those three categories or you don't have to worry. Again, it's a very visual way of talking about that.

In addition, I added information that explicitly states that FDA will provide more information. Did the original do that by implication? Yes, I think it did. FDA is looking into these data, but cannot conclude that recommended doses -- no, I'm sorry. That's my rewrite.

At this time FDA cannot conclude that

recommended doses of Adderall can cause SUD but is continuing to carefully evaluate this data.

Notice that then big parenthetic comment that isn't made is "and we'll let you know," and that's what people are going to really want, is tell us that you will let us know.

Now, this is very focused. It's really looking at what was only a paragraph on that page, but if we apply these same kinds of standards trying to set up a very strong structure that a consumer can recognize, the idea of what's happening, why is it happening and what will happen next, that type of basic plain language, technique can give us a clarity that we don't currently have on these.

Clarity is not a simple quest. If people are complicated, I assure you that coming up with a rewrite of this, balancing all the different policy issues that people have talked about and incorporating some of these very basic, plain language techniques is a lot more than rocket science. It is complicated. It is difficult because we're not merely trying to inform people, but we're trying to influence people. At least the first step of this is to give them the knowledge, give them the understanding, give them the clarity around what this information is.

The next step, getting them to act, is a whole new kettle of fish and a big one at that.

How do you know if you've got clarity? There's only one way of knowing. I can do all sorts of things about this because I have a lot of plain language techniques that I can bring to bear on something. Experts can go through, and they can get it technically accurate, but there's really only one way of knowing and that is to test it and test it and test it again because the ultimate judge of a document's success is going to be the consumer.

Measure everything you want, but know what the consumer knows, and I'm not talking about merely doing surveys. I am talking about being able to do usability testing, doing one-on-one conversations, one-on-one tests with consumers to be able to understand, to see if they comprehend and if they know what it is that they need to be doing, if they know what the consequences of inaction are.

This is how we're going to find out what to do, and this type of ongoing, iterative testing can be done in very small n's. It doesn't have to be 800 people or 1,000 people. You can get very valid information by talking with seven consumers. Seven consumers who can tell you where the sentence goes

wrong, where the paragraph goes wrong, who can tell you that "I don't know what that means," and who can give you clues on how to fix it so that you can fix it.

We have to ask about the consumer's questions. We have to know what those questions are, not try to guess what those questions are. We have to know what the structures are that they want to hear based on those questions, and we have to be able to get the language right so that they can understand it.

Let me end with Frank Lloyd Wright. "Out of clutter find simplicity."

Thank you very much.

CHAIRMAN SELIGMAN: Thank you very much.

I must beg everyone's permission. I'd like to take a ten-minute break if I may. So we'll reconvene at 2:30 with the last three speakers.

Please, I'd like to invite the four speakers to remain on the panel so that you're available for questions at the end.

So ten minutes. We'll reconvene at 2:30 with Peter Mayberry.

Thanks.

(Whereupon, the foregoing matter went off the record at 2:21 p.m. and went back on

the record at 2:33 p.m.)

CHAIRMAN SELIGMAN: Okay. Let's begin the last session and then we will have some time after the next few speakers to entertain additional questions.

Our next speaker is Peter Mayberry from the Pharmaceutical Printed Literature Association.

MR. MAYBERRY: Yes, thank you.

I do have a prepared statement which I've submitted for the record, and it's pretty short. It basically just simply notes that in terms of the electronic means that FDA has sought comment on, all of them have their good points and their bad points, but none of them did any good to folks who were stranded in New Orleans earlier this year or people who were living in the Super Dome.

The biggest benefit of PPIs and med. guides, especially as FDA has done them with the antidepressants, is that FDA has taken the med. guide and married it to the concept of a unit of use package such that rather than the manufacturer, shipping a product in a bulk bottle, a bulk container of, say, 1,000 pills and leaving it up to the pharmacist to take that product out of a big bottle and put it into a smaller bottle and then print something off from first data point and then give it to a patient, what

FDA has said is here we're going to have information that's prepared by the manufacturer, approved by the agency, and it's shipped in the manufacturer's original packaging so that the pharmacist can simply take it off the shelf and give it to the patient.

Now, I am here today on behalf of the Pharmaceutical Printed Literature Association, but through the course of my career I've worn many hats, and one of the hats that I've worn the longest that I'm the most proudest of is I've developed quite an expertise in the area of patient compliance, and I believe that I probably read 90 to 95 percent of every study that's ever been published on the issue of patient compliance, and to my knowledge if there's a study out there that shows that patients do not comply with their pharmaceutical regimens because they're afraid of the label, I am not aware of that study. Perhaps such a study could be provided, but I do not know of such.

Compliance is driven by a number of very complicated factors. Antihypertensives are incredibly difficult to insure compliance, but a recent study, the most recent study, released in May of this year by Ohio State University and funded by HHS, sponsored by and funding from Representative Price of Ohio,

basically found that when patients are given their medication in the manufacturer's original package with the compliance profiting feature and the bare minimum amount of information needed to insure that they take it properly, they get a higher therapeutic outcome. In other words, patients, you have got their product in the traditional cap and bioclosure had either no reduction in their blood pressure or very minor, whereas the people who got their product in the special packaging had significant reductions in both their systolic and their diastolic blood pressure.

Mr. Kamp said that we need to protect FDA's jurisdiction. I agree wholeheartedly. But we also have to keep in mind that FDA's jurisdiction by and large stops at the manufacturer's door.

The gentleman from First DataBank said should we be thinking about paradigm shifts. Most definitely. We have to be thinking about getting product not being shipped from the manufacturer in bulk containers that have to be repackaged in the pharmacy where errors happen, where product is exposed, where all of the stability data is thrown out the window and product cannot work 100 percent as it was intended.

Plus we have the opportunity now, as shown

through both the NSAIDs and the antihypertensives to have information, reliable information, approved information dispensed with medications every time a prescription is filled.

That's my basic message. Thank you.

CHAIRMAN SELIGMAN: The next speaker is Harry Sweeny from the Dorland Global Health.

MR. SWEENY: Thank you very much.

By way of background, I'm here. I'm the chair of the Coalition for Healthcare Communication. I also am an unreformed copyrighter of some 40 years standing in the business, and I wanted to, along with several of the other speakers, compliment the FDA on these last two days of hearings and, by the way, two days a couple of weeks ago on DTC.

I think about the FDA like I think about the Flying Wallendas, that famous circus act that worked without a net all the time and managed to pull off some amazing feats. I think that the pressure that the agency works under sometimes served up by people like me and by others, I think they function very, very well. And as you'll hear later, I think they do it under some constraints that we need to fix.

So here's the three topics that I would like to talk about. I saw the questions that the FDA

asked for, and I thought about the topic itself, and so these are the three that I've lined up.

First, how safe are prescription drugs?

And what makes a prescription drug different from an ordinary chemical?

And what steps do we need to take to help assure an understanding on the part of the public about the risks of prescription drugs?

Well, last Saturday night I was having dinner with a long time friend of mine, a trial lawyer who has survived two heart attacks and heart surgery; his daughter who had a GI incident this summer where they took out about half of her intestines; my friend's wife, who is a cancer survivor and who is now doing twice a week dialyses; my own wife, who is a communications professional; myself, and two friends of the daughter of my friend, one of whom was a pediatric pulmonologist and the other of whom was a dentist.

So there's seven of us sitting there, and I said, "Look. Before we get rolling here, I'd like to play a little game with you. Bear with me. Imagine a line. At one end is a zero and at the other end is a ten. So it's a ten-point scale. I'm going to ask you a question, and I want you to put your

finger on that line on the number where you think it belongs."

And they said, "Well, what's the question?"

And I said, "How safe are prescription drugs?"

Now, before I give you their answers, since it's after lunch and we're all having postprandial meltdown, I'd like you to think about that line, and where would you put your finger on that line?

Okay. Now, everybody who put their finger on four or less, less being dangerous or unsafe, show me your hands.

(No response.)

MR. SWEENY: Nobody at all? Okay. How about eight and above?

(Show of hands.)

MR. SWEENY: Okay. I'd say about a third. Is that fair?

CHAIRMAN SELIGMAN: We're going to abstain up here on the --

(Laughter.)

MR. SWEENY: Abstentions? All right.

Okay. So we had nobody below four. We

had perhaps a third of the people eight and above. In my little group of seven, we had two ones, a three, a four, and let's see. That's two ones, a three and a four, two fives, and one seven.

That's what we need to be doing on a population basis before we do anything about risk. We need to understand where people are in their understanding of how safe they think prescription drugs are.

There's a book by two fellows out of Harvard, Center for Risk. Some of you may be familiar with it, and in that book they distinguish two polarized points of view which drive all conversations about risk. All topics about this are very contentious, and in fact, the authors write that you can almost not have a noncontentious discussion these days on any of these topics.

But they outline two principles, one called Edmund Burke's precautionary principle, which basically says that all technology is not to be trusted and that you must prove it all. It's guilty until proven innocent, versus a more contemporary view that we've heard about in the last two days here about trying to balance risks and benefits so that we get some serious benefits out of it.

How safe are prescription drugs? Well, here's an example of the polarization. Safe enough to make them the fourth leading cause of death, said the head of the National Nutritional Foods Association a couple of years ago, not a group that's very fond of pharmaceuticals.

But Ropeik and Gray in their book on risk attempted to do something that is maybe unprecedented, and interestingly they did not do it for prescription drugs, although they did it for some disease entities, cancer and high blood pressure, I believe, and some others. But you can't probably read it on the bottom. They said we don't explain risks from drug reactions which are so unique to each individual that the discussion in the book about risk in general might, in fact, be dangerous for the reader.

Now, if this is what a couple of experts from Harvard believe about risk and they're dealing with all sorts of risk, airplanes and, you know, all of the rest of it that we know about, then how in the world can we expect an agency to deal with the topic in any sort of a meaningful way?

What makes a prescription drug different from the chemicals? Information. We used to say a prescription drug is a chemical poison wrapped in a

protective capsule of information. The more information you have about it and about its use and about its risks, the better off you are.

What is the value of the information? It separates reality from perception. It tells us what we know versus what we don't know or what we're uncertain about. It lets us make judgments about what's safe and what's dangerous, what we need to be fearful of and what we can be relaxed about.

But remember at the bottom of it all, familiarity breeds contempt. That's why we have campaigns like "Speed Kills," to remind us, and that's the kind of thing that we need in relation to prescription drugs.

There's another book that's out there now that's on the best seller list that's called Freakonomics. There's a very interesting set of observations in there. Steve Levitt, the economist is known for his in some cases bizarre applications of economic analysis to problem solving in problems that no one has approached before, and one of the things that he's very clear about is information asymmetry in the role of experts, and one of the only examples that he gives in the book is that of a doctor who was a cardiologist, interventional cardiologist, who was

getting patients from people in the community, and when he was asked why he was performing some procedures that probably shouldn't have been performed, he hesitated and then he said, "Because if I didn't do them and I sent them back to the primary care doc, they wouldn't refer patients to me anymore."

One of the things that hasn't been said here today is that in this complicated world that we work in, with all of the competing entities, it's extraordinarily difficult to try and make a move because it's a mexican standoff kind of a world where any move on one part is going to affect a move on the other part, and the unexpected consequences can be severe.

The other point that I wanted to make that Levitt talked about was about incentives. Now, the incentives for the doctor that I just described was clearly an economic incentive, but there are others. There are social incentives, and there are moral incentives, and in any given situation those are the arguments that are going to be brought forward, and in many cases that's what's going to be the decision point.

So what steps do we need to take to help assure an understanding of the risks? Well, my first

recommendation would be start low and go slow. What does that mean?

Well, a few years ago we made some recommendations to the agency. One of them was for a prescription drug warning box. If the problem is that the general public believes that prescription drugs are not potent, then we need to raise that awareness so that they understand it.

And I know the arguments about warning boxes on smoking, on tobacco and all of that business. Whether that's worked perfectly or not isn't the point. The point is that if you want to move the needle and if you believe that the public thinks that prescription drugs are trivial, then we need to move that needle in the other direction and a warning box might be a very good place to start.

We've heard also at this meeting about standardized icons and at an outreach public health program to inform the public as to what they mean. We thought that would be an excellent step five or six years ago, and we think it would be an excellent step now.

What else? We need to understand the barriers that consumers have to behaving the way we want them to behave. About two and a half years ago I

was asked to address a DTC conference on compliance, and I looked around, and as our last speaker indicated, there wasn't very much information on compliance as a result of DTC, and I was extremely frustrated.

So I typed this question in and I Googled it. "Why don't people do what they're supposed to do?" And I was amazed at the long list that I received. But one of them was from a book by an author by the name of Ferdinand Fournies, and Fournies knows why people don't behave the way they're supposed to. He's a consultant for some 30 years now. He was a professor in his youth at Columbia. He did a 15-year study of 25,000 employees, and then he wrote a book called Why Employees Don't Do What They're Supposed to Do and What You Can Do about It.

So I bought that book, and in there he had 16 different reasons, but I just picked these top ten on why people don't do what they're supposed to do. The first one, they don't know why they should do it. They don't know how to do it. They don't know what they should do. They think your way won't work. They think their way is better. They think they are doing it. They think they're going to be punished for doing it. There are no positive consequences for doing it.

It's beyond their personal limits. Nobody could do it.

Think about these things when you get an opportunity and think about relating them to some of the health care decisions that have to be made.

But then I went further, and I found that there was also interest in why physicians don't do what they are supposed to do according to some others. Cabana and his group sets forth a group of practice guidelines here or -- I'm sorry -- the reasons that doctors don't follow practice guidelines. A very thoughtful analysis of why not, and here's why.

Lack of awareness, easily overcome. Lack of agreement, more difficult. Lack of outcome expectancy, it won't work. Inertia. Lack of familiarity. Lack of self-efficacy or confidence, and the external barriers. My partners will make fun of me. They don't want to do it either. There's restrictions for managed care.

The problem is pervasive among human beings, not just doctors of patients. Patient expectations in the clinicians' role was treated in another article, and this goes back to the incentives. This was an article about what doctors ought to do in order to avoid litigation. It's stunning in its

simplicity. They need to talk to patients. They need to communicate better. What a surprise.

So we say start low and go slow. Understand the barriers. Connect the dots, and then what about risk perception itself?

Well, there's a fellow up at Rutgers. He and his partner, Neal Weinstein, he invented and put together a formula that he calls the risk equals hazard plus outrage formula, where hazard is a product of outcome severity and probability, and outrage is the soft stuff, trust, shared control, fairness, courtesy, all measurable.

And using this model for some 35 years, he and his group up there have worked on things like what's riskier, radon or radiation or nuclear waste, and what's consumer perception? And how does that industry communicate on that subject?

The risk perception people have a whole literature of their own. It's somewhat less than crisis management, but it's a lot more than the kind of communication skills that many of us bring to the party.

So we have those things, and what would the last admonition be? This one comes from Professor Bill Kissick at the University of Pennsylvania. He

told a story at a meeting I was at. He said, "You know, when I was a young doc," he said, "I used to lay asleep at night worrying about all the problems I was trying to solve, and I'd get up and I'd go charging around in the morning," and he said, "I did that until I got into my 40s."

And he said, "I got up one morning, and I realized, do you know what? There's always going to be a top ten cause of death." And he said, "I decided I would just slow down and think problems all the way through and not try to solve them so instantaneously."

Not a bad thought for what we're trying to deal with here.

Last but not least, I think we ought to be using the mental models approach. This one we've heard now from at least five speakers over the last couple of days. Remember Mrs. Robinson in the movie? Remember what the famous word was from the uncle? Plastics. Well, the word I'd like to leave everybody with coming out of this meeting is research, research before, research during, research afterwards. That's going to be our way out of the jungle.

I'll be happy to answer any questions you might have.

CHAIRMAN SELIGMAN: thank you very much.

Our final speaker is Vanessa Cullins from Planned Parenthood Federation of America.

DR. CULLINS: Thank you very much for giving me the opportunity to speak on behalf of Planned Parenthood Federation of America.

I was trained as an obstetrician-gynecologist and practiced for over ten years. I'm now Vice President for Medical Affairs for Planned Parenthood Federation of America.

Planned Parenthood Federation of America is the world's largest voluntary reproductive health care organization. It was founded in 1916 by Margaret Sanger, and now is composed of 120 affiliates plus the national office. The 120 affiliates have over 850 health care delivery sites and it serves over five million men, women, and teens each year.

The overwhelming majority of Planned Parenthood's health care services are preventive, and as such, we are striving on a daily basis to promote understanding of risk and benefits of preventive care activities. While most people we serve understand that the benefits of preventive care vastly outweigh the risk associated with preventive care, this information is always competing with sensational headlines about rare but expected adverse events and

with unfounded myths that circulate within a community.

PPFA's commitment is to advance consumer understanding and control of personal reproductive and sexual health care. So we find it imperative to increase health care provider and consumer understanding of individual and population risk factors.

And the reason why we find this to be so imperative is because a better understanding by both provider and consumer of both individual risk factors and population risk factors should serve to enhance informed decision making about health care.

Now, whether we're imparting information about immunizations, contraceptions, cervical cancer screening, STI screening, diagnosis, and treatment, or pregnancy options or any other preventive health care option, we find that we're in the situation where no medication and on intervention is without risk. Nothing is perfect in preventive health care.

In addition, the statistical information from the population based studies and also from the clinical studies appears to be poorly translated into individualized decision making, whether you're talking about decision making that is being pushed by health

care providers or clinicians or decision making that is made in conjunction with the health care provider and also the consumer.

In the interest of time, I'm going to limit my remarks about the FDA informational documents to those that are intended for consumers. My remarks are based on Ortho Evra consumer information, FDA News, FDA updates labeling for Ortho Evra contraceptive patch, and questions and answers, Ortho Evra.

The reason why I chose these three documents is because we're now currently struggling to help clinicians understand the new warning for Ortho Evra as it relates to the pharmacokinetic data, and we understand that the providers need to be able to place this warning in context in order to convey the information appropriately to consumers, to the women that they see that want to either initiate Ortho Evra use or continue Ortho Evra use.

In all three documents, the actual content that was covered was very good. However, as many of the speakers have already mentioned, the reading level and also the medical literacy level is very high.

These and other consumer information documents would benefit from a section that generally

and briefly outlines issues that the consumer in consultation with the health care provider might consider when trying to decide whether a risk, whether we're talking about a side effect or a serious adverse event, is worth taking because the risk-benefit balance in terms of whether or not you're going to start a medication or continue a medication or start a preventive activity and continue a preventive activity is based on individualized decision making that should take into account not only what that particular individual is at risk for as it relates to their population, their demographic characteristics, but also their personal behaviors and their personal medical risk factors, and personal medical risk factors including risk factors based upon behavior.

So the type of conversation that would need to occur is actually alluded to within one of the documents. It's actually within the Q&A. In the Q&A about Ortho Evra, there is a question: what should I tell my health care provider?

And there's another question: what are some possible side effects?

Now, missing is an explanation that such information should be used by the consumer in conjunction with the health care provider to make the

health care decision that this is information that will help to inform the risk-benefit equation for that particular individual.

Now, interestingly and appropriately, a specific example of risk-benefit consideration is found in the November 10th, 2005 FDA News, FDA updates relating for Ortho Evra contraceptive patch. Paragraph 3 gives balance and allows for individualization of the product through this particular statement.

Furthermore, women taking or considering using this product should work with their health care providers to balance the potential risk related to increased estrogen exposure against the risk of pregnancy if they do not follow the daily regimen associated with typical birth control pills.

Because Ortho Evra is a patch that is changed once a week, it decreases the chances associated with typical birth control pills that a woman might miss one or more daily doses.

Now, a similar helpful statement is found in a document titled "Questions and Answers, Ortho Evra." In this document it states, "When thinking about prescribing or using Ortho Evra, health care professionals and women need to balance the increased

exposure to estrogen against the chance of pregnancy if a birth control pill is not taken daily."

Now, granted, the sentences are too long. There isn't much clarity as we learned from our previous speaker, but the content is correct. The approach is correct.

What we need to be able to see is more of this approach in order to help both consumers and providers understand risk and benefits and determine that individualized risk-benefit balance.

What the speakers have conveyed today is that that information needs to be clearly understood and, therefore, the issues about research, testing, developing of tools, we're all in agreement or at least I'm in agreement and PPFA is in agreement that that work definitely need to be done.

At PPFA we applaud the FDA for having this public hearing specifically to receive comments on risk communication tools. PPFA, and I personally hope that this is the first of a more expanded process where the public will be invited to continue to participate and there will be focus group testing of tools that are developed by the FDA.

It's important that we use every day and, to quote our previous speaker, plain language and that

we begin to use comparisons that resonate with the individual learner, the individual decision makers, educational, cultural, social, personal health, and personal behavioral context.

Now, this implies that there is audience segmentation of messages designed to inform about risk. No one document is going to do it for every single audience, and that also was spoken to by earlier speakers.

To move in this direction regarding messaging of risk, many must be involved in first deconstruction and then the reconstruction of risk messaging. PPFA, Planned Parenthood Federation of America, offers its input and assistance in this effort, especially as it relates to reproductive and sexual health risk.

PPFA has already begun to work to improve clinical messaging about risk. Planned Parenthood Federation of American in partnership with the Association of Reproductive Health Professionals, which is usually called ARHP, is launching a multi-phased educational program designed to provide health care providers and consumers with improved understanding of risk associated with hormonal contraception.

Now, ARHP, Association of Reproductive Health Professionals, was founded in 1963, and it is an international nonprofit association of health care providers, researchers, educators, and other professionals. ARHP serves as an information and education resource for health care providers, the public, policy makers, and the media on a full range of reproductive and sexual health issues.

Our program is entitled "Putting Risk into Perspective, Making Informed Health Decisions." Now, we hope that we will be able to have this program ongoing for years and years because it is our intent to tackle various topical areas in preventive health. We hope to be able to have a module on immunizations, a module on laboratory screening tests, nonhormonal contraception, unintended pregnancy and child birth.

Also, we want to be able to address the myriad of preventive health measures and interventions that, while associated with small, measurable health and well-being risks, are extremely important for both individual health and also population public health.

We at ARHP and also PPFA would welcome further collaboration with the FDA and with others that have spoken, both today and also yesterday, as we

embark on this multi-phase project.

thank you.

CHAIRMAN SELIGMAN: Thank you, Dr. Cullins.

We'll turn to the panel to see if there are any questions. Yes, Nancy.

DR. OSTROVE: Mr. Ratto, and I apologize if I missed this because you had a lot of information out there. Now, your group actually puts together the information, the CMI. Can you speak more to what do you do?

I mean, what we heard here is research, research, research, test, test, test. You don't need to have large groups. How do you test the information?

I mean, you believe that your information is consistent with the Keystone criteria. How do you make that determination? What do you do to test with consumers? What can you tell us that might be helpful for us in terms of looking at our tools in that sense?

Can you give us more kind of specifics about that?

DR. RATTO: There haven't been any formal tests with our data, and I'm not sure about other providers as well, and that's why we're looking for

some collaboration via NCPIE since FDA has commissioned NCPIE to work on this CMI project in order to do research on this topic.

There have been a number of discussions and attempts to get funding, and at this point what we've done, we certainly have had input from our customers. We have millions of patients that are receiving our documentation, and we get pretty much daily feedback from the field from pharmacists and physicians about information. That's clearly not testing, but it is information that tells us areas that might be perceived as problematic in some way, and we certainly answer all of that in terms of research.

We use basic information. We have a detailed policy that we use, and basic information in terms of clarity and sentence structure and that sort of thing, and I think every one of our group has a considerable amount of clinical experience in working with physicians, patients, and other health care professionals, and it's based a lot on personal experience in terms of what works in terms of educating patients.

But we definitely feel that there needs to be more work done in this area. We've also been

involved with the NCPIE group in constructing a guide to the Keystone guidelines, essentially a working document from which we can essentially use as a way to operationalize the Keystone guidelines. We came up with that through the NCPIE criteria committee, and we certainly abide by some of those, all of those types of guidelines.

FDA has issued their own version of this with not as much detail or not as much concreteness to it, if you will, and so we've submitted that information quite some time ago to FDA in terms of that particular piece of data on the interpretation of Keystone.

So we're also looking basically to collaborate with the agency on this sort of thing in terms of getting a systematic approach to research established and the logical vehicle would be through the NCPIE organization.

Does that answer your question, Nancy?

DR. OSTROVE: Yes. Thank you very much.

DR. RATTO: Okay.

CHAIRMAN SELIGMAN: I had actually a question really more for point of clarification. In your presentation, Mr. Kamp, as well as in yours, Mr. Mayberry, you talked about conservatisms related to

the protection of the FDA jurisdiction. I wonder if you could just say a little bit more about what you mean by that protection and what the nature of your concern is in that realm when it comes to communicating safety information.

MR. KAMP: There seems to be a panoply of "wanna be FDAs" out there. Most importantly I see it in state legislatures, state Attorney Generals using their consumer protection area, perhaps most dangerously for the drug companies, plaintiffs' attorneys bringing cases on against drug companies on failure to warn.

California is one of the states that have had state laws that essentially require warnings that are inconsistent from the warnings of the FDA. That was a case actually that the General Counsel's Office of FDA intervened in, and in that case the drug company had to make a choice whether it followed the federal law or the state law.

These kinds of incursions on the jurisdiction of the FDA, I think, are very dangerous for all people involved, as I said, because I think we need one regulator that's professional, that knows what it's doing. The FDA is the right one, and that the FDA General Counsel's Office and others inside the

FDA must, I think, be very careful to insure that their regulations are understandable, have the reputation in the world as the gold standard or in the United States as the gold standard, and essentially through law and its prestige cause the rest of them to go away.

CHAIRMAN SELIGMAN: How would you apply that to information that in large measure we're talking about today that isn't really formally part of the label but is, you know, information about emerging risks, things that go out to consumers or to patients or to health care providers, you know, related to appropriate use of medications, concerns about on label or off label use.

I'm trying to sort of put it in the context of the discussion you've been having in the last couple of days, your concern about what various Attorneys Generals and state legislators are doing.

MR. KAMP: It's about the professional labeling part where the FDA -- the FDA's job in approving drugs is essentially the chemical entity approval and the communications envelope around it. When other entities get into the business of deciding what should be in that communication envelope that surrounds the drugs, you create a very difficult

situation for drug companies that want to do right. They just want to do it right, but it also adds to the confusion.

Now, my comments about that were not about the stuff that we talked about much of yesterday where, you know, how can we make our Web site more consumer friendly. That's not the issue. It's sort of the legal requirements of what an entity, most specifically the drug companies who are the regulated kind of companies, what kind of safety warnings they must have in order to follow the FDA regulations and to insure as much as possible that the professionals and consumers know what they need to know in order to take a drug safely.

DR. TRONTELL: We've talked today about communicating. We talked as well yesterday, and I think we've had, in my opinion, some implicit assumption that we're talking about risks where we have some degree of confidence that they're real. We believe that there's a degree of certainty attached to them.

I'd appreciate hearing from all of the panelists, from their own perspective, from the stakeholders that they represent's perspective. What is the best mechanism to describe risks that might be

classified as uncertain, where there's a glimmer or signal where telling people too much information might have unintended consequences of frightening them when it's not a certain risk, but where failure to warn might be considered paternalistic or less than fully transparent about what risk information is available, since a lot of safety information falls into this region at least for a period of time, until the risk is fully clarified.

Can you speak to how do we warn people when we're not quite sure what we're warning them about?

CHAIRMAN SELIGMAN: Dr. Cullins.

DR. CULLINS: First, I think that you're not warning people. You're informing people when you don't know that a particular adverse event is necessarily correlated to actual use of a medication, and I think that's the way to look at it, that there's a certain amount of information that people have a right to have, and the information as outlined by our previous speaker in that the main thing the needs to know is that the FDA is watching this. And the FDA will inform providers and consumers if anything different needs to be done as it relates to their individual health care.

I think people need guidance. Providers need and want guidance in terms of how they should really be processing the information, and that's some of what has, I think, been missing.

And I can understand the reluctance of a governmental agency to move in that direction, but if we're really talking about helping both providers and consumers to put the potential risk into context, there's guidance associated with that, and I think actually the sticking point is going to be in terms of how much guidance you can really give.

CHAIRMAN SELIGMAN: In that vein before we go on, I would be very interested, Dr. Cullins -- I know you talked about Ortho Evra -- the degree to which you or your association or your organization who can provide specific comments to us about those materials in way that will allow us to approve either the questions and answers or the alerts that will provide that kind of context will be much appreciated.

DR. CULLINS: I will.

MR. MAYBERRY: To my mind it gets really to the role of FDA and what your jurisdiction is, and the fact that the biggest tool that you have is the CGMPs in my mind, and you know, these are prescription drugs. They are only dispensed pursuant to a

prescription. So that implies a learned intermediary, you know. A doctor is going to inform you of anything that the doctor is aware of, and the pharmacist certainly plays a huge role in the learned intermediate growing role as well.

But, now, for FDA's side, to my mind, it's your responsibility to publish what is known without a doubt and what is largely suspected. That's what your job is, is to make those determinations.

And I know that Mr. Kamp will tell you that, you know, everybody is going to get sued and all drug businesses, all of the pharmaceutical manufacturers are going to go out of business, but at the end of the day, these are prescription drugs, and they all have some inherent amount of risk to them because they're prescription drugs.

CHAIRMAN SELIGMAN: Comments from the other side? Yes.

MR. KAMP: Yeah, I'm not sure everyone is going to get through. I think that Dr. Trontell asked a very good question, and I think I'd like to separate it out in two different things.

The most important one and the one that's central to the FDA is to decide when there's enough information to say something definitive about a risk,

and that's the job of the FDA. The FDA is and should continue to be the gold standard on the making of that judgment using the scientific evidence it has before it.

Now, I think there are going to be some, of course, who are dissatisfied with the Adderall message. We're watching it, but we don't know. But that is the answer. That was exactly the answer that the agency in an expert judgment came to at the time, and that's exactly what you should do, you should continue to do.

I don't have any idea what the right answer is on those kinds of things as they go forward. I trust the FDA to make the right decisions.

The other half is the one that we talked about today. Once you have made those decisions, once the decision is made that additional information needs to be out about possible new risks and situations like that, then it's a behavioral. It's a consumer communications issue.

My thought if I were in your position would be essentially to do the best job you can, explain it to the professionals, and then let the rest of the world, all those other folks who have a stake in this, the drug company itself, the pharmacists and

all of the other health care providers and supporters, the press and whatever, to do with it what they will.

But if you give the best information possible, you make the judgment you make, you explain them as well as you can, particularly to the professional community that needs to know them the best, then that's pretty much your job and you've got it done.

DR. RATTO: I would say that for the emerging safety information, one thing to do, adding onto the Planned Parenthood comments, would be move the disclaimer up to the top of that particular documentation and indicate clearly that it is preliminary information.

If the first thing you see which is the current situation is the bolded information about the fact that this drug can kill you if you're asthmatic, and you already are asthmatic, I think that's a problematic issue in terms of information that clearly is emerging and not proven.

CHAIRMAN SELIGMAN: Others wish to comment?

DR. KLEIMANN: Yes. Again, a very simple way of thinking about this, and I'm not trying to gloss over the complexities of this, but label it.

Maybe there is something that says we don't know, something that doesn't make people process through the sentences, process through the language, process all the way through the this hand and on the other hand and on this hand, but simply gives them the bottom line very simply up there.

Now, I know that that is complicated to do it simply, but, again, I think we see again and again that people need the label, the label that sums up, the label that directs them, that helps them know exactly what it is is being said, not simply having to process through all of the language themselves.

MR. SWEENEY: you asked the question yesterday about the role of the FDA, and I think this part of the meeting gives an opportunity to sum that up as the most trusted source of this kind of information. I think the rest of your role flows from that.

You are the consumer advocate and protector. You are the convener of experts. You are the consensus former. You are the information clearing house, and then you become the disseminator of information, and I think when we talk about the dissemination, some of the ideas that we've heard to set up some templates so that consumers can become

accustomed to dealing with this information in a readily understandable format, a road map of the information, if you will, that's what we do in the rest of the world and it doesn't make sense that we're not doing it for drug information.

CHAIRMAN SELIGMAN: Thank you for that comment.

Any other questions or comments from the panel?

(No response.)

CHAIRMAN SELIGMAN: Is there anyone else remaining in the audience who wishes at this time to say anything or make a statement?

(No response.)

CHAIRMAN SELIGMAN: Before I conclude, let me remind everyone that is here that we are, indeed, accepting statements and comments to the docket. Clearly many of the panelists have already provided their statements, which we already have, and I thank you for those.

Let me just simply add in conclusion then that I really appreciate not only this particular panel, but everyone who participated and contributed to our meeting in the last couple of days. I think everyone has been not only blunt, but fair, but also

very constructive in their comments, and particularly because I think at the end of the day, we all share ultimately the same goal, which is to insure that information that is provided out there to all of those, since we all at one point in our lives are either patients, consumers or in some cases, even health care givers; indeed, this information be given in a fair and constructive way, and that it be accessible and available to all.

Clearly, I've heard lots of messages about the way the FDA faces the world and I've heard a lot about our Internet site. We've also heard a lot about the panoply of messages and communication tools that we use as an organization, and the desire amongst many who have spoken here today about trying to certainly at least reduce that number or simplify them or at least certainly make clear what the purpose of these various tools are.

I've heard a lot about the importance of partnerships and about collaboration and about interaction and, you know, the needs to really engage not only the health care professional community, whether they be physicians, nurses, pharmacists or other organizations, as well as the specialty health care organizations.

I've heard a lot this last couple of days about the importance of standards and consistency and the need to insure that we not only have consistent approaches, but that the standards that are used for the development of this information be well and clearly understood.

And then finally, if I didn't say the word research, it's clear that we all need to not only understand the scientific underpinnings of good risk communication and clarity, but also that we need to have the kinds of resources that would allow us to both pretest, test during, and test after the development of many of these messages.

It was a delight, and I again thank you all for taking the time to be here, for traveling, for preparing your presentations and your submissions to the docket. It really left me with a profound appreciation as well as respect for not only the breadth of the community out there in this world that are interested in effective and valuable risk communication, but also a profound respect for the tremendous amount of expertise that's out there. It's certainly my hope, and I hope I speak on behalf of the other members of the panel that we can work together in the future to corral this tremendous amount of

energy and expertise and caring that exists out there.

So with that, thank you and I will close the proceedings on that note. Thank you all.

(Whereupon, at 3:27 p.m., the meeting was concluded.)