U.S. FOOD AND DRUG ADMINISTRATION

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CENTER FOR DRUG EVALUATION AND RESEARCH

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USE OF MEDICATION GUIDES TO DISTRIBUTE RISK INFORMATION TO PATIENTS

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PUBLIC HEARING

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WEDNESDAY, JUNE 13, 2007

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The public hearing convened at 8:30 a.m. at the National Transportation Safety Board Boardroom and Conference Center, 429 L'Enfant Plaza SW, Washington, DC, Paul Seligman, M.D., M.P.H., Associate Director, Safety Policy and Communication Staff, CDER, presiding.

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JOHN JENKINS, M.D., Director, Office of New Drugs, CDER
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REBECCA BURKHOLDER, National Consumers League
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LISA VAN SYCKEL, On Behalf of Janet Sisk of the Juvenile Justice Foundation
SUSAN NELSON, Consumer

I-N-D-E-X

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

8:34 a.m.

DR. SELIGMAN: Good morning and welcome to the second day of FDA's Part 15 hearing on medication guides.

My name is Paul Seligman. I'm the Associate Director for Safety Policy and Communication of the Center for Drug Evaluation and Research, and will again be serving as the presiding officer for today's Part 15 hearing.

Before I call the next panel to the table, I'd like to just go over briefly a few of the ground rules that I covered yesterday just to remind those of you who were here yesterday and to inform those of you who are new to the discussion today.

First of all, this public hearing is being held in accordance with Part 15 of the Code of Federal Regulations. As such, this hearing is a informal one and the rules of evidence do not apply.

We ask that no participant be interrupted during their presentations by another participant. And that only the presiding officer and the FDA panel may question presenters during

or at the conclusion of each presentation.

If there are those individuals in the audience who are attending the meeting but did not sign up in advance to speak, and if you wish to make such an oral presentation at the conclusion of the meeting, should time permit, please see our staff at the registration desk out front.

I also want to remind everyone that written comments on this topic may be submitted to the FDA's Division of Documents Management by July 12, 2007, as well as a transcript will be made available as well as a summary of the hearing proceedings on the Internet within 30 days after this hearing. And, again, please see the *Federal Register* notice in the blue folder for the information on our website.

We ask that individuals in the audience please turn off their cell phones, pagers, blackberrys or other devices that could interrupt the proceedings.

And finally, remind again everyone that our host the National Transportation Safety Board requests that no food or drink be brought into this auditorium.

We are joined today, again, by the same

distinguished panelists who were here yesterday. I don't think I need to reintroduce them at this time, other than point out that we have, starting from my right, Ilisa Bernstein, Toni Piazza-Hepp, John Jenkins, Bob Temple to my left, Jason Woo. And at the table on the floor Jeanine Best, Lillie Golson, Janet Norden and Dave Roeder.

So with that, may I invite the first panel, please, this morning to the table?

Once again, we will be using the sophisticated timing system that's on the podium to inform speakers as to when it's time to summarize their remarks and when their time has expired.

Our first presenter this morning Dr. Alex Michaels.

Dr. Michaels?

DR. MICHAELS: Good morning.

DR. SELIGMAN: Good morning. Yes, I think we can hear you. Thank you.

DR. MICHAELS: Good.

My name is Alex Michaels. I would like to thank the FDA, Dr. Seligman and his colleagues for this opportunity to present my professional perspective on medication guides, their

distribution and development and their use.

I will address questions posed in the *Federal Register* meeting announcement for consumers as well as touch on some points in the manufacturer's and academician researchers sections. Where other presenters have covered some of the ground yesterday, I will keep my comments brief.

By way of disclosure, I'm a primary care physician by training. I trained the pharmaceutical industry some 20 years ago and had the opportunity to work on late phase clinical trials, clinical drug safety and surveillance and product labeling.

I have no current pharmaceutical industry affiliation and have received no industry sponsorship in association with this presentation or this meeting.

To offer comments on the ways to improve communication to patients it is important to focus on the intended use of medication guides. What does the FDA expect them to do?

Where a drug product was known to pose a serious and significant health concern, medical guides are to provide information the FDA has

determined is necessary to the safe and effective use of these drugs by patients. Specifically, medication guides are intended to make patients aware of information concerning the known risks, risk or risks associated with drug products. That is, they identify and where possible quantify risks and with this information allow patients to make informed decisions about starting use, continuing use and discontinuing use of drug products. So they contribute to the patient's decision making process.

Now I want to step aside a bit from the prepared comments I have and just work through two concepts. The first is really a concept around medication guides and how the program has been put together. And I'd like to challenge the audience to comment on whether they think this is a push program or a pull program as it relates to how information is distributed. What principles were used?

Of course, the background is that the FDA mandated that manufacturers prepare and make available medication guides and that pharmacies or dispensers make them available to the public. So, do you see this as a push program or a pull

program?

Any thoughts from the audience? Okay. It's early.

I think it's a push program.

DR. SELIGMAN: Would you like a show of hands or --

DR. MICHAELS: Yes, please. A show of hands?

A pull program would be something like a pharmaceutical industry advertisement DTC where a patient sees and advertisement in *Newsweek* or *Time* or one of those journals and then goes to their doctor and says "Doc, we've tried diet, we've tried exercise, my cholesterol hasn't come down, what's next? What about this product X, would it work." And the doctor says sure, that's one of the ones that works, we could use that. So there's a pull, there's a demand that's created as opposed to a push program where information or product is pushed in the market.

Push program or pull program for medication guides? Push? Okay. Pull?

I agree. I think it's a push program, and I'll discuss why I think that's relevant later.

The second point that I wanted to touch on is how many of you have done a risk assessment when your physician has suggested that you take a medication? You're sitting in the doctor's office. Think back. The doctor said "Well, you need such-and-such a product to treat such-and-such a condition and here are some of the side effects, you know, nausea, vomiting, diarrhea, tummy ache, headache. Oh, and in a few cases perhaps there's been sudden death and maybe a heart attack or two. How do you deal with that? Is there a formal way that we as health professionals understand that? Is there a way that consumers have been conditioned or have been taught to assess risk?

It's a rhetorical question. Having been a consumer and having been in this position, I think it's difficult. And I think even with some, but not all of the medication guides, it remains difficult for even a trained health professional to really come to a conclusion about risk.

So those are really two points that I think are relevant as it relates to medication guides and the program.

Now to see how the medication guide program was working, I undertook an inquiry at a small number of pharmacies in the Bethesda and Rockville, Maryland areas. My findings were limited, but they parallel information that was presented yesterday.

I can say that all of the pharmacists that I spoke to were dispensing CMI with prescriptions. All pharmacies had medication guides provided by manufacturers. These were attached to the primary packaging, although this came as a surprise to the majority of pharmacists. They were not aware that there was a second or origami-folded document tucked onto various containers.

Only 25 percent of pharmacists were aware of the medication guide program. This knowledge came through internal work flow processes, as was discussed yesterday. And only medication guides for anti-inflammatory drugs and antidepressants were dispensed routinely.

Overall, only 25 percent of the pharmacies were dispensing medication guides and none of the pharmacists were aware of an FDA or other program designed to review or audit their

information dispensing practices. Having looked at the FDA's website and its content of medication guides, I think that what it reveals is that there is variation in the quantity of information provided and in their quantification of risk. I think some are very well done and I think others would benefit from change.

Based on the presentations yesterday, pharmacy practice appears to be served by a single succinct one or two page information document dispensed with new prescriptions. The information would be written at a grade school level and would contain a subset of known adverse effects. I'm not convinced that there is one best way to inform all consumers about medication risk. Consumers are heterogeneous. They differ in intelligence, education. language, income and many other characteristics. Some will be comfortable with making a decision with a 6th grade explanation while others will need a doctoral thesis. A one page tear-off will please some, while an extensive Medline search will satisfy others.

Can a medication guide be all things to all people? I don't think so, but it can certainly be a good starting point.

There are already many information sources on the Internet, for example, that purport to provide patients with reliable information. I suggest that the FDA actively set standards for patient information in an accessible way.

The package, which includes the medication guides where one is required, is the current information standard for product and risk information. I suggest the agency set up collaborations with existing information providers to develop what I've described as authentic patient information, be it printed or electronic, derived from the PI and reviewed by the agency.

As was alluded to yesterday, a logo or a symbol would be used to identify the material as FDA approved. In this way, the varying needs of consumers and health care professionals could be met.

This proposal would provide alternative distribution channels for the information in medication guides, PPIs and possibly additional adapted information instruments.

The need for current medication risk information begins before a treatment decision is made and continues after the medication has been

discontinued.

As was discussed yesterday, medication guide provided at the pharmacy comes very late in the decision cycle. The risks identified in the medication guide need to be considered before the treatment decision is made by the physician and the patient and long before the patient has paid for the prescription and gone home.

Once taking a medication, the patient should have continuous access to adverse event and risk information so emergent symptoms, that is new findings, can be accessed. New findings for the patient can be accessed and timely decisions about adverse event management or drug continuation or discontinuation can be made in consultation with treating physicians.

With the wide availability of electronic communications, it is probably time to consider methods of notifying patients about new black box warnings, the recall of lots or the withdrawal of medications from the market.

Here is some specific suggestions that can be applied to information documents like the medication guide.

The precise nature, content and

distribution channels for risk identification documents like those mentioned earlier should be the subject of additional systematic research involving all stakeholders, including consumers with diverse backgrounds. And follow-up studies should be used to determine how well these documents and distribution channels work and they should be the basis for building on success.

Information should be product specific or if a generic description it used, it should be annotated where a product differs from the description of its class.

Information should be understandable, that is include aides like a glossary of terms with simple definition. I'm not sure that patients are comfortable understanding the terms mania and psychosis without some assistance.

An FDA approved information source document should provide comprehensive information. Derivative documents should confirm with the intent of the source document and sources that comply with the spirit, emphasis and content of the FDA's standard source document should be identified with, as I mentioned, a logo.

The essence of my message is that there

needs to be provision of multiple sources of information, both content and distribution channels targeted at consumers and health care professionals with varying levels of education and understanding.

I think there's a need to create a demand, that is a pull, for product information and risk assessment through a concerted campaign.

I think there should be education of consumers and health care providers about the need to be informed and to consider risk when making treatment decisions.

We need to establish a common understanding among health care providers and patients and pharmacists and increase health literacy.

I think it is also important to publicize the availability and sources of FDA approved information. The medication guide program appears, unfortunately, to be one of the agency's best kept secrets despite efforts to stimulate distribution and use the documents.

I think it's prudent to provide assurance that information complies with the FDA standard. Again, the concept of logos or some sort

of identifying mark or symbol. This approach would give the agency a higher profile, a higher profile role in the creation and dissemination of consumer friendly efficacy, safety and risk information.

And I think there's a need to maintain an oversight program with regulatory powers to assure distribution of reliable risk information from key sources like pharmacies.

Since I've run out of time, I'll just briefly make a comment that I think it's important that the public be guided in their decision making. And I think there needs to be identification of the purposes of the medication guides, in some cases that's been done excellently, so that patients realize what they're for, how to use them, and how they're an aid in their decision making.

And I think it's time to consider, for example, a primary school curriculum that helps the public to understand drugs, the complex processes involved in approving them and risk.

I think there's one gap that has not been filled at this point, and that is the communication of emergent risk; that is risks that are identified after the patients start taking a

medication. And I think that, as I mentioned, relates to product recalls and withdrawals and newly identified safety risks. With modern communication techniques such as emails, cell phones, text messaging and instant messaging and automated phone dialing I think it's now possible to consider distribution of risk information to provide patients with current information.

Thank you.

DR. SELIGMAN: Thank you for your comments.

Are there any questions from the panel? Yes, Dr. Woo?

DR. WOO: Thank you, Dr. Michaels, for that broad overview of the helpful education needs that we need to address.

I'm interested in if you could speak directly to physician knowledge of medication guides and how it may effect their practice?

DR. MICHAELS: What I can tell you is that I haven't done any kind of formal assessment of that. But anecdotally, I think physicians are unaware of the medication guide program in general. I think there are some groups and organizations that are very aware of it, but I

think in general it's not well understood and certainly not used as a formal tool.

DR. SELIGMAN: Yes, Dr. Temple?

DR. TEMPLE: You indicated that once people get beyond the two pager or something and perhaps get beyond the approved product labeling there ought to be some program for qualifying, validating or something, other sources of information. Do you have more thoughts about that? It strikes me with terror, of course, because I think we'll need a very large increment of people to read everything.

The current information that's provided, you know, is not reviewed piece-by-piece. The current information that it's called, what, CMI? Yes, that's right. Is not reviewed piece-by-piece although there's general statements about how it should go. Are you thinking of something like that or an actual piece-by-piece review of large volumes of materials?

DR. MICHAELS: I don't have a knowledge of the inner workings of the FDA and what resources they have available. And I think it would be inappropriate for me to make recommendations in that regard.

But I think the essence of my comment is that a single document can't be all things to all people and that there should be additional sources of reliable and accurate information available that contained the FDA's core messages. And that information should be available at different levels of understandings. And it should be available from different distribution sources.

So maybe there's a call center that people, you know, have a 1-800 number and call into. Or perhaps they get it from Internet sources that aren't just putting information out but rather have some measure of compliance with the FDA's intent and content.

DR. TEMPLE: We're thinking about how to do that.

DR. SELIGMAN: Yes, one final question. Mr. Roeder?

MR. ROEDER: I have to confess that I never read anything that the pharmacist gives me.

DR. MICHAELS: You'd be shocked.

DR. SELIGMAN: This hearing is not for those kinds of confessions.

MR. ROEDER: I'll stop there. However, to get to what's been a common theme throughout

most of yesterday, too, I really listen to my physician. And for those like me who do risk benefit with somebody in an oral -- I mean in that kind of an exchange, is there something -- because what we're truly talking about, things that the FDA can do, are written documents. Is it essential that in this whole program that there be some component of a direct interaction with another person? Can we get to where we need to be purely through written documents, Internet, things like that?

DR. MICHAELS: I think for a proportion of the consuming public, yes. I think there will always be those people who are comfortable with a face-to-face dynamic discussion.

Sort of a pathway process would be the video processes that can be streamed over the Internet.

And then I think it's also possible to use a telemedicine approach, you know where you don't have to necessarily be face-to-face but there could be a knowledgeable intermediary whose available either through the Internet or phone who an individual could interact with.

Again, these are concepts. I'm not

suggesting that they just be implemented because they're probably more fantasy than they're reality at this point.

DR. SELIGMAN: Thank you, Dr. Michaels.

Our next presenter is Mr. Ray Bullman from the National Council on Patient Information and Education. Mr. Bullman?

MR. BULLMAN: Thank you.

Can you hear me?

DR. SELIGMAN: Yes.

MR. BULLMAN: Okay. I'll just stay here at the table since I don't have any slides.

My name is Ray Bullman. I'm Executive Vice President of the National Council on Patient Information and Education, NCPIE.

NCPIE is a nonprofit coalition of over a 100 organizations whose mission is to stimulate and improve communication of information on appropriate medicine use to the consumers and health care providers.

Please note that my comments do not necessarily reflect those of every individual member of the NCPIE coalition.

In the comments that I presented to the agency in December of 2005 at the public hearing

on communication of drug safety information, I posed a number of questions for your consideration about medication guides. Such questions that call for research and testing of medication guides remain relevant and will be reiterated in written comments submitted to the docket by NCPIE.

As noted in December of '05, there exists a nationwide pharmacy information delivery system with the capacity to disseminate written consumer medicine information with every prescription dispensed. How can this nationwide capacity to deliver timely, authoritative information to consumers be engaged, equipped, enabled and supported by government and the pharmaceutical industry to generate and disseminate emerging drug safety and risk information is a reasonable and a productive question for the agency to consider as opposed to how an externally developed medication guide program be force fit into such a system after the fact.

I would like to address several of the questions posed in the *Federal Register* announcement of the hearing. Two are directed at consumers and one at pharmacy supply chain

stakeholders.

The first question: What is the best way for consumers to be informed about the serious risks of a drug product or other important prescribing information?

The most effective way for consumers to be initially informed about the serious risks of a drug product or other important prescribing information is through meaningful communication with their health care providers. Oral counseling should be reinforced with adjunctive written information that the patient and the caregiver can read, understand and act upon when so advised.

In the U.S. we have in place a vast risk communication network made up of health care professionals. It consists of hundreds of thousands of health care providers including prescribers, pharmacists and nurses. In theory when medicines are prescribed in the outpatient setting, patients and their caregivers have several opportunities to be informed about any serious risks of a drug product: At the time the prescription is considered and written; when the medicine is dispensed at the pharmacy. This backstop process which theoretically provides a

safety net for consumers before starting a new medicine provides opportunity for health care providers to counsel and communication about specific medication benefits and risks for the exchange of relevant medicine and health information and question asking and answering.

In practice, FDA's consumer survey research points out as recently as '06 that consumers reported receipt of medication counseling at the prescriber's office and at the pharmacy, voluntarily provided or as the result of question asking has increased only marginally relative to instructions for use, precautions and side effects over the past decade.

Currently consumers routinely receive adjunctive written information at the pharmacy in the form of CMI. In 2003 FDA research found that nine of ten new prescriptions were accompanied with such CMI.

Is it helpful to produce separate drug risk information to inform consumers about serious risks of a drug product?

As noted, consumers are not regularly receiving risk information orally because there is n infrastructure to deliver such information or

because there is a shortage of opportunities or prescribers or pharmacists or nurses to deliver such information. Rather, consumers are not routinely receiving such risk information because current health practice doesn't recognize or value the time for the critical exchange between health care provider and patient.

Prescriptions are often written and provided with little communication about the medicine's risk or benefits and prescriptions are dispensed with the company's CMI that is not mediated by the pharmacists to point out, to clarify or reinforce key benefit or risk information. Patients are left with an information sheet stapled to the pharmacy bag and little or no encouragement from health care professionals to read and to heed such information.

Medication counseling guidelines exist for both prescribers and pharmacists, as do countless continuing CE programs or CME programs to improve oral counseling and communications either broadly or related to specific disease and/or conditions.

For example in 1998, NCPIE collaborated with the AMA which published guidelines for

physicians for counseling patients about prescription medicines in the ambulatory care setting. Those guidelines call for an updated medication record as part of the medical record and for a treatment plan noting that decisions regarding the use of prescription medications are best accomplished out of a collaboration between the physician and the patient. This requires that the patient be aware of relevant information regarding the prescribed medication as well as available alternatives. Therefore, the physician should discuss with the patient expectations of treatment and appropriate information regarding risks, benefits and appropriate alternatives of all medications that may be prescribed prior to deciding on a treatment plan.

The AMA guidelines also point out that physicians should counsel patients on their medications emphasizing what is medically significant.

Part two of question one: Do medication guides have a unique or important role in the education consumers? Compared to other written information distributed at the pharmacy, should it be combined or simplified?

In May of last year, '06, NCPIE commissioned IPSOS Public Affairs to conduct two consumer focus groups among daily prescription users in Rockville, Maryland. The following is limited to feedback on medication guides as requested in the *Federal Register* announcement for this meeting.

No respondents, even in the second group, who should be receiving them were familiar with medication guides or recalled receiving one.

In both groups, respondents indicated a willingness to read one to two pages of well formatted information in plain English: Keep it simple and keep it short was by far the respondents' preference for written information including medication guides.

In both NCPIE consumer focus groups, respondents felt that the type of information in the guides would best be discussed with the prescriber before they decide to fill a prescription or take that type of medication.

Due to the warning nature of the medication guide, most respondents felt that medication guides should be distributed both in the doctor's office and in pharmacies.

It could also be very helpful to consumers, who wish to have access to medication guides for those documents, to be posted in various formats on credible well-publicized websites including DailyMed and medlineplus.gov, for example. Yet to locate a product for which a medication guide is required, site visitors on DailyMed must work through multiple clicks and then scroll down past other patient information to reach the product's medication guides. Alternatively, a button off the DailyMed homepage entitled "Medication guides for select high risk medications" could take site visitors to an alphabetic rooster of all published medication guides available in various formats, including HTML and PDF for downloading.

Medlineplus program provides detailed information about prescriptions and OTCs yet refers consumers to the FDA website or the manufacturer's website to obtain a medication guide.

Question seven: What process improvements could be made to ensure that patients receive appropriate drug risk information at the pharmacy?

Between January of '05 and September of '06, NCPIE participated in two teleconferences and helped arrange and participated in three face-to-face meetings with FDA staff and stakeholders to discuss the feasibility of practicality of producing and disseminating medication guides electronically in conjunction with generation of CMI at the community pharmacy. During those meetings FDA was presented with examples of what was dubbed electronic medication guides or e-med guides. These e-med guides, which were generated as separate documents appended to corresponding CMI were produced on current pharmacy computer systems. Med guide content was produced in its entirety, but some layout and formatting stipulated in 21 CFR 208 was lacking with these e-med guides.

Meeting participants asked FDA to allow for electronic printing in conjunction with printing of CMI. FDA was encouraged to provide pharmacies that wished to do so with such waivers as needed to enable them to electronically print med guides. The agency has continued to stipulate that the onus for disseminating or establishing the means to disseminate med guides falls to the

drug sponsors and that the pharmacies should take up the issue with the various sponsors.

In addition to concurring with those who have recommended considering shortening the length of medication guides, I would also encourage the FDA to collaborate with these same stakeholders in developing and promoting a broad based medicine risk communication plan that builds on progress that has been made in the private and the public sectors. Consider what has occurred in relatively short fashion.

The private sector developed consensus guidelines for what constitutes useful written information, i.e, the action plan. The FDA issued its opinion of those action plan guidelines in the form of a final guidance on CMI, which signals to the private sector how those guidelines must be operationalized to be deemed useful by FDA. Drug information publishers have worked diligently to revive CMI clinical content in their monograph databases to meet action plan criteria.

Consider that there is a convergence of events and timing occurring now that if exploited aggressively could make it possible for the U.S. to have in place a comprehensive workable medicine

risk communication program by the end of this decade.

First, the FDA has lead agency status for helping ensure that key drug safety objectives for the nation are met. These are delineated in *Healthy People 2010*, Chapter 17 Medical Product Safety, 1704 of states to increase the proportion of patients receiving information that meets guidelines for usefulness when their new prescriptions are dispensed. Those guidelines refer to the action plan.

Increase the proportion of patients who receive verbal counseling from prescribers and pharmacists on the appropriate use and potential risks of medications.

Second, just two weeks ago the FDA announced creation of a new advisory committee to address risk communication. The risk communication advisory committee will help the agency understand the communication needs and priorities of the general public, advise FDA on development of strategic plans to communicate risks and benefits of products and make recommendations to FDA on what current research suggests about crafting risk and benefit messages as well as to how most

effectively communicate specific product information to vulnerable audiences.

For the short term, that is through 2010 and in order to avoid even more unintended consequences wrought by what I've heard some call a runaway med guide program, I would suggest in engaging in challenging the critical thinking and the academic rigor and the expertise of those who will constitute the new Risk Communication Advisory Committee as to the complexities and as to the opportunities brought by this problem at hand. Hold their feet to the fire and force them to look and think forward on this particular issue. This will require of them demanding more of technology than the pending document A to document B with a hard break separator. They will, as will we all, to ensure relevance have to consider integration and communication of risk information into the technology applications like electronic prescribing, personal health and medicine records and electronic medical records to account for how health care providers will communicate among themselves and with their patients and caregivers in the very not too distant future. Let's not continue to build from

a paper base when momentum, critical thinking and technology in health care is moving forward. Otherwise, as in the situation at hand, the tracks won't connect when we arrive at what we think we think is our destination.

Thank you very much for your consideration.

DR. SELIGMAN: Thank you, Mr. Bullman.

Questions from members of the panel for Mr. Bullman?

Yes, Bob Temple?

DR. TEMPLE: I guess my main worry is that one of the points that's made is that everything that needs to be kept at a relatively simple conceivably grade school level. Is that compatible that the presumably same people will use electronic media and be able to handle those things? Those strike me as different populations, but maybe I'm wrong.

I mean, there are mixed goals here, I realize, and I guess the question is how does one get at all the parties who take drugs?

MR. BULLMAN: Information would not in its entirety have to be limited to fifth, sixth, seventh or eighth grade reading level.

Particularly with technology it's possible and potential to deliver that perhaps by drilling down consumers can access as much or as relevant of level of information as they seek.

DR. TEMPLE: So you'd need at least some at a relatively low reading level to get started and access? It's sort of what Dr. Michaels was saying, and access to more detailed material as they wanted it?

MR. BULLMAN: Yes.

DR. SELIGMAN: Okay. Thank you, Mr. Bullman.

Our next presenter is Ms. Rebecca Burkholder from the National Consumers League.

MS. BURKHOLDER: Thank you.

I am Rebecca Burkholder from the National Consumers League. The National Consumers League is a private nonprofit advocacy group representing --

DR. SELIGMAN: Excuse me. Can you get a little closer to the microphone or just move it down towards you? There you go. Thank you.

MS. BURKHOLDER: The National Consumers League is a private nonprivate nonprofit advocacy group representing consumers on marketplace and

workplace issues. We are the nation's oldest consumer organization. The League provides government, businesses and other organizations with the consumer's perspective on various concerns including medication information.

Our mission is to protect and promote social and economic justice for consumers and workers in the United States and abroad.

NCL has worked extensively on the issues surrounding communication of information to consumers about the drugs they take. NCL is one of the participants on the Steering Committee for the Action Plan for the Provision of Useful Prescription Medicine Information. Furthermore, NCL provides patient education on medication uses issues and convenes a coalition of over 80 organizations called SOSRX dedicated to improving outpatient medication safety.

We're also a member of the Board of Directors of NCPIE and we support many of the comments made by NCPIE at this hearing this morning.

NCL is pleased to be able to comment today on FDA's medication guide program. We commend FDA for undertaking this effort to obtain

feedback regarding the medication guides.

In our comments, we will be addressing some of the questions posed in the *Federal Register* around the following issues: Communication of risk information; coordination with other patient information; delivery, and content.

The first *Federal Register* question for consumers was what is the best way for consumers to be informed about the serious risk of a drug product or other important prescribing information?

NCL believes it is vitally important that consumers receive information about drug risks, and we recognize that there are a myriad of factors impacting the delivery and comprehension of risk information. FDA should approach this question holistically and we are pleased to see that some of the key questions, such as what is the best way and place for consumers to receive risk information, are being explored today.

We also believe it is important to be aware of the context in which consumers receive risk information. We know that consumes can potentially receive information about the

medications they take from a variety of sources; physicians, pharmacists, the Internet, magazines, newspapers, directed consumer advertising, health plans, friends and families. Consumer understanding of risk information they receive is influenced by a number of factors including personal concepts of benefit and harm, subjective value judgments, cultural perspectives, different levels of fear and the existence of other risk factors.

Our recent SOSRX oral anticoagulant education campaign demonstrates the challenges of risk communications. Patient may say they understand medication risk information but still engage in risky behavior. While over 80 percent of the patients surveyed said they know they should tell their doctor or pharmacist when they are taking an OTC or dietary supplement with their blood thinner, less than half do so. And while the bast majority has experienced some type of side effect including bleeding or bruising, more than a third did not talk to their doctor about the reaction. These survey findings highlight the need for continuing consumer education on medication risks.

In light of the challenges of effectively communicating risk information, the FDA should evaluate the form and content of medication guides before it expands the program further. We do not know enough about consumer comprehension of medication guides to know if they are doing what they are supposed to do. Research is needed to answer such fundamental questions as: Are the medication guides useful to the patient? Are they comprehensible? Are they too long? Are they redundant? Should they be more balanced with both risk and benefit information?

FDA has tested or is researching other risk communication vehicles and should be applying the knowledge from those areas to medication guides. FDA research and other regulatory actions show the agency is looking to make print communication essential risk information more concise.

For example, professional labeling now will be including a highlights of prescribing information to help the health care professional quickly identify the most important information about the drug. And in light of data showing that consumers do not read or use the typical lengthy

brief summary of the prescribing information that accompanies prescription drug print advertising, FDA has needs to make an ongoing effort to find a better, more concise way to communicate risk information in print.

We understand that the Division of Drug Marketing, Advertising and Communications will be testing alternative brief summary formats, including a long format, a Q&A format, highlights and a drug facts box similar to the other drug facts now used on OTC drugs. The knowledge gained from this research should inform the medication guide format and content as well as the agency's own final guidance document entitled "Useful Written Medicine Information" from July 2006.

The *Federal Register* also asked, do medication guides have a unique or important role in educating consumers about these risks compared to other written medication information distributed at the pharmacy? Should the information be combined or simplified into fewer or one communications vehicles?

We recognize FDA has authority over the medication guide content and more limited authority over the CMI or consumer medication

information content, and that consequently the agency is trying to use the content it does control to assure that patients receive it. The result, however, is sometimes lengthy duplicative information and a broken delivery system.

The medication guide delivery system needs to be fixed. Some pharmacy systems cannot accommodate the formatting requirements of the FDA medication guide. Until such times as they upgrade, FDA should permit compliance with the rule, if the pharmacy delivers the medication guide content even if the precise formatting cannot be achieved.

Pharmacies and information providers should be permitted to incorporate medication guide content into CMI content and then distribute one document. So long as the medication guide risk information is clearly and promptly emphasized to the patient, the spirit of the medication guide program is maintained. That is necessary to avoid both overloading consumers with vast amount of potentially conflicting or duplicative information and to ensure that the information provided is clear and readable.

While the numerous pieces of medication

information, medication guides, CMI, brief summaries and PPIs may fulfill some distinct regulatory purpose of the FDA's, the nuance and distinctions between these documents are meaningless to the consumer. Consumers may not understand and probably don't care about the difference between the medication guide and the CMI. What they do care about is receiving understandable and useful information about the drugs they take.

A holistic approach to communicating drug risk should emphasize coordinating all patient information and consider using the same consistent format to convey information to consumers in various settings.

We commend the FDA for considering the prescription drug facts box, similar to the nutrition facts and OTC drug facts which already have widespread consumer acceptance as a potential way to satisfy the brief summary requirements for prescription drug advertising. The FDA should consider using the same prescription drug facts format, something consumers are already familiar with or the drug facts format for patient/pharmacy communications. This will promote greater

consistency in communicating drug risk information whether in advertising in the doctor's office or the pharmacy.

The *Federal Register* also asked: How do consumers prefer to receive the medication guide information and when should they receive the medication guide information?

Coupled with the content analysis of the medication guide there should be a reevaluation of when patients should receive the guides. The point of dispensing in the pharmacy should not be the first time the patient receives the medication guides warnings. Risk information in the medication guide needs to be communicated by the prescribing physician, in the first instance. If the point of dispensing is the first time the patient has received this information, the medication guide may discourage the patient from beginning the prescribed course of therapy.

The prescribing health care professional should be an integral part of any patient education process, including education on medication benefits and risk. NCL education campaigns often educate patients about the key questions they need to be asking their health care

professional, and at the same time provide health care professional with the patient educational materials so they are able to respond appropriately and answer patient questions. In the same way, the FDA's medication guide could do a better job of highlighting the items patients should discuss and share with the health care provider. And they should make sure they're not buried in the sometimes voluminous text of the guide.

Medication guides could serve as a basis for health care professional medication counseling if the first distribution is in the physician office with follow-up delivery at the pharmacy. Armed with the medication guide, health care professionals could be prepared to discuss the risks and benefits with the individual patient in a way that is clear and understandable and takes into account the individual's patient risk factors.

There should be alternative mechanisms for delivery of the medication guide if the patient wishes, including by email or first class mail.

We commend the FDA for its newly

redesigned FDA consumer webpage where consumers can access a medication guide for a particular drug whether searching by drug name or active ingredient. While it is important to offer alternative delivery systems including the Internet, we do need to recognize that not everyone is online. According to the 2003 U.S. Census Bureau data less than a third of those over 65 have Internet access and racial disparities also exist with regard to online access.

Finally, the *Federal Register* also asks: How can medication guides be improved?

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

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

to obtain more realistic rates of adverse events, the FDA should actively encourage reporting directly from patients. To achieve this, FDA needs to add a consumer portal to the existing system and then to promote the system's new features to consumers.

As part of this effort, FDA should revamp over the telephone and Internet interfaces to make them more user friendly and develop a separate event report form that is easier for consumers to use.

The medication guides provide an excellent opportunity to promote the MedWatch system. The guides should direct patients to report adverse events to their health care professional and also provide consumers with the MedWatch web address and toll free number to encourage direct reporting.

Thank you for this opportunity to comment.

DR. SELIGMAN: Thank you for your comments.

Do we have any questions or comments from members of the panel?

Yes. Ilisa Bernstein?

DR. BERNSTEIN: Thank you very much.

You said something that we heard yesterday as well, in that consumers don't know the difference what's a med guide, what's CMI; it's just all information to them. And then we heard Dr. Michaels suggests that there be some sort of logo or imprimatur on the medication guide. What do you think the impact or influence that that might have on consumers that if there is some sort of imprimatur that this is FDA approved information? Because we heard that people aren't reading it. And if they don't know that it is FDA approved or just information that's just being provided, do you think that would give any more credence to the information that people would read it?

MS. BURKHOLDER: I think that's something that should be considered, absolutely. But I think what's probably more important is to have consistency in format. And one of the things I talked about is if you have it in the medication guide, then also have it in other ways that you're conveying risk information to consumers, whether it be direct to consumer advertising. But I think having some type of very simple, understandable

with some research into it, FDA logo could be helpful for consumers.

DR. SELIGMAN: Lisa Mathis?

DR. MATHIS: Thank you for presentation.

I just was wondering as far as the logo goes, would it also be helpful to have the logo on packaging so that way pharmacists and physicians could easily identify those products which had an attached medication guide?

MS. BURKHOLDER: Well, I guess from our standpoint there needs to be consistency across the board. We wouldn't want consumers to be confused that the logo is FDA -- that that drug is FDA approved and the other medications aren't, if I understand what you're saying. So I think it would need to be looked at very carefully.

But you're saying with those that have that information that somehow that that's identified?

DR. MATHIS: Right. Because it seems like right now physicians when they are prescribing the medication even on electronic systems don't get any cues or may not be aware that there is a medication guide that exists. And

then when the pharmacists pulls the bottle off the shelf -- yesterday we saw a bottle that actually had marked on it a medication guide accompanied this prescription. But I don't think that that's consistent. And so I don't think that there's anyway for physicians and pharmacists to readily identify those drugs to which they should be handing medication guides or discussing the medication guides with the patient.

MS. BURKHOLDER: That would be helpful for that piece of information. For the pharmacist, the one thing you want to be careful is not to create a two tier system in the sense of the eyes of the consumer that this information has those risks I particularly need to be aware of, but what about that other medication. I don't need to be aware of those risks.

So, you would just want to be careful how you present it.

DR. MATHIS: And I do understand that. But in some sense, that's the point of the medication guide.

MS. BURKHOLDER: Exactly.

DR. MATHIS: This drug has a special safety concern that people need to be aware of.

MS. BURKHOLDER: So again, it would depend on wording and presentation.

DR. SELIGMAN: Yes, Bob Temple?

DR. TEMPLE: I think I have something of the same question. Many people have said, and it seems obvious, that the time to at least begin these discussions is with the prescriber who should be talking to the patient about this and why the prescriber thinks it's a good deal for the patient and here's the -- do you see any particular way of getting these things into the doctor's office in a way that would make the physician actually use them? You know, my physician types everything he does into his computer and conceivably could get feedback that said there's a med guide here, why don't you talk about.

And I already know that pharmacies signal potential drug interactions that no one ever tells you about. I got a call from my pharmacist when I prescribed something that triggered a signal, and they said do you know you're not supposed to use those two things together? I checked back and went back to the pharmacist, found the person who called me and

said "This is my 12th prescription for this. No one ever told me that before." And what she said was that the signal comes up all the time and they just push the off button.

MS. BURKHOLDER: Yes. Yes.

DR. TEMPLE: So it seems at least possible that busy people can ignore any conceivable thing. So I just wondered if you had thoughts about how to get the prescriber/patient interaction better? I mean are there mechanisms for doing that?

MS. BURKHOLDER: Right. Well, if I had that answer, then I would be probably not very rich, I think. But the electronic health system I think offers a perfect opportunity for what you're talking about when the physician is prescribing. But, again, if there's too much noise on the system, they're not going to be paying attention to it.

I do not have any perfect answer to this. I do think that the more -- I mean, you don't want to put the onus on consumers, but the more they're aware of to ask questions of their physician about a medication they're taking, then they can start the conversation. Fortunately we

would hope that physicians would also have that information, and I think the electronic health system is a perfect way to do that.

DR. SELIGMAN: Very good. Thank you very much.

Our next speaker is Dr. John Kamp from the Coalition of Health Care Communication.

Dr. Kamp?

DR. KAMP: Thank you, Doctor, and thanks for inviting me on behalf of the Coalition for Healthcare Communication. Just briefly, the Coalition for Healthcare Communication is a coalition of a group of trade associations and companies that care about communication, effective communication. Most of them work for word device and biocompanies, it includes publishers who do medical journals and CME, advertising and public relations and other agencies.

I'm going to try and make just a few major points today so we can maybe even catch up on some time. The first one I want to make is I want to applaud the agency for creating an Advisory Committee on Risk Communications. The IOM report in FDA clearly gets it. You're on the right vector. Keep going on that right vector.

My second point is that communication to consumers is incredibly hard. The FDA must really appreciate its own limits and its limited ability to operate in this area. The limits of printed materials and the great panoply if not the assault of information that's now available to consumers on these and related issues that could tend to confuse and otherwise get in the way of good compliance.

I also want to recommend that the agency expand its progress in recognizing the clear distinctions between professional communications and the needs of consumer communications in these areas. And because you've heard me before, I will discuss a few of the First Amendment issues and also I will again recommend that the agency work very aggressively to protect its jurisdiction, especially against those that I call the FDA want-to-bes who are creating inconsistent rules from time-to-time.

What are the reasons for this new focus of FDA and others beyond the concerns, maybe hyper concerns about safety? The most important concern I suggest is of the high rates of noncompliance with the drug regiments that doctors are

prescribing. These jeopardize the patient's health and the public health. Let me just use two examples that I think you very well appreciate.

A recent study on hypertension drugs suggests that the rates of noncompliance are somewhere between 30 and 60 percent. In my own case, a Type 2 diabetic, I'm appalled to find that most treated Type 2 diabetics have an ALC of over eight, which as the medical folks in this room know, the standard of care is 6.5, in some cases 7 in others.

Noncompliance is rampant. We need to do all that we can to fix it.

Unfortunately, patients do understand when they have these chronic diseases for the most part that there are long term effects to noncompliance. But they have not for the most part totally connected these sort of theoretical, it almost seems to them, concerns about noncompliance with their own particular current and future health. We need to do a better job with medication guides and all the other things that we do to communicate to consumers to do this.

Focusing just for a moment on the advisory committee and the advisory committee

process, the 10 to 20 year process where the FDA has been focusing much more effectively on communication to consumers. We need to make sure that the new advisory committee and other activities inside the agency take into account the communication needs of consumers do not systematically exclude many of the people through conflict of interest provisions, systematically exclude many of the people who can serve on those committees most effectively.

We must also develop, I think, a set of social scientific standards that the agency and the outside world understands and appreciates like the gold standard that the FDA uses in other places. The rules must be simple, the enforcement must be clear, direct and respected throughout our system.

We also must somehow, and I don't know how to do this I know, we must somehow respect the fact of off-label prescribing. As a Type 2 diabetic I take eight drugs everyday, six of them are off-label. We have to figure out a way to deal with that reality of the consumer marketplace in a way that makes sense for us, for the American public and for drug safety.

On the advisory committees and on this activity I suggest that we start with a very basic premise that may sound revolutionary in this room. I suggest that we start with the consumer and the understanding of the consumer when we look at all of these. Let me put it another way that will put a finer point on it. Maybe it's time for us to throw out all the academic, doctors and the lawyers in the room as these decisions are made and begin with a basic understanding of the consumer patient on each drug and let them develop a set of principles and a set of information that must be in these med guides before the doctors and lawyers go in and focus instead on the label, in some cases, or in liability in other cases.

Somehow we must begin with the consumers in a better way. The good news about consumers is consumers do want to know more about how to use their drugs safely and effectively. The other piece of good news is they trust their doctors. We need to begin with that kind of information and then develop information and messages that don't confuse them and also reassure them. One of the great notions in consumer behavior is the one of cognitive dissidence. After

making a decision, and for the most case drug decisions are made by the doctors, there's always some consumer dissidence about that. How do we help them get over that dissidence? How do we use these med guides as a way to reassure them that they're on the right course and to pay attention to the details they need to pay attention to, and then comply appropriately with the directions?

The messages must be developed, I think, much more directly than they have been now with the prescribing physicians that know patients very well.

Now I wanted to suggest that although you may be tired of listening to Dan Troy and his successor Sheldon Bradshaw about the First Amendment, I will suggest that it's not so hard to follow the First Amendment in these areas, and I think the agency has been doing a much better job in the last decade and a half than it has done before. But let me simplify this First Amendment requirements and all these kinds of activities.

You must do first essentially what you're doing right here, and that is develop a public record. But you must remember that the FDA under the Central Hudson test of the First

Amendment, the FDA before it does a communication mandate must accept the fact that it has the burden of proof on four areas. It must articulate a need for the new rules; it must know -- know that the policies worked, the limits on speech will work; it must consider all the alternatives to speech mandates, and; it must use marketing limits only as a last resort.

Finally, I want to talk about the market jurisdiction. The FDA must protect this jurisdiction to develop the communication to consumers around us. I want, by the way, to start by praising Dr. Lutter yesterday who in the House Commerce Committee hearing on the new PDUFA bill told the Committee that he was very concerned about late night additions of preemption language in the PDUFA bill that would have limited the preemption ability of the FDA to get in the way of many of the FDA wanabes who might create new different, maybe even inconsistent communication mandates. We must resist the inconsistent State laws and Attorney General enforcement where the states are beginning to believe that they are the ones that are the expert in this communications issues and they can develop new rules sometimes

inconsistent with the FDA's.

The FDA must continue to very actively participate in those state cases and those tort cases where the public interest and the public health is put at risk by these.

We must resist the private actions for failure to warn in false advertising. I read last night again the 1998 report and order on this, and I think it was although it was perhaps the right response at the time, the FDA said there that these threats from FDA wannabes, as I'll call them, were not sufficient to force the FDA at that time to go to a very strict preemption standard. I think in the last ten years we have found out that that's not true, that these wannabes are getting in the way.

I think we also must respect and understand that even others inside the Federal Government, including the HHS IG under False Claims Act jurisdiction is getting in the way sometimes of this good FDA policy driven consume-based social science understanding of what consumers need in this area and perhaps developing inconsistent rules.

You can only blow away that kind of FDA

wannabe action by consistent and effective leadership in this area. That requires clear understandable rules, effective enforcement, and more importantly with new understanding of consumer behavior for and about their needs for effective and efficient and understandable communication. You're well on your way. Congratulations. We're here to help you if we can.

Thank you very much.

DR. SELIGMAN: Thank you, Dr. Kamp.

Do we have any questions from members of the panel for Dr. Kamp? Yes, Jeanine Best?

MS. BEST: Yes. Thank you for your presentation.

I'd be very interested in hearing how you would propose language to reassure a patient when we're discussing serious risks in a med guide? What would you propose we could do to reassure a patient?

DR. KAMP: I think we need, again, to start with patients and understanding. Patients are reading those because they want to do it and want to do it right. But I remember when I first was prescribed a statin in the mid-'80s, my doctor told me don't read the fine print in the package

that comes with this drug because it will scare you and you will stop taking it. I want you instead, just to do, and she gave me the things that I needed to do, including making sure I see her regularly to make sure that a liver test be done and other kinds of things.

I think we're past that. But I think we need to focus on the need for compliance and these med guides can be used actually to increase compliance as well as to increase the awareness about drug safety. I don't really know how to do that without talking to consumers about each drug and each contact source.

DR. SELIGMAN: Ilisa Bernstein?

DR. BERNSTEIN: I certainty don't want to go down the road and challenge you on any First Amendment issues, but I just have a question in that when you were referring Central Hudson four factors you said the fourth one was -- you related to marketing material. You're not implying that med guides are marketing pieces, are you?

DR. KAMP: It's a very interesting question. If it's not marketing materials, if it is in fact is the exchange of basic scientific information, we could even have a tougher test. I

don't know for sure which test would apply there. At the very least, though, it was be the Central Hudson test, and that's easier.

And so I think what we need to do to make sure that we stay way out of the way of those kinds of mandates. But if it's in effect in the same category as political or in here public health exchange of information, the burden would be even higher. Almost impossible, frankly. And we don't want to go there.

DR. SELIGMAN: Yes, Lisa Mathis?

DR. MATHIS: When you say that physicians need to be more --

DR. KAMP: I'm sorry, I can't hear you.

DR. MATHIS: I heard you state that physicians should be working with their patients on their programs and safe use of medication. And we've heard that plan throughout yesterday and today that communication between the physician and patient are vital to the proper use of medication. And yet when you look at the medical school curriculum, pharmacology isn't up there and one of the most frequently taken classes. It tends to be in the first two years of school. So I think physicians are not always adequately armed to use

medication in the most safe and efficacious way unless they keep up with the information.

Is there some suggestion that a medication guide being required to be given by the physician would be a starting place or would you resist that as well?

DR. KAMP: Well, I'm not sure that that isn't a good idea, frankly. I'm not sure that it should be mandated. I don't think that the FDA wants to get the cross hairs again of physicians by mandating what they do in those conversations. But I think what the agencies have found in their studies of doctor/patients' communications that there's a serious trust level there and docs, when they have tools available to them to help them explain to patients, we could call it a leave behind in the advertising agency business, a leave behind that the patients can refer to that works for them that they really like those kind of tools because those tools help them get across the important compliance information. And I think perhaps with more information even in these about the value of the compliance, the discussion of the efficacy of the drug being totally depended upon appropriate compliance. And I was looking at a

few I get. And that's there. There is a theme there about in order for your drug to work like it's supposed to, you're going to have to take it in these kinds of ways.

Maybe we need to do a better job of that communication. Talk to the patients a little bit more.

The advertising agencies who are studying these doctor/patient conversations tell me that doctors are looking for better tools. And making those available seems to me like a no brainier almost in this context.

I don't think you and I can fix medical education these days. But having been a surrogate student through my daughter's four years through just recently, I have to say it's pretty darn good in this pharmacology area. At least it was in her case.

DR. SELIGMAN: Thank you, Dr. Kamp.

DR. KAMP: Thank you.

DR. SELIGMAN: Our next presenter is Ms. Marcie Bough from the American Pharmacists Association.

MS. BOUGH: Good morning. Thank you.

I am Marcie Bough, a pharmacist with

the American Pharmacists Association and serve as the Director of Federal Regulatory Affairs for the Association. Thank you for the opportunity to present the views of the nation's pharmacists today.

APhA was founded in 1852 as the American Pharmaceutical Association and represents over 60,000

pharmacists, student pharmacists and scientists as part of our members and is the largest and longest serving association for pharmacists.

Pharmacists are committed to improving patient health through the appropriate use of both prescription and over the counter products. Pharmacists help patients manage their medications with patient education activities through written information, oral consultation and medication therapy management. Med guides are one method that pharmacists use to provide this information for medications that the FDA has determined has an immediate risk. Unfortunately, the med guide program is becoming a burden on pharmacists' time, work flow and the ability to provide patient care.

Therefore, APhA not only supports the agencies initiative to reevaluate and improve the

medication guide program, APhA's concerned with the growing number of med guides, the logistics for handling them in the pharmacy and getting them to patients and the impact and disruption to pharmacy work flow, and the information overload being experienced by patients receiving these medications.

While not officially APhA survey, my following comments will be based on 396 respondents to a recent poll APhA did to its members addressing the questions in the *Federal Register* and the pharmacy professions general concerns. Many of the comments are also similar to those that are addressed within the white paper in June 2006, "Patient Safety Implications and Implementation To the Current FDA Mandated Medication Guide Program" supported by APhA and many of the other associations at this meeting.

More than three quarters of the respondents to the survey said the program is working poorly or is more of a hassle and they're doing their best to make it work. Less than ten percent said that it's working well or moderately well.

Pharmacists are receiving med guide

notification through a variety of ways. Less than ten percent said via electronic notification. Roughly a quarter said that they received information through written notification from the manufacturer. Nearly a third said they received notification via FDA notices and updates. And nearly a third said they receive notification from their employer or company communications. And approximately 40 percent said they receive notification about med guides from pharmacy publications.

In the interest of time in this session, I hope to address questions that the FDA raised to the pharmacy profession in the *Federal Register.* Questions two, three, four, six and seven.

APhA members reported that they receive med guides in several ways. Hard copy from the manufacturer either attached to individual bottles, bundled as tear-off pads or pamphlets or as part of the package insert. By searching and accessing an Internet site such as the FDA's site that includes all of the med guide information our company Internet sites to print the med guide PDFs. Or the med guides print automatically

through the pharmacy's labeling program that is already printing the patient information monograph.

Unfortunately, many of the pharmacists reported significant administrative burden and the logistical problems trying to comply with the med guide regulations. Pharmacists are experiencing disruption in pharmacy work flow and that sometimes impact the overall quality of care patients receive.

The growing number of med guides is becoming unmanageable and potentially decreasing the program's impact on consumers.

Consumers are also confused with med guides and ask pharmacists why they are receiving it, especially when the warning does not apply to them and they've asked how come they haven't received this from the physician.

The majority of responders said that med guide information overlaps with other information they are receiving, such as the CMI, and that there's too much information in the med guide for some patients to understand, and it is not written in a consumer friendly health literacy level. That the information overload means that

much of the material is simply not being read.

Many of the pharmacists responded to our survey that the challenge that they face with trying to meet the med guide regulations included:

Not receiving med guides from manufacturers in a timely manner or in sufficient quantity;

Continually trying to reorder med guides to provide them with the first fill or each refill of the prescription, often with limited success on those reorders, and;

Dealing with multiple formats of med guides with varying storage requirements.

Of concern, we had a noticeable number of members state that they have never received med guides from manufacturers or if they did receive the information, they received it only the first time and have yet to receive another shipment of med guides. Often med guides are not shipped with the actual product, and there's extra time required by the pharmacy staff to match those med guides to the product.

Pharmacists are also concerned with the lack of reimbursement for the time and attention that is required for pharmacy staff to manage the

med guide programs.

Members did note that med guides that come with the unit of use packaging worked better than others. Similar to the examples we heard yesterday, med guides that come as part of the packaged insert are cumbersome and require pharmacists to unfold the labeling information glued to the bottle, find the med guide information that is often nondistinguishable from the other information and cut off the med guide information, sometimes leaving text that's for the professional information on the back side of the paper. Often leaving patients wondering what it is they're missing.

One of the biggest complaints and burdens that we've heard from pharmacists is that multiple dose bottles typically come with one med guide attached, thus requiring the pharmacist to either photocopy, print or reorder med guides for the remaining prescriptions being filled from that bottle.

What are some recommendations of changes that can be made? APhA recommends streamlining the med guide program to allow pharmacy software vendors more flexibility to

integrate med guide information within the patient information already being automatically printed with each prescription.

We recommend investigating whether the med guide section should be separate and distinct from the rest of the information or integrated within the CMI. However, the agency must address how the cost shift from manufacturers to pharmacy would be addressed in this system understanding that manufacturers are required to provide med guides. Any change to the current system must take steps to prevent substantial cost shifts related to printing expenses and explore possible reimbursement solutions.

As mentioned, some pharmacies have already retooled their systems to automatically print med guides with their patient information and CMI as an appendage. I will show you an example of this at the end of my presentation.

APhA strongly encourages the agency to consider how to facilitate systems to automatically print this information with the other information.

As for the current system, we recommend exploring ways to enforce the requirement for

manufacturers to supply an adequate number of hard copy med guides to pharmacies. We also recommend streamlining the reordering system so pharmacists can go to one website or call one number to reorder all med guides instead of trying to track down the number of locations as they do now and finding ways to help improve the distribution system so that med guides come automatically upon reordering medications.

We also recommend standardizing the information that must be included in the patient information and require:

Consistent format, look and feel to the med guide information;

Scientifically evaluating the usefulness of this program and to see if it's reaching its intended use, and;

Determine relative value to other safety measures and patient care services that could be used with these same resources;

Also removing the requirement to provide med guides with every refill and limit it to the first refill and then once a year thereafter upon prescription renewal;

In considering how prescribers could be

better informed that these products require med guides and that prescribers should have the opportunity to provide med guides at the point of prescribing.

APhA also recommends that the med guide information be combined with the package insert material and CMI so that one piece of material is provided to the patient.

We recommend that the agency refer to examples of consumer friendly drug information produced by the agency's own Office of Women's Health. While not as detailed as the med guide and not a complete balance of benefit and risk, the material is easy to read, written at a fourth or fifth grade level, well formatted and includes health information focusing on safe medication use.

Two page factsheets are available on a wide variety of health issues and longer guides provide an overview of the medication used to treat certain conditions, the side effects and what a consumer should know about the treatment.

I addressed electronic distribution previously in my comments, but wanted to take this opportunity to highlight electronic availability

of med guides to consumers. Pharmacists support the electronic availability of all med guides on a central easy to access user friendly online location that is maintained by the FDA similar to the site now, but easier to access.

Electronic med guides should be easy to access, download and print for all pharmacists, other health care providers and consumers.

Additionally, APhA supports the electronic distribution or emailing of med guides to patients, but only for those systems that support an email distribution process and for those patients that request and agree to receive the med guide electronically.

Back to survey results. Only a third of the responders said that they felt that med guide was a valuable tool in counseling patients and are somewhat useful. Over half of the respondents said that the time dealing with med guides could be better spent by pharmacists talking to the patient about the medication.

Improving medication use requires the patient understanding their medication and how to use them. Provided the opportunity, pharmacists working with patients and physicians are the best

equipped and positioned to address many medication related problems and improving medication use. While not within the scope of this meeting, and it does address a previous question about talking with the patient face-to-face, APhA strongly encourages the agency to include in its review of the med guide program the prospect of expanding access to pharmacists' provided medication therapy management or MTM services for patients on medications that require a med guide.

APhA also recommends that the agency consider changing the med guide program when information covers a class of drugs when the risk information is of class effect.

The med guide system should be streamlined and if the med guides were based on a class, and the logistics of the handling of med guides would be improved, thus decreasing pharmacy storage issues and the administrative burden on pharmacy staff. However, for medications that do have a unique and rare side effect that are not shared with the other drugs in the same class, this information would need to be specifically highlighted in the med guide.

The agency should consider having a

class med guide that specifically lists perhaps per paragraph each drug in the class while highlighting those specific information.

In conclusion, an improved med guide system is critically important to:

Better balance the benefit versus risk information;

To incorporate into one piece of patient information;

To streamline the logistics and work flow within the pharmacy practice setting, and;

And to propose solutions to avoiding a substantial cost shift to pharmacy.

Reengineering the med guide system will help decrease the administrative burden so that pharmacists can focus more time and resources on getting the right medication with the right directions to the right patient in helping patients manage their medications.

Thank you. And we look forward to working with you on this important issue.

And I'll show you some examples right now.

This is an example of the sheet that would actually come from one from one of the

stores, Target, is this particular example. And they have integrated the PDF format of the med guides with the labeling that's printing off. And you may be aware of this, but when the prescription comes out for the label itself, it would print off -- this is a dummy mockup of the label. It would come out printing like this. The very next page that prints is the med guide. This one's for NSAIDs. And it prints out. So this helps with the pharmacy work flow knowing that it's attached to this particular product for naproxen, and that technicians and pharmacy staff know that this is attached with this product.

Another example that I don't have with me actually happens at Safeway where the labeling marks an M on the label so that pharmacy staff know that there's a med guide accompanying that product.

We have discussed the possibilities of marking the actual prescription bottle, the stock bottle, with a symbol. That may or may not be helpful depending on if pharmacists actually see the bottle or if they have automatic dispensing systems where they wouldn't see the bottle, the source bottle for those prescriptions.

But these are opportunities for at least alerting the health care providers that a med guide would be available. And to address some of the electronic prescribing opportunities and electronic health record information, there are innovations and opportunities so that when someone who is either entering the prescription for these products with med guides that, yes, something would pop up on that screen so that they are alerted there's a med guide. And they could click on that, see the med guide. And also at the pharmacy level sometimes based on filling the prescription by the NDC number similarly that we heard yesterday, some of the programs have integrated a popup that alerts them that there's a med guide.

That's all the information I have. And I'll be happy to answer any questions.

DR. SELIGMAN: Thank you, Ms. Bough.

I'd love to see those materials if you wouldn't mind sharing them with the panel.

MS. BOUGH: Yes. Yes.

DR. SELIGMAN: And ask if there are any questions? Yes, Lillie Golson?

MS. GOLSON: Yes. I was wondering. I

work in the Office of Generic Drugs and often times we have the larger package sizes of like 5,000.

MS. BOUGH: Yes.

MS. GOLSON: And we always ask that they provide more guides for the refills, as you were mentioning that you often run out and have to photocopy.

MS. BOUGH: Yes.

MS. GOLSON: What my question is, is do these additional med guides or extra inserts, do they actually arrive to the pharmacies, number one? Is that helpful to have that extra number of med guides sent to the pharmacies or is there a storage problem where you really don't find them useful and end up discarding them? And what's the preferred format? We've done the pads, which I work also, I find the pads very helpful but I don't know if that's helpful in the pharmacies; if we have them attached at the end where they can be torn off? And I know the young lady showed it yesterday where they weren't perforated where they could be easily torn and she had to cut them. So that's not useful.

Do you have any feedback on whether

you're getting them in the pharmacies, whether it's useful to do that or does it create a storage problem and which format is preferred?

MS. BOUGH: Well, that's a good question. And based on our feedback many are not receiving them with those refills of manufacturer provided products.

One of the problems is that many of the distribution systems from the manufacturer through wholesaler have a hard time matching packaging for the actual prescription drug product bottles and then this paper information that's not integrated well within their distribution systems.

Often times, med guides will show up to the pharmacy either attached to those boxes as part of a shipment, but you still might not know which it is that they're going to or as a separate shipment, especially on the reorders for those products. So it causes a problem for matching up the products with the med guides because there's also a storage issue for paperwork within the pharmacy. There's prime real estate on a pharmacy counter for what's going to be here. And where can be med guide information be stored efficiently, especially when there's such a varying format for

how they are provided. If it was a standardized process so that pharmacists and other health care professionals knew that these were all going to be supplied in the same way, have kind of the same look and feel, it would standardize the system and it would really improve patient safety because pharmacists and patients would be familiar, more familiar with how they should be receiving this information.

But I think the overwhelming feedback we heard was that the best system would be to integrate med guide information to the automatic printing process that already are in pharmacies for printing the prescription label, the consumer medication information, the CMI. And then as the example I showed, being able to either print as an appendage the med guide information or integrating it into the existing test but with an appropriate format and look. But that way it would at least be efficient and with the product based on filling that prescription.

DR. SELIGMAN: Dr. Woo?

DR. WOO: It's a broader question to the panel, and again as I expressed earlier with the comments Dr. Michaels, that I appreciate the

breadth of the problem of getting good information to consumers being the end objective. And also by the understanding that this panel has demonstrated about their understanding of the limited authority that the agency has over the practice of medicine and pharmacy.

I'm just kind of summarizing the solution that I'm hearing. It's similar to what Dr. Jenkins had mentioned yesterday. That in an effort to streamline and standardize and provide a central -- at least a recognized authority on credible information that what's being recommended essentially is a Back to the Future where the issue that addressed the CMI in the past where the agency didn't have the authority or didn't take the stance to standardize that information but leave it up to the manufacturers or sponsors to provide that is not a good solution. That you would prefer to see the agency have more authority on putting out the actual CMI and improving that. And I'd just be interested in your comments in response to that as a solution.

MS. BOUGH: I think looking at the information that is provided, it's all well intended. And everyone agrees that patients should

be aware of the information of the medications that they're taking. But we also need to let them know that there's benefit and risk evaluation between what they're taking and talking with the prescribers, the pharmacist, the patient; that triad so that there's a health care team helping them manage their medication. And this med guide and the CMI information are products to help in that, but nothing should replace as a paper product actual conversations and discussions with the health care team. But anyway that we can help facilitate this piece being more efficient would benefit the entire program and streamline the process.

The other panel can address this, too.

DR. SELIGMAN: Other comments from the panel before we -- yes? Mr. Bullman?

MR. BULLMAN: On this issue of potentially combining a combined product, CMI and med guide information I certainly, and I think we've heard this, that I think the issue or the feasibility deserves close attention and consideration, but it would appear to be doable by embedding key risk messages into the CMI monograph with attention paid to offsetting this particular

section of this particular information there would need to be a continued discussion about the mechanics of how this could be accomplished and about the still present issue, obviously, of it were an appended type process where the information comes through in the whole as a separate element of the document of the issue of, as we've heard in terms of cost shifting between the pharmacy and the PhRMA sponsors. And to whether such a combined program or if the content of CMI and med guides were combined into a regulated program, would that be more useful or how useful that would be for consumers and caregivers, you will hear I think from panels that are coming up from those in the private sector that the system that's in place and their pharmacy information network that's in place in the nation today can much more quickly move emerging risk information into the marketplace than the existing current med guide program. And so I think that's an important consideration that would have to be considered as well; that information can be entered into monographs and can start being disseminated such that updated information reaches consumers in a much more timely fashion than the

current program.

Thank you.

DR. SELIGMAN: Do you have any additional questions? Toni Piazza-Hepp and then Ilisa.

DR. PIAZZA-HEPP: We can really appreciate the many logistical issues surrounding the receipt and distribution of med guides, and you expressed this very well. So we thank you very much for that.

Your survey was very interesting and it did look like your respondents were aware what medication guides were and that they should be distributed, et cetera. We've heard in other surveys and also from a few comments from consumers yesterday that actually many pharmacists are not aware even of what medication guides are, even if they're asked can I have the med guide, they don't know what they're talking about.

And I guess my question is how can we -- assuming we can get to these other logistical issues and we certainly want to do that, how can we better educate our practicing pharmacists about what medication guides are, why they're important, that they should be distributed? Has APhA made

any efforts to this effect or what would you consider mechanisms that pharmacists would best get this information, like you know pharmacy, et cetera?

MS. BOUGH: Well, you have a good comment. And I think that the overall educational campaign that we all should work on together, whether it's FDA information or specific pharmacy association, other health care providers process and distribute out to their members really can improve on our focus on med guides. And I know that as this information is becoming more available and we develop continuing education programs on these products that require med guides, we're trying to include this type of information within that CE presentation or whether that's oral and written. And as the pharmacy profession itself moves forward with medication therapy management, pharmacists face-to-face services with those patients, we're developing a lot of information of what information needs to be portrayed to the consumers, educational materials. Med guides falls into this because it's a tool that the pharmacists can use to actually sit down and talk to the patient about that. So, you know,

we plan on integrating that type of information and what tools and resources are available. But I think we can highlight on our own information and in our publications to members and to the pharmacy profession what med guides are. And we may need to step back and everyone really put out a med guide 101 so that all the health care professionals are aware of what they are and that it's not just pharmacists' responsibility to provide this information. But we've heard we need to educate the prescribers, consumers and the pharmacists and all the other health care providers on their benefit and their use.

So I think as we move forward we're definitely going to try to highlight this activity more and do what we can. We'll be publishing information in our publication about this particular meeting, and that can help jump start our activity in helping to educate the profession.

But I think you raise a good point that we also need to loop in the state pharmacy associations and boards of pharmacy and look at what they look at on an inspection or their educational pieces to help really educate the profession.

DR. SELIGMAN: Thank you very much.

In deference to the next panel, I'm going to conclude this discussion, thank the panelists for their input.

We'll take a 15 minute break at this time and reconvene at 10:30. Thank you.

(Whereupon, at 10:17 a.m. a recess until 10:34 p.m.)

DR. SELIGMAN: If everyone would please find their seats, I'd like to begin in a couple of minutes.

Thank you.

And I'd like to welcome our next panel, and begin by inviting Dr. Catherine Melfi from Lilly to the podium, please.

DR. MELFI: Good morning. I'm Dr. Catherine Melfi, Scientific Director of U.S. Regulatory Affairs at Eli Lilly and Company.

On behalf of Lilly thank you for the opportunity to participate in this public hearing on medication guides. I'm pleased to be here today.

At Lilly we're --

DR. SELIGMAN: Please stand a little closer to the mike, if you don't mind. Thank you.

DR. MELFI: At Lilly we're committed to provide --

DR. SELIGMAN: No, I can't hear you at all. Try that again. The button should be open, okay?

DR. MELFI: I'll start over. I'm Dr. Catherine Melfi --

DR. SELIGMAN: Perfect.

DR. MELFI: -- Scientific Director in U.S. Regulatory Affairs at Eli Lilly and Company.

On behalf of Lily, thank you for the opportunity to participate in this public hearing on medication guides. I'm pleased to be here today.

At Lily we are committed to providing answers that matter through medicines and through information for some of the world's most urgent medical needs. Lilly is committed to patient safety and considers medication guides an important communication tool for appropriate products, as described in FDA's final rule. And we support efforts to provide balanced and meaningful information that patients will receive, read and understand. We support efforts to find better ways to make sure patients receive med guides,

including leveraging any processes or technologies that may evolve from the ongoing paperless or electronic labeling initiatives.

In short, Lilly believes that med guides can provide patients and their families with timely, accurate and understandable information about the benefits and risks of particular treatments in order to enable more informed decision making and to help patients and their families know what may happen during treatment.

Med guides can be an important way to warn patients about potential risks but again, as others have stated, they should not be written in such way that frightens patients so that they're afraid to take a medication that could provide substantial benefits. Patients and their families must have necessary information to make fully informed decisions.

I hope this hearing can help all of us work together to find better ways to make sure patients and their families are receiving clear, understandable and timely information about the products that require med guides.

The questions posed by FDA in the

meeting notice for this hearing to each of the relevant parties are very important. Lilly's pleased that FDA is seeking input from developers, providers, distributors and even researchers of medication guides, but most importantly from patients and their families, the ultimate consumers of the information.

I'll provide answers to the six questions posed to manufacturers in FDA's meeting notice and I'll make some additional remarks regarding communication of important information about medications to patients based on Lilly's experience.

First, FDA asks how we ensure compliance with the med guide requirements and how we ensure that pharmacies are receiving a sufficient supply of med guides.

To ensure compliance with the med guide requirements Lilly has policies and procedures in place that define and control how work activities are completed. These documents are approved by management, reviewed and updated on a regular schedule, and compliance is expected of all employees whose work is governed by these documents. So Lilly's policies and procedure for

U.S. labeling, which includes medication guides, are consistent with the FDA requirements and Lilly corporate labeling policies. All areas involved in the creation, printing, packaging and distribution of med guides must comply with these policies and procedures, and they all have monitoring and auditing plans in place to ensure compliance with the area policies and procedures.

Once a med guide is developed, approved by FDA and printed the packaging of med guides is conducted according to the corporate policies. The med guides are physically attached to or included with the product in adequate quantities so that a med guide is available for each prescription, typically a 30 day supply. In addition, instructions for dispensing med guides are included on cartons and labels of the applicable products.

In addition, Lilly provides a central call center to which any questions and concerns can be directed, including requests for and questions about medication guides. Together, these efforts ensure that we meet regulatory requirements for pharmaceutical manufacturers regarding med guides and that dispensers of our

products will have enough med guides so that one can be provided each time the product is dispensed.

Next, FDA asks whether means other than paper, such as electronic files, have been used to supply med guides. Lilly does not currently use means other than paper to supply the med guides. Pharmacy and third party vendors have a range and variety of technological capabilities around receiving and distributing electronic files, thus making standard electronic distribution difficult. Having said that, however, utilizing advances in technology to rapidly communicate approved product information to health care professionals and patients such as using the NLM DailyMed database continues to increase. As such, Lilly supports leveraging the evolving paperless labeling initiatives for use of med guides. In fact, Lilly is actively involved in the paperless labeling initiative on which PhRMA and FDA are also collaborating.

In addition for applicable Lilly products, med guides are available on the Lilly product websites for easy electronic access. The med guides for these products are accessible with

one mouse click from each product's home page with the link clearly labeled.

Next FDA asks how we instruct pharmacies that med guides must be disposed with certain prescription drugs. As stated in response to question one, instructions for dispensing med guides are included on cartons and labels of applicable products. Specifically, instructions such as medication guide is to be dispensed to patients is printed in bold font on the cartons and the labels of these products.

And related to that question, FDA asks about a standardized language or a uniform symbol on the container label for the required instruction to dispensers. As you know, space limitation on container labels can make it difficult to require an additional statement on most labels. With other required information such as bar code, NDC number, active ingredients, dosage strength, quantity, storage conditions and more an additional standardize phrase is likely to be missed.

Regarding a uniform symbol if one is adopted, an appropriate introduction of the symbol and its meaning would be very important. Lilly

does not have a specific symbol to propose at this time, but if one is used it should be one that's prominent but does not take up a lot of space and is universally recognized.. It would be great if the symbol had such easy prominence and recognition as that bright green Mr. Yuck sticker that was introduced in 1971 for poisons. I just read somewhere that within six months of when it was introduced, it had a 96 percent recognition rate in the general public.

Anyway, this notion of immediate notification that a product is one that requires a med guide is an area where technology can be helpful. Many pharmacies already have software that automatically notifies the pharmacists when he or she enters a prescription for a product that requires a med guide. With paperless distribution and standardized software the med guide could be printed out at the time that the prescription is dispensed.

Furthermore, and as others have mentioned, as physicians move toward electronic prescribing it could also be possible for a med guide to be printed out right at the time a prescription for one of these products is written.

This may be advantageous so that patients and their families have an opportunity to look at the med guide while still at the prescriber's office and have it with them when they go to the pharmacy to fill their prescription.

FDA's fifth question asks what can be done by means of packaging such as unit of use so that a med guide can be distributed with each prescription. Again, to help ensure that pharmacies receive a sufficient supply of med guides, Lilly attaches the medication guide to each sample and pharmacy trade bottle for effective products. One medication guide is provided for each 30 day supply of the product. So if a medication is packaged in bulk rather than in individual 30 day supplies, then multiple medication guides are provided in the bulk container in order to facilitate distribution of the med guide with individual consumer prescriptions.

One difficulty with unit of use packaging, however, are things like insurance coverage or prescribed dosing may require that some packages be opened and split anyway, if something other than a standard 30 day supply is

appropriate. Again, this is an excellent example of where paperless labeling could have a significant impact and represents an area where industry, pharmacies and the FDA can collaborate to help patients receive the med guide when each prescription is written rather than trying to combine them by providing extra pieces of paper.

FDA's final question to manufacturers asks about advantages and disadvantages of medication guides to cover a class of drugs rather than having a separate med guide for each product in a class. If there is a class of drug that all have the same risk that needs to be conveyed, ideally this should be done in the context of each individual product rather than as a single document covering the class. This way that class risk information can be balanced by the information about each individual product, including things like dosing instructions, known benefits, proper use and any other key information that can provide benefits with accurate, understandable and useful information. Again, so that patients and their families can make more fully informed decisions.

Also with effective use of electronic

labeling initiatives, med guides could be associated with an NDC number, then there wouldn't really be any efficiencies gained by having med guides that cover a class of drugs. As stated, it's important for patients and their families to know and understand what might happen during treatment. If only potential risks are included in the med guides, then patients aren't getting the full picture. With med guides that cover a class of drugs, it might be more difficult to provide that balanced information that's relevant for a particular product.

Now I've gone through the six questions that FDA posed to manufacturers in the meeting notice. I'd like to make a couple of additional points about communication of risk information in general and the use of med guides as a communication tool in particular.

Regarding a communication of risk information, earlier this year the *Drug Information Journal* published an article that had some Lilly authors on it and it presents the results from research conducted to evaluate risk communication specifically in print DTC ads. The study used a questionnaire-based method to

evaluate the effectiveness of risk communication in print ads that varied the risk information both with regard to format and content. The highest scoring ads in terms of effectiveness, comprehension and recall of risk information contained the risk information in a prominent window. Further, as the number of side effects listed in the ads increased, more consumers recalled no side effects correctly.

Realizing that this research focused on a different communication vehicle so it may not be directly applicable to med guides, it still further emphasizes the need to conduct studies specifically in med guides to evaluate the effectiveness of the current approaches and how improvements may be made.

Other recent research, including that piece late last year in the *Annals of Internal Medicine* that examined comprehension of information such as dosing instructions and the recent article in *Health Affairs* that focused on the usefulness and limitations of written drug information showed that there's a lot of work that needs to be done in the area of appropriately informing patients and health care providers about

the benefits, risks and proper use of medications.

As emphasized throughout my statement, Lilly is committed to patient safety and considers med guides an important communication tool for appropriate products. And we support efforts to provide balanced and meaningful information that patients will receive, read and understand. If you think of med guides as food, people need to receive it, they need to consume it, and they need to digest it. In addition, people need a balanced and nutritious diet. The same is true for med guides. People need to read them, receive them and understand them, plus they must contain useful and balanced information.

Many of the questions explored in this hearing have focused on the way to improve patient access to medication guides. Again it's equally important, as we've heard, to evaluate and to try to improve what's in the medication guides. Risk information should be put in context with known benefits to allow for the balanced assessment of these medications in order to make informed decisions.

Finally, research is needed to evaluate comprehension and understandability of the med

guides. So again it's not just the access, but really it's the ABCs, access, balance and comprehension. The ABCs must not be looked at as individual letters, but must be looked at together as the ABCs.

Thank you for the opportunity to participate in this discussion today.

DR. SELIGMAN: Thank you for your comments, Dr. Melfi.

Any questions from members of the panel? Dr. Woo.

DR. WOO: Yes. Just a quick question about -- and thank you, Dr. Melfi for your presentation.

We heard from a couple of the pharmacy associations that some pharmacists reported difficulty in getting med guides when they ran out. Have you heard of any of those complaints or how does your company address it?

DR. MELFI: I personally have not heard of any of those complaints, and I typically would through our labeling department.

I do know that Lilly tends to over supply med guides in some cases. This wasn't a med guide, but it was a PPI. It's just one anecdote

that I think illustrates. But it was a case where we had printed the tear-off pads of the PPI when a product was approved, sent them out to pharmacies so that they would all have them, and then our quality groups said no, no, you actually have to include them with the product. So in addition to the tear pads, we included several PPIs right in the package. We had to ripe open the boxes and put the PPIs in.

But I know that in general Lilly does tend to over supply. And they present the med guides and PPIs and literature like that as a separate entity so that they don't have to be torn off or scissored off from the other labeling as well.

DR. SELIGMAN: Janet Norden?

MS. NORDEN: It sounds like you're using paper to get the med guides to the pharmacy. We have heard from others that they receive these from different manufacturers in electronic PDF files or CD ROMs, things like that. I'm just curious as to if you've explored that or if you've considered any other means besides paper?

DR. MELFI: Well, Lilly as I mentioned is actively involved in the paperless labeling

initiative, and so we're certainly thinking about that. But as far as med guides we have those SOPs and standards in place that really relate to the paper provision of them. That being said, I think if we were to receive a phone call to our central call center to ask about access to a med guide, we could certainly steer someone toward our product page and direct them to the link on the product homepage where they can get to the medication guide.

DR. SELIGMAN: Bob Temple?

DR. TEMPLE: Because we've been aware of the difficulties of getting people to recognize that there's a med guide that needs to be handed out with medicines, we in my ODE office have strongly encouraged people to develop unit of use packages when there's a med guide. Sometimes when a drug is about to be approved, we usually gain acceptance of that approach. But if it's after the fact, we encounter considerable resistance. Where are you on this?

My understanding is that European marketing is almost entirely unit of use. And of course, OTC marketing is entirely unit of use, so it can't be that expensive.

Where are you on this and how would you feel it become more the rule than the exception?

DR. MELFI: That's a tough one for me to answer on behalf of Lilly. But I can talk about the experience that we have with the products I'm familiar with on unit of use. I know that fairly recently, one of our products had a med guide revised and we have been providing that as unit of use packaging, where the med guide is physically attached to the 30 count units that are sent to the pharmacy. But again, we're also hearing that in some cases --I've actually heard that some insurance companies now cover a 34 day supply of medications. And so what the pharmacists are doing is then, they're opening up another one of those unit of use, dumping out four pills and I don't know what they do with the med guide in that case.

So again, we could provide "unit of use" but I think in some cases with some medications it's even hard to determine what a unit of use really is.

DR. SELIGMAN: Thank you, Dr. Melfi.

Our next speaker is Dr. Isma Benattia from Wyeth?

DR. BENATTIA: Good morning. My name is

Isma Benattia. I'm the head of the Global Labeling Division at Wyeth, part of the pharamacoviligance and epidemiology group.

On behalf of Wyeth, thank you for the opportunity to participate into this discussion and this public hearing. I'm very pleased to have this opportunity to present today.

I'll be addressing the questions posed to the manufacturer through our experience in the implementation of the recent med guide, especially for the class med guide with the antidepressants.

The Food and Drug Administration may require a medication guide to prevent serious adverse effect for products that poses serious and specific health concerns. Medication guides are a special form of labeling specifically targeted to patients.

When a medication guide is required, it's the responsibility of the pharmaceutical manufacturer to ensure that the FDA approved patient labeling are available in enough quantities to deliver one to each patient for whom the product has been prescribed. The authorized dispensers are pharmacists and health care providers.

Before addressing the specific implementation, again, of the class medication guide I'll be referring a lot to the recent antidepressant example, it is important for the agency to know that we at Wyeth are committed to supporting the safe and appropriate use of our prescription medication. Accordingly, Wyeth shares the agency's view regarding the important role of medication guides as a communication to help patient and their family make fully informed treatment decision in consultation with their health care provider.

In this regard, Wyeth according to our internal procedures and in compliance with the Food and Drug Administration requirement distributes the FDA approved medication guides to pharmacists.

We also, Wyeth also makes medication guides available by additional needs, including online outlet and the toll free number that the patient can call and speak with a person with our medical communication specialist who will provide current prescribing information and further product information upon request.

Now I'm going to go into more detail

and share our experience with the implementation of the medication guides as part of the new class labeling when we were asked to implement antidepressant medication guide effects to unit of use packages.

Following the FDA Public Health Advisory Committee on October '04, work began on dissemination of medication guide entitled "About Using Antidepressant in Children and Adolescents." The preparation was conducted in closed consultation between the FDA and consortium of antidepressant manufacturers of branded and generic. That included Wyeth.

In order to expedite the distribution of the medication guide, the consortium contracted with a service provider to print and distribute tear-off pads to pharmacists and physician throughout the United States. And the distribution to patients began in July '05.

In addition, Wyeth has implemented with manufacturing plants for our antidepressants Effexor XR and Effexor product line to achieve Wyeth and FDA ultimate goal of ensuring that medication guides are systematically provided to patients through unit of use packaging.

In December '05, Wyeth introduced its unit of use packages with medication guides and prescribing information leaflet firmly affixed to all marketed strengths of Effexor and Effexor XR. In this regard, Effexor and Effexor XR are now sold only in unit of use packages for retail pharmacy.

Wyeth efforts in providing medication guides did not end with the unit of use packages only. We also changed the physician sample packages. In February '05 Wyeth begun including an antidepressant medication guides in its sample packages for Effexor XR.

We also recognize that for whatever reason, there might exist the situation where the medication guides may not be available or provided with the prescribed product. For example, a medication guide may inadvertently become detached from the package, a patient or his or her family may displace this information, or in some cases generic manufacturers may not offer unit of use packaging as a means of ensuring distribution of medication guide. To help to mitigate these circumstances, Wyeth makes the antidepressant medication guides available at Wyeth's online location including the corporate

website, the Wyeth corporate website, the product specific website and a patient education program and support program for depressed patients taking the product. Time to Talk is the name of the program, will offer access to the medication guide.

Furthermore, a patient or their family can also call, as I mentioned, the medical communication department, an 800 number, to request current prescribing information and additional product information.

In conclusion, and I just want to again stress that Wyeth is in compliance with our internal procedure and with the FDA requirement regarding the distribution of medication guide. We have taken numerous steps to ensure that the patients who are prescribed our product that necessitate a medication guide, including our antidepressants, receive a medication guide when their medication is dispensed or have access at other means at other times to medication guides throughout the course of the therapy.

With that, again as I mentioned, I tried to share with you our implementation plan I would like to ask and welcome your questions now on the specific details.

Thank you.

DR. SELIGMAN: Thank you, Dr. Benattia.

Are there any questions from the panel?

Dr. Jenkins?

DR. JENKINS: A couple of questions. The antidepressant medication guide was our first experience with a class medication guide. And we worked with the various players in the industry to come up with the consortium to distribute a common version of the medication guide. My understanding is that that consortium fell apart about a year after it was put together and now we're in a situation where every manufacturer is having to distribute their own medication guides. And we had someone sitting here yesterday showing the various ways that's happening.

Can you elaborate why did that effort fall apart? It seemed like it was working very well.

DR. BENATTIA: Yes. And I took this specific example because I shared with you the initial impression, it was working pretty well. But I will say after that it was important to maintain a structure or a driver behind the discussion across the different manufacturers. I don't think that that group reacted to a specific need and an urgent need. It was not the structure in place to handle ongoing needs. It was a

response to a very specific need at one time. It was not built with the idea with a long term in place and a structure in place to handle additional changes.

DR. JENKINS: But it seemed to be working very well and now we find ourselves in the situation where every company and every generic manufacturer is providing the medication guide in a different way.

DR. BENATTIA: I would say at the beginning it was interesting to see that the alignment, because it was a requirement coming from FDA and there was need to act urgently. I think over time what we are seeing because of, in lack of other words, a lack of structure behind and driver behind this kind of consortium that we've seen some different direction being taken by different companies.

DR. JENKINS: I also noted that you've mentioned that you're now including medication guides in your sample packs that go to the physicians' offices. We heard a plea for that type of situation yesterday from one of the panel members.

DR. BENATTIA: Yes.

DR. JENKINS: Is that common practice across the industry that every product that has a medication guide that is sampled to physicians, the medication guide is included with the sample pack?

DR. BENATTIA: I cannot answer on behalf of the other sponsors.

DR. MELFI: I can answer on behalf of Lilly, and we have always included for products that have medication guides, we've included with our samples.

DR. SELIGMAN: Yes. Ilisa Bernstein?

DR. BERNSTEIN: Going back to the consortium, because as John as saying, it was working and then it didn't. Just to be blunt though, when you say "lack of structure," was it a matter of FDA involvement to keep it going or was it a matter of funding from the manufacturers to keep it going, or was there something else? What kind of structure was lacking?

DR. BENATTIA: My initial reaction and response would be it's really by structure I mean a driver. And when I mean a driver, FDA could be the driver behind. Initially we have seen this reaction and immediate response because FDA was driving this discussion. And I think it's important that FDA being present and the driver within this type of structure.

DR. SELIGMAN: Yes, Dr. Woo?

DR. WOO: Yes. And one more question about the physician sample packages. I applaud you on

providing that type of information. My question is just because the variability of what type of sample would go out, is that actually intended to be provided to the patient or to educate the physician? Because I imagine little boxes where I have 50 little samples, but I'm not going to get 50 medication guides with that, right?

DR. BENATTIA: It's intended to go to the patient. It's attached to the patient sample.

DR. WOO: Really?

DR. BENATTIA: Yes.

DR. WOO: Okay.

DR. SELIGMAN: Thank you very much for your comments.

DR. BENATTIA: Thank you.

DR. SELIGMAN: Our next presenter is Dr. Jeffrey Stoddard from Covance.

DR. STODDARD: Good morning.

I'm Dr. Jeffrey Stoddard, Vice President of Medical and Scientific Affairs for Risk Management and Post-Marketing Programs at Covance.

I want to thank you for giving me the chance to make a statement on this issue, so important to ensuring patient safety while also maintaining a positive balance between benefit and risk.

Covance is the largest publicly trade contract research organization. Covance is heavily involved in all stages of drug development after discovery. And we are particularly involved now in some very large and very important risk management programs including risk minimization action plan implementation. And I would be remiss if I didn't mention the fact that we implement the iPLEDGE program, which is the largest performance linked access program in existence.

The March 2007 guidance on drug safety information, FDA's communication to the public, includes the circumstances that must exist for a medication guide to be required. And these include:

(1) The drug product is one for which patient labeling could help prevent serious adverse events;

(2) The drug product is one that has serious risks relative to the benefits of which patients should be made aware because information concerning the risks could affect the patient's decision to use or continue to use the product;

(3) The drug product is important to health and patient adherence to directions for use is critical to the effectiveness of the drug.

It is on the second point that I wish to focus my comments this morning. And this really speaks to the content of medication guides. Several points here are of note.

First, we know that compliance with medications in a number of conditions including hypertension and diabetes, obesity and pain management is poor.

Secondly, there has been a paradigm shift in medical practice and in consumer health generally from paternalism; the sort of notion that I am the doctor do as I say, to a much more agreed upon course of treatment arrived at through a mutual discussion between patient and physician. And this concept of mutual buy in to the treatment approach increases the likelihood of patient adherence to the therapeutic regimen, and thus a positive therapeutic outcome.

In order to arrive at a mutually agreed upon treatment approach it is imperative that the patient understand both benefits and risk so that a truly informed decision regarding the balance of benefits and risk can be made.

Third, current medication guides are aimed solely at the risk side of the equation. Thus, in order for the patient to obtain the benefit side of

the equation, the physician must either provide education to the patient directly or through a separate education program. In essence, the patient must digest information from at least two separate sources to arrive at their personal risk benefit balance. This seems inefficient and in all likelihood shifts the balance more toward the risk side of the equation.

We recommend that the agency consider adopting a model for medication guides similar to that utilized by the Centers for Disease Control and Prevention in their vaccine information statements, or VIS sheets. And I've brought a couple of examples this morning of vaccine information statements. And you can see that these are easy to read, a single page, two side statements. They exist for every licensed vaccine. And they present balanced information on FDA licensed vaccine products.

The VIS is written in a nontechnical language, approximately at the sixth grade reading level and provides a summary of benefits and risks. The benefits portion is brief, but it effectively portrays the benefits of the vaccine as well as the risks.

For example, the rotavirus vaccine VIS

states that the vaccine is the best way -- and this is taken right out of the VIS -- the best way to protect children against rotavirus disease. That it is taken orally, not injected. It will not prevent diarrhea or vomiting caused by other germs, but it is good at preventing diarrhea and vomiting caused by rotavirus. About 98 percent of children who get the vaccine are protected from severe rotavirus diarrhea and 74 percent do not get rotavirus diarrhea at all.

And finally, children who get the vaccine are also much less likely to be hospitalized or to see a doctor because of rotavirus infection.

Note that to the extent possible benefit and risks are quantified. The remaining one and three quarter pages of the rotavirus VIS are devoted to the risks; who should get it and who should not get it, and what to do if there is a moderate or severe reaction.

In summary, Covance believes that for patients and their physicians to make mutually informed decisions regarding the balance between risk and benefit, a single document that includes risks and benefits such as the VIS model is an effective way to communicate this information.

Thank you.

DR. SELIGMAN: Thank you for your comments.

Questions from the panel? Yes, Dr. Woo?

DR. WOO: Yes. Thank you.

I'd be interested in trying to achieve a better balance of the type of information that goes out to the consumer. How would you compare what's provided already in the CMI versus what we're trying to do with the medication guides or what the objective of the medication guides in terms of providing consumers better information specifically about the risks? How would you see mixing those?

DR. STODDARD: Yes. And that's an excellent question. I think other panels and earlier presenters have touched upon it. In a nutshell, particularly the panel yesterday afternoon I think was all sort of coming to the same point.

I think a couple of points are important. One, we have to start with the consumer; what does the consumer need, what are they going to understand? You know, the VIS interestingly enough, all the VIS statements say right underneath the title what you need to know. And it's called out, it's very clear. And I think this is a good model. We sort of start from the consumer's standpoint, ask ourselves what

does the consumer need to know? I think we then need to work backwards and determine what's the effective way to communicate fairly and in a balanced fashion both the benefit and risk calling out where appropriate the risk information in a very clear cut way. The VIS seems to be a model that does that pretty well.

I think with respect to your question specifically, and I'm not an attorney. I'm a pediatrician and I know a lot about vaccines, and I know quite a bit about risk management, but I'm not an attorney so I don't want to say that I know what's required with respect to changing the regulations that affect both the CMIs and the medication guides. But I would presume that there may have to be some modification of those regs.

DR. SELIGMAN: We've heard a lot in the last couple of days about the importance of providing information at the time that a decision is made to prescribe the product between the physician and the patient. And I was wondering if you would care to give us some of your impressions and experiences based on the risk minimization action plans or Risk MAPs that your organization conducts on behalf of sponsors and sort of what it takes to effect communication at

that point, given that there is a fairly large component of those plans that do involve patient and prescriber interaction?

DR. STODDARD: No, that's absolutely right. And I think for risk MAPs to be effective, particularly large scale risk MAPs but really any risk MAPs, the risk communication piece and the risk communication evaluation component ultimately is really essential. One has to be able to understand how effectively the risk information is being communicated. There have to be clear cut mechanisms by which those evaluations can be conducted. And Covance has been extensively involved in all aspects of that type of work.

It's very clear to us that the content, the message if you will, the content has to be clearly understandable, clearly accessible and with respect to virtually all the products that we're really talking about here that have medication guides associated with them, an evaluation component is also very important to assess how well are those messages getting through.

I don't have specific data as to, you know, specific risk MAP programs and how well that's done. But I can tell you that certainly in any risk MAP implementation that that piece is a crucial piece.

In other words, ascertaining and measuring over time the effectiveness of the risk communication, that is critical.

DR. SELIGMAN: Do you have any feedback on how well these are accepted by practitioners either --

DR. STODDARD: The VIS sheets specifically?

DR. SELIGMAN: Not VIS, or the requirements to engage in that kind of communication whether it involves, you know, patient consents or other forms or the actual formal communication. It's clearly obviously placing a burden on physician's time, and I was curious as whether you have any feedback as to how well this communication -- you know, the requirements for communication that occur at that level are accepted and whether you have any formal feedback?

DR. STODDARD: Yes. My sense is that increasingly physicians are acknowledging that risk communication is a critical part of what they have to do and that often that does involve formal mechanism, including documentation and later assessment mechanisms including surveys and other mechanisms.

I think we're entering an era where the professional autonomy of the physicians is essentially

undergoing an adjustment in recognition that may licensed products do carry very significant risks and with that risk of maintaining those licensed products on the market comes a responsibility and a burden to very concretely and very clearly communicate the risk information. And, again, to be able to document that, to be able to monitor that.

So my sense is that we are entering an era where all stakeholders recognize the significant responsibilities associated with what we're talking about.

DR. SELIGMAN: Other questions, comments from the panel? Yes, Lisa Mathis?

DR. MATHIS: I'm a pediatrician, too, so I can appreciate the use of the VISs, the vaccine information sheets. And they're actually kind of a unique situation. Because when kids come in for the vaccinations it's in general in conjunction with a well child check. So you have more time, more time is allotted on the schedule for a well child check than it is for, say, an acute visit.

In addition, the parents tend to be more prepared. They know that their children are going to be getting shots and will frequently have looked the shots up on the Internet and come in with specific

questions.

That being said, even though it's a little bit different of a situation, often when parents do have questions, and they often have questions about the MMR and autism or rotavirus, I can use those sheets as a good jump off point to give anticipatory guidance to the parents on the side effects and what to expect. In addition, those sheets are reviewed for the consent by the Immunization Clinic, the people that are actually giving the shots. And then those sheets go home with the parents and in general they keep them in order to be on the lookout for side effects.

So they are very utilitarian. Although again, they are used in a very different setting than most medications. We don't in general have longer time for acute visits, so with every medication the physician could counsel the patient, although you would hope they would. And also you don't have somebody specifically administering the medication so that way they could counsel them and consent them again. But in theory, that would be a really good tool.

DR. SELIGMAN: Yes, David Roeder?

MR. ROEDER: Hi.

In looking back over the past day and a half the one issue in which seem to be getting stuck here is many of the presenters have advocated for a simple no more than two pages balanced document. And that's not what -- you know, the FDA's having a hard time with that. You know, we write longer documents. And it's very difficult for us to present something that we don't feel is complete.

DR. SELIGMAN: Right.

MR. ROEDER: So what is it that we're doing wrong? What is it that's in those documents that shouldn't be there? Or not that it shouldn't be there, but that we could get by without? I mean just in more general terms? I mean what are we doing with these documents that are just making them too bulky?

DR. STODDARD: Well, as I look at the medication guides that exist, I see a reflection really essentially of virtually all known risks. You know, the contraindications of warnings and precautions are really all spelled out to varying degrees, even hypothetical or theoretical risks tend to appear in medication guides as we know them today. That is not what you tend to see in the CDC's VIS statements. What you tend to see with respect to risk communication in the CDC's VIS statements are really

the most significant and most likely adverse events that are likely to occur.

I think it's a matter of really staying focused and being disciplined about providing and communicating the risk information again with a starting point of what does the consumer really need to know, what is within a reasonable likelihood going to occur that is of significance. And making sure that that risk communication occurs.

When you do that you actually end up being more effective in really communicating what matters. When you try to be comprehensive and convey each and every potential risk and the document goes on for five or six pages, then you run the risk that the whole thing will be ignored. And I think that's really, particularly that panel 8 yesterday afternoon I think was really sort of trying to convey that.

So I think we all want to get to the point where we're conveying the information that matters, we're conveying it in a way that it's going to be read and digested. But maybe that involves in some cases stripping back some of the lesser likelihood, the risks that are lesser in importance.

DR. SELIGMAN: Dr. Stoddard, thank you for comments.

Our next speaker is Marissa Craddock from Roxane Laboratories who will be speaking on behalf of the Generic Pharmaceutical Association.

MS. CRADDOCK: Good morning.

Again, my name is Marissa Craddock. I'm from Roxane Laboratories and I'll speaking today on behalf of the Generic Pharmaceutical Association.

I'd like to thank the Committee for giving us this opportunity to speak today. And I'd like to touch briefly on each of the questions that were presented in the *Federal Register* notice and the ones that were proposed specifically to the manufacturers.

The first question is in regards to compliance with medication guide requirements. To ensure compliance with the medication guide requirements we in the generic industry typically provide a dispensing statement, such as pharmacists provide medication guide to patient with medication.

The biggest challenges we've been facing are technical issues in package engineering. We're facing more obstacles in designing, folding and affixing the increasing amounts of information to the containers.

Another concern comes with patient safety in ensuring that pharmacies are receiving and

dispensing the medication guides as required. We believe that by taking advantage of technology, electronic files may enhance compliance.

Next we were asked about our experience with electronic forms of medication guides. Generic firms have typically not provided medication guides as electronic files. The roadblocks that some firms have come up against is that there has not been a way to ensure that all pharmacies could receive, view, print and distribute the medication guides electronically.

There is a strong interest among the generic industry to take advantage of the technologies available to us and work towards a paperless solution, both in the distribution of prescribing information and medication guides. We ask that a central database, possibly accessible through DailyMed or the National Library of Medicine websites be considered.

The third question deals with pharmacy instructions for dispensing medication guides. The current practice for instructing pharmacies to dispense medication guides is to prominently display the dispensing statement. The objective is to provide one medication guide for each prescription dispensed. I'll get into more detail concerning unit of use packaging in the next couple of slides.

The medication guides are typically issued as perforated or tear away pages. Manufacturers are starting to supply additional medication guides to wholesalers and other members of the supply chain.

Pharmacies are also able to contact the manufacturer or third party vendor to request additional medication guides if necessary.

Next we were asked for a proposal of standardized language and/or a uniform symbol. We support the idea of a uniform symbol to be placed on the bottle label to let pharmacists know that a medication guide should be dispensed, especially for smaller bottles where text space is an issue. However, we have no specific recommendations for a symbol at this time.

As far as the standardized language is concerned, we are satisfied with the statement currently in use, which states "Pharmacists provide medication guide to patient with medication."

The next question deals with unit of use packaging. As I mentioned earlier, technical and engineering challenges have become more prominent. We've had to work harder to be more creative in fitting all of this information on the bottles. But there are practical limits to what can be done, and we

feel that this calls for an exploration of the technologies available to us.

One of the advantages to unit of use packaging is that there is little to no repackaging by the pharmacists. And because the information is attached during the manufacturing process, there is no additional work in supplying the medication guide.

One of the biggest challenges to unit of use packaging is actually defining unit of use. Because the definition is so broad, it's difficult to provide for the numerous variations of dispensing.

Additional disadvantages to using a unit of use package are that it is impractical for all products.

First, medication guides cannot be affixed to all unit of use container types, such as syringes.

Second, facilities such as hospitals and clinics tend to buy in bulk and repackage into their own dispensing units. It is much more efficient for the amounts they are receiving and dispensing.

And third, as needed dosages supplied as unit of use may provide patients with too much or not enough medication.

Products administered in multiple dosing regimens are often difficult to dispense as unit of

use due to the variations of the dosage amounts.

All of these factors will result in increased cost to the patients.

Finally, the last question addressed class-specific medication guides. One of the chief advantages of creating class-specific medication guides is the FDA and industry can collaborate on standardized text and work in a consortium to provide information to pharmacies. Consortiums have already been successfully implemented with NSAIDs and antidepressants. When changes need to be implemented, there is one point of contact which allows the changes to be made much more efficiently. As a result, pharmacies have access to the most current information in a more timely manner. And to go one step further, pharmacies would have even faster access if that information was available electronically in a centralized database.

Our main concern with using class-specific medication guides are the variations of data and side effects within each drug class. Patients could become confused with which information applies to their specific product.

In summary, the Generic Pharmaceutical Association is focused on patient safety, education

and communication. We believe that every patient deserves to have the information they need to take their medications effectively. We're willing to collaborate to find a system that satisfies all stakeholders. We'd like to focus on the technologies that are already available and build onto a system in order to efficiently provide pharmacists and patients the most up to date product information.

Thank you.

DR. SELIGMAN: Thank you for your comments.

Any questions from the panel? Seeing no questions, again thank you for your presentation.

Our next speaker is Paul Johnson from Wolters Kluwer Health. Mr. Johnson?

MR. JOHNSON: Thank you. Good morning.

My name is Paul Johnson. I'm a pharmacist and clinical manager for Wolters Kluwer Health. We're a major provider of patient education materials and other clinical information frequently used by hospital and retail pharmacies, pharmacy software vendors as well as the general public.

Wolters Kluwer Health along with other information and database providers has been actively involved in both the CMI and medication guide

initiatives. And as database providers, we all work to develop ways to help those who use our products and services to comply with the FDA regulations and guidances that have been published in relation to these initiatives. WK Health has spent actually considerable resources to be proactive in this regard.

Our broad challenge is that we're often pulled in many different directions in trying to meet the needs of our users, the needs and desires of our users and at the same time by trying to satisfy the regulatory requirements together. So I would like to focus my comments at a high level around two specific questions asked of database and information vendors in the *Federal Register* notice for this hearing.

Number one: What challenges or issues regarding distribution of medication guides have you encounterd? What changes should be made to the medication guide program to address these challenges?

And secondly, what challenges do information vendors face when offering electronic versions of medication guides in the FDA approved format? What idea do you have regarding how medication guides could be integrated into other consumer information?

Regarding our overall challenges with the

medication guide program, as you can probably see, the challenges that we face with regard to distribution often mirror that of the pharmacies and software vendors that we serve. Many of the issues that I had planned to speak about on this line I think were covered quite extensively yesterday, so in the interest of time and simplicity, I don't want to further belabor these points except to say that Wolters Kluwer Health is essentially in agreement with many of the sentiments expressed yesterday as they relate to the content and format issues, particularly with respect to excessive medication guide length, poor or inconsistent format and the negative impact that these problems may have on patients who become frustrated because they cannot read the information or will not read the information, or who may avoid therapy because they really don't receive a clear balanced and accurate picture of the medication risks relative to the risk of nontreatment of their disease state.

We further agree that many patients and practitioners are often unaware that a medication guide exists for a particular drug. Currently no standard process exists to efficiently notify practitioners, database providers or the public

regarding the availability of new or updated medication guides.

Access to new and/or revised medication guides as they become available is just as difficult for us as it is for our users. There's currently no single location where one may find every medication guide that has been approved by the FDA. Also, the CDER medication guide website is incomplete. Currently, we have identified and collected approximately 80 individual medication guide compared to the roughly 60 or so found on the CDER website.

Although the CDER website includes medication guides for many branded products, it does not often contain medication guides that correspond to the respective generic or branded generic products.

Wolters Kluwer has an entire team of people who spend a great deal of time tracking down medication guides along with other information from manufacturers and/or the FDA. It's very disheartening when one of our customers actually stumbles across a new version of a medication guide that we were either unaware of or unable to obtain and asks why aren't you giving it to us? So imagine how much harder it must be for patients or busy physicians to obtain that information when we're sometimes unable to do it with

a concerted effort.

We also agree that there is a significant amount of inefficiency on a number of levels within the medication guide program as it stands today. The cost in time, effort and dollars to overcome these inefficiencies is very high, both for database providers as well as for pharmacies, and may arguably be the main reason why the program does not work today. Those who choose to integrate medication guide distribution into their work flow unfairly are forced to assume the financial responsibility for acquiring, generating and distributing medication guide information that was intended by the regulation to be born by the drug product manufacturers.

Also, as all of these problems compound exponentially as the program grows and expands, a new medication guide for one branded name drug today may translate into an unknown number of separate medication guides for all of its generics when they come to market. And those, in turn, carry along with them all the costs and inefficiencies and concerns that exist currently.

Well, actually, I should back up.

Regarding challenges with electronic distribution of medication guides, in an effort to

help our customers deal with the acquisition problems, Wolters Kluwer Health roughly two years ago, successfully developed and released work flow integrated software that enables users to print both medication guides in the FDA approved format, as well as to print CMI that was specifically created to be consistent with action plan content and format guidelines. We have a number of pharmacy chains and pharmacy software vendors who either have or are in the process currently of adopting this technology. Wolters Kluwer also includes medication guide content in an electronic version of Facts and Comparisons which is a common drug information reference used by physicians in their offices as well as in hospital settings and so forth which then allows the person using that product to --if they're looking up information on a drug that requires a medication guide, they can then directly print the medication guide from that product as well for use in counseling the patient.

Despite the availability of these integrated work flow tools we've experienced a certain amount of resistance to it. The reasons are not always exactly clear, however some pharmacies may find it difficult to manage the technical or programmatic

changes necessary to implement the technology to distribute medication guides in the exact format in which they were approved. Some may have difficulty working with certain file formats, such as PDF files. Others may be concerned about cost issues and the current regulatory ambiguities that exist as they relate to both CMI and to the medication guide program.

As to the question of what changes should be made to the medication guide program to address these challenges, first we agree that we need to improve the usefulness of the documents if the program is to be successful. There are currently no standard content or format criteria defined for medication guides outside of the heading criteria and the 10 point font requirements outlined in 21 CFR 208. Regardless of whether or not medication guide information remains a separate document or if it is incorporated into other patient information such as CMI, it needs to be clearly defined and focused in its scope. If the purpose is to convey specific risk information, it should do only that and refer the patient to CMI for other information. As a separate document it should serve the same purpose and be simple and concise.

I would note that all CMI produced by Wolters Kluwer Health for drugs that require a medication guide contains a statement advising the patient to read the medication guide available with this medicine in order to alert them to the availability of the risk information. There's no reason that medication guides should not do the same for CMI in order to provide balance, assuming of course that there are two separate documents that exist.

We further submit that all medication guides should follow a defined standardized format useful for patients to provide consistency. Specific format criteria, including 10 point front, use of bullets, et cetera, is included within the action plan for CMI to define useful formatting for that information. We see no reason why the same logic would not apply to medication guide information.

We also need to have a specific alert mechanism regarding availability of new or revised medication guides. The CDER News Listserv might serve as an appropriate medium for this, however information regarding medication guides needs to be separated out from other information. Currently medication guide changes for a drug are often included within the term

labeling revision which does not specifically convey the availability of new or changed medication guide information.

Medication guide info should also be made available in one centralized location in its final format for use as soon as it is approved. It is frustrating when you utilize the FDA website to learn of a labeling change, click on the label information link but then find that the most recent label or medication guide is unavailable at that link.

Thirdly, we support the idea of distribution of medication guide information through as many avenues as a patient may conceivably use, whether it be from their physician or pharmacist, on paper, through email or via Internet access. As has been noted, I think definitely patients are not homogenous and as many avenues as we can use to get the information out, we support that.

Obtaining clean useful copies of medication guides for electronic distribution to pharmacies is difficult when it only exists as part of another document, such as the last several pages of a PI. If the medication guide is to be used as a stand alone document, we suggest that it should be written and reviewed and approved as such.

We also support the idea of using alternative file formats when it may facilitate the distribution of medication guide information to patients who otherwise might not receive it, to the extent that the document content and overall readability would not be adversely affected.

To prevent the rapid expansion of problems that exist with the current medication guide program, we suggest that steps be taken to minimize the physical number of different or separate medication guide documents. The current criteria used to determine the need for a medication guide for a particular drug is fairly vague. We suggest that FDA evaluate and develop specific criteria to ensure that added risk information is indeed needed for a given a drug and useful for patients.

We further support the use of class medication guides whenever possible so that only one document is necessary to cover a number of affected drugs. This would have been particularly useful for the ADHD drugs and should definitely be considered for the sedative hypnotic drugs.

Also, avoiding proprietary information within a medication guide document allows for a single document to be used for any number of brands or

generics of a single drug entity. A perfect example would be isotretinoin. There are four different brands of isotretinoin, but the only medication guide available at the FDA website is for Accutane with a reference to the other three brands.

Coumadin is another example of a medication guide that initially came out and contained information for a brand named Coumadin, yet only recently did medication guides for generics as well as other branded generics of warfarin become available.

As to the question: What ideas do you have regarding how medication guides could be integrated into other consumer information? We hadn't really given this option serious consideration because we never really thought that it would be an option acceptable to the FDA. However, it is definitely something that we would certainly be very willing to investigate if it appears to be a viable option in the context of private sector CMI. It is already our current practice to make sure we include as much of the substance of medication guide information as possible within all of our CMI for which it applies. Specifically because we know that many patients may not actually receive the medication guide.

In conclusion, I would just like to say

that I agree with Diane Dorlester's comment yesterday that we are at a point where we face a real opportunity to craft a new program that can present balanced information, acknowledge risk and educate patients and practitioners on how to mitigate these risks. As a practical matter I kind of wish that the discussion we're having today, it could have taken place ten or 12 years ago because it would have -- kind of we got the cart before the horse I think a little bit. But it's good that we're having it today at least.

At this point I think a lot of information has been presented regarding what needs to be done to accomplish this goal. What now has to be figured out is how we're going to accomplish it. Wolters Kluwer would very much like to be actively involved in any efforts as it can be useful to the FDA in achieving this end.

I thank the FDA for holding this meeting and for its consideration of all of the comments that are being presented. I urge FDA to continue to involve all interested parties as it moves forward in evaluating this important issue.

Thank you.

DR. SELIGMAN: Thank you very much.

You indicated that you all have developed an ability to provide electronic access to medication guide in the FDA format. And I was curious given your ability to do so whether you would comment further on a request made yesterday by some groups to request either a waiver or some latitude in some of the format, and also in particular in the second to last slide you mentioned a desire for allowance for format alternatives. I was curious why you make that request given your ability to essentially provide electronic access to the medication guide as currently formatted?

MR. JOHNSON: I think there's some differences in meaning in terms of allowances for format.

DR. SELIGMAN: Okay. Could you explain?

MR. JOHNSON: From Wolters Kluwer's perspective when we're talking about changes in format, we know that certain people have problems using PDF files, whereas they might be able to use the same information in, say, a Word file or a different electronic file format that doesn't really seriously affect the content and so on. And that is what we suggest. Is that an answer?

DR. SELIGMAN: That clarification helps a lot. I mean, whether it's a Word document or a PDF

document, I think our greatest concern and issue is related to format is sort of look and the feel of the document in terms of the wide space and the headings and the chunking or the varies aspects of the document that make it a more effective communication tool.

MR. JOHNSON: The other problem that we run across is that many of the documents and even documents at the FDA website that you see there are draft copies with lines down the side and so forth, and our customers complain to us, "why does it look so bad"? And so, you know, there needs to be flexibility to clean up these things and so forth.

DR. SELIGMAN: Yes. I know. We appreciate your comments regarding the website. And some of those are, how should I say it, copies that we made and put up on the website. And I think the whole notion of having the original document in a clean electronic form is a critical one. My understanding is that with the DailyMed and the National Library of Medicine Initiative that you will be able to actually download that portion of the label that does refer to the medication guide. But that's something that I need to look into more carefully. Because that indeed would provide a sort of clean electronic access that you all would be looking for in trying to reproduce that

portion of the label.

Are there other comments from members of the panel? Yes, Toni Piazza-Hepp?

DR. PIAZZA-HEPP: Yes. Since you are one of the pharmacy database providers, I would guess you would have some knowledge of some of the features that the other pharmacy database provide supply as well.

But a couple of questions. What sources do you typically use to update information like knowing that there's a medication guide for a new product or even knowing there's a new product, or any changes in updates, what do you find are the best sources for that? And also do pharmacy systems typically have any kind of prompts that would alert a pharmacist that a medication guide would need to be provided with this particular medication?

MR. JOHNSON: Well, as far as acquiring information, we have a team of people whose job it is to basically scour the news, FDA websites -- I don't know all of the sources they use, but things of this nature. And then that information is compiled into a report that is generated several times daily as new information develops. There's two to three reports on a given day. So that's how we then know that there is a new medication and if it needs a monograph, CMI

monograph or if it needs a medication guide or whatever.

What was the second part of your question again? I'm sorry.

DR. PIAZZA-HEPP: Do pharmacy databases typically prompt you for drug interactions, that kind of thing? Do they prompt for a medication guide to be distributed with this product?

MR. JOHNSON: In our case, if they're using the software that I spoke of, when a prescription is filled for an NDC that requires a medication guide, the software knows it. And so automatically, the CMI is generated and then following that would be the medication guide. So that's the design of the product.

I think as we heard yesterday some other systems apparently flash a warning saying that a medication guide is associated with this product. But my assumption was from what I heard that then they have to go separately to print that document.

DR. SELIGMAN: Thank you.

MR. JOHNSON: Thank you.

DR. SELIGMAN: The final speaker on this panel is Dr. Kala Paul from the Corvallis Group.

Dr. Paul?

DR. PAUL: Good morning. It's still morning. My name is Kala Paul. I am a physician. I have over 13 years experience in the pharmaceutical industry in the development of drug products and in clinical safety surveillance. And for the past seven years I have been working as a consultant with the Corvallis Group developing risk communications for patients and for health care providers or health care professionals.

I want to thank the FDA for the opportunity to be here today to present information that we have gleaned from consumer research in over 40 products for ten different companies. I an not here to represent any company or any company's viewpoint. I am here as an advocate for patients and for what they tell us in the course of this comprehension testing about how they understand the information that's being presented to them.

I'm presenting universal findings from consumers. Our testing is in predominately low literacy patients. But these findings are consistent with what consumers want to know and what consumers tell us across the entire education spectrum.

As we know, and everyone has said, consumers are now more involved in health care

decisions and they want to have this information. I used the term "they're useable product information," meaning both useful and understandable. If the information is neither something they can use or something they can understand, it doesn't fit the bill.

We have talked about whether or not patients need this to have conversations with their health care provider, we use the term doctor as a general term there, and how they would use this to participate in a risk benefit decision. Obviously if there's only risk information, this information isn't sufficient to help in a risk benefit decision. One of the things that consumers tell us when they read our information is "Gee, is that what the product is for" when we put in the indication. And when we put in any information about what the product might be expected to do, they'll tell us the physician never told them why they were taking the product.

Not only do patients need this information when they make that decision to take the product, it's very clear that throughout the life of their product use, they will need the information that we provide or that is provided to them in these documents in order to continue to make decisions throughout the life of

the product use. They use information to minimize the risks, to maximize the benefits. They need to know how to respond appropriately when something arises, when they perceive an adverse experience when there's question. And we have heard from these patients that this information, which they will keep with them, influences their attitude toward the product and their decision to comply.

This is a comment about a patient label. This is a patient label I wrote. And it's not -- it's a patient label with the person reading it said "They finally are realizing that you can't read those small print documents, they're a waste. There's too much information. This gets to the important points."

And the question is what are the important points and what is the point of this document? And I would raise the issue that this is a starting point. We're talking about something that can be accessible cognitively to all patients and serve as a basis for their understanding drug risk and benefit.

In spite of the fact that we have heard a bazillion times here today that these documents need to be focused and easy to read in order to low barriers to comprehension and reading, the current documents that are out there do not always deliver

this. Our patients tell us, our subjects tell us "I didn't understand what they were trying to tell me." Again, these are documents I wrote. These are the documents they're talking about, of course. "They don't highlight important information adequately. They're not inviting to read." And if they're not inviting to read, they won't read them. And we heard Congressman Ferguson say yesterday that he won't read something at his reading level if it looks too dense. And I'm from New Jersey so I can understand that.

They say that it's still too hard to read these. That the content is still too hard. We try and try and try. And I will present to you information, sixth grade reading level is very, very simple writing. Very important to understand that.

I think this is one of my major points. We have two things about the medication guide program that we're hearing here today. Delivery, delivery, delivery. Delivery of the information is the first in terms of it making readable and delivery of the document, otherwise they won't get it. But the medication program cannot work if consumers don't understand the message.

And this is true regardless of whether you deliver it by the Internet, or regardless of whether

you deliver by any other manner that uses the written word. If they can't read it, they can't understand it, they can't act on it and you might as well go home.

When writing for consumers, we can't assume that they can read what we wrote. That absolutely is critical. Even those with high literacy may not understand health literacy terms. So you can't assume that they understood what you wrote.

You can't assume they will read what you wrote. You can give them the document, but nothing says they have to read it. So that's tremendously important.

You must make the information appear relevant to them or they won't read it.

And you don't know that even if they can read it, that they understood what they read. And once we even know that they've comprehended, we don't know that it influences behavior entirely. But we can always hope.

We want to maximize communication to consumers, we need to focus the content. There was a question here earlier, how do we get these documents smaller? Focus the content. What is it that is necessary to know and how do you get rid of all the other stuff that isn't necessary to know?

How can you simplify the language? And I'm not talking about making it simple, leaving things out. I'm talking about simplifying it to make it accessible.

You format to enhance delivery, and I'll talk about format later.

And absolutely test these documents with consumers to find out if you made your message understandable to them. And this is a critical issue where we think we have made something that is perfectly understandable, most of us here, I assume, read above the sixth grade reading level. We understand it. We wrote it. We know what we mean. The consumer does not. And that is critical.

We have heard this back from consumers when they look at the documents, and I'll tell you about the documents that we're giving them. We write it in such a way that they don't have to deal with the big words, the big phrases, the difficult information transfer.

We did qualitative testing. We did this in, as I said before, we've done it over 600 hours of qualitative comprehension research in risk management documents; medication guides, patient package inserts, patient's instructions for use and risk MAP documents

across over 40 brands for more than ten manufacturers.

Our respondents were from age 13 to 70. We had a wide range of ethnicites in our population. We tested English and Spanish documents and the interviews were in English and Spanish.

Our subjects' estimated reading level, and we used a REALM testing, which is the Rapid Estimate of Adult Literacy in Medicine, just as a categorizing tool. Ranged from third grade through high school. We did have some college level respondents in a few of our testing. But, again, as I will say our learnings we feel are absolutely applicable across the entire educational spectrum.

The documents we tested were in general in a two column format, 10 point font, distillation of the PI. They contained all the risk information that was serious, precautions, contraindications, common adverse experiences, indication, what to tell your doctor beforehand, how to take the medicine, what to avoid, how to store. All that information was on one page.

Low literacy consumers and the elderly. You cannot, cannot, cannot, cannot over estimate how difficult it is for these people to read and to understand product information. They read sentences

word-by-word, they're discouraged by difficult looking text, they skip text, they won't read through to the end, they miss clauses that modify. They go through a document and pick what they can read, read it and for that reason many times with these documents for these consumers, the opportunity for communication to them is lost.

This is why we say you need to limit the information on a need to know basis and to ease the reading burden, to focus the reader on the most important information. This is a comment from the reader that the extraneous information, and they did not use the term, really erodes their ability to remember the key facts and erodes their ability to find the key facts.

Information that we consider extraneous, there's usually an introductory paragraph that says read this before -- when you get the medication guide, read it when you get it refilled, blah, blah, blah. And it in some respects is recapped at the bottom about getting more information, ask your doctor, ask your pharmacist. I'm not sure that that's entirely necessary. There are other parts throughout the document which we can look at in particular.

The last paragraph that's required by the

regs, which is medicines are sometimes prescribed for conditions other than those listed in the patient leaflet. I took a long time to understand it. None of the consumers who have ever read that paragraph understood what it meant or where it was there. Okay. Too many words and you get too side tracked.

Clear and concise layman's terms work across cultures and ethnicities. We run into some problems, obviously, when we're describing bodily functions. We do have to keep this to a certain level. But clear simple sentences, simple terms.

The fewest words possible. We don't need to write sentences that have lots of elegant terminology in there. A three word sentence that says "don't do this" is probably more effectively than a "you should not do this because" when the end of the sentence is totally lost.

Medical terms confuse patients. One of the ways that we have handled this is using the simple definition, using too many words and the definition, the medical term in parenthesis logorrhea. I thought that was appropriate for this content.

Clarify with format. Again, I'm sounding like Ruth Day and she and I have talked about this many times. Format, such as two column format, void

space, bullets, headings; these organize and enhance the information, focus and emphasize it. And this is what a consumer tells us. "I will read it. If it's too hard to read and things are dense and blocky, I'll walk away from it." Okay.

And I want to make a point here, which is I've seen some of the documents. The Q&A format and some white space don't make for easy reading just because it's a Q&A format and white space. There are other elements that need to be added in order to get to an easily read document.

This is one my pet peeves. We talked to patients, the term health care provider means insurance company to many. You say why should I call my insurance company if my gums are bleeding?

Late pregnancy from some of the NSAIDs, they say I'm not an older lady, what difference does it make? I used the term "older lady," I was offended. But, okay.

Sugar pill for diabetes; that's what people think when you say sugar pill. Not placebo, but why are you talking to me about a diabetes medication?

Health problems better than medical conditions. Medicine or drug better than medications. Simple things.

And pictures are also potentially a problem, and Ruth Day alluded to this. We don't know what those icons mean until we ask consumers what they mean.

Why we test? Okay. Ruth would be thrilled. I did this beautifully. Simple sentences, clear, very clear instruction, okay. Don't -- simple sentences, very clear instruction test it. It says lay down for 45 minutes. I can't do that, I have kids to take care of. Where did this come from? The patient reads don't, ready the first one, read the simple sentences. It says lay down for 45 minutes. In order to understand what the patient takes away, you need to ask them this worked where we repeat the do not, do not, do not; the patient got the information and avoided the issue of a potential side effect.

Okay. When I said you can't just use a simple sentence and white space to get the message across -- actually this is interesting it's going to go backwards. All right we'll do the whole thing all at once.

The left hand side is an instruction to the patient what to do while using a medication. The right hand side takes all that information, bullets it and even adds an extra line for the same amount of

space on the paper referring the patient back to the physician for additional help.

Defining a role for the medication guides. We've talked about this over and over again, defining overarching communication goals and looking at product information. If the medication guide is to communicate risk and be useable, it has to communicate benefit. If you're going to do that, you need to have the information there to give the consumer what they need to know about the product in order to use it safely. I'm speaking about apple pie and motherhood.

General health and public safety messages that dilute the product safety information. And I think this is something that we need to consider. Safety information on storage. Keep it out of the reach of children. Is the medication guide to give risk information or is to educate the public? That is something that is a policy decision, not mine. But I can tell you for all the information that we put on that very precious piece of real estate, that one page, each time we take away something and simplify it, we can magnify the other pieces of information.

Another piece that I wanted to mention, we use the term in the medication guide what is the most important information I should know about product X?

When I'm going to do a two column format, that's a two line sentence. If I were simply to say most important information, I would catch the patient's eye, could make it a 12 point font, still fit it on the page. But they would know, right at the beginning, that that's what they had to looked at. That's what they had to see.

Okay. We want to use language and formats that consumers can understand.

And then you have been asked by other speakers to enforce health literacy standards, to set goals and enforce them. I think that part of the problem that's happened with the medication guides and the program in general for patient communication is the surgical rigorous application of cutting out everything that isn't necessary in the sentence to the core meaning has been lost. And therefore, for not only low literacy consumers, but for all consumers getting the message becomes harder.

Okay. I'm going to go through this because basically we have discussed this, said this time and time again.

My feeling on using class labeling, it's an opportunity to simplify a message, simplify the language, to focus the risk message across all

products in a class. Flexibility is needed when specific drug product information is needed. And this is absolutely de rigeur -- simplify, simplify, simplify the text and the format using the fewest words, deleting all extraneous information, focusing on key points, maximize white space, use bullets and heading and at minimum, access reading level.

The SMOG is one, it's not as popular as the FRY. But I like the SMOG simply because it says what it does. It is the Simple Measure of Gobbledegook. That's what it stays for.

The Flesch-Kincaid, which is on Word, very nice, but it underestimates reading level. The Flesch-Kincaid is easier if you use percent reading ease.

We have so much more information. We've gone through these. When we do our testing, we go through these section-by-section in in depth interviews for an hour. And I could keep going for more hours. You don't want me to do that.

Use health literacy experts as resources.

Test everything that's written in low literacy consumers quantitatively or qualitatively, test for comprehension, readability, useability, validate the content, format to ensure meeting good

communication goals, which we said earlier, we talked about setting them.

My rules of thumb: Simply, test in low literacy consumers, simplify again. But by adding more, you communicate less.

Thank you for the opportunity to present this information.

DR. SELIGMAN: Thank you very much for your input.

Can you spell gobbledegook?

DR. PAUL: Actually it's too many syllables. If you have that many syllables in one of these documents, it will throw it into a tenth grade reading level like that.

DR. SELIGMAN: Like that?

Thank you very much.

Any questions from the panelists?

Well, thank you all for your input today.

It was a very valuable session.

And we will reconvene at 1:00. Thank you.

(Whereupon, at 1:00 p.m. the meeting was adjourned, to reconvene this same day at 1:03 p.m.)

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

1:03 p.m.

DR. SELIGMAN: Good afternoon. If we could have the first panel to the table, we'll begin shortly.

Good afternoon and welcome back.

The first speaker in this afternoon's panel is Dr. Gerald McEvoy from the American Society of Health-Systems Pharmacists.

Gerald?

DR. McEVOY: Thank you, Dr. Seligman.

My role at ASHP is the Assistant Vice President of Drug Information. And ASHP as a professional association represents pharmacists who practice principally in hospitals and other health system settings. Our members in the vast majority of their practice are not really affected directly by the medication guide regulations because they are principally dispensing drugs in an inpatient basis. However, there are groups of our members, for example, pharmacists practicing in the VA, pharmacists who practice in institutions which have outpatient pharmacies who are directly affected by the medication guide regulations. And in addition to that as a publisher of consumer medicine information that is accessed principally electronically we also are directly affected as a professional society by the

medication guide regulations.

I first became involved with this issue by being one of the pharmacists that was invited to the first meeting with the drug industry, pharmaceutical industry to try to come up with a way to distribute the paper solution that FDA had come up with for antidepressants. And I can tell you going into that meeting I had no idea that that was what was going to be proposed. And I came to the mike at that meeting and predicted that that paper solution would fail, and indeed it has.

ASHP has been publishing consumer medicine information for over 25 years. As I mentioned, most of the access to our information is electronically through the National Library of Medicine's MedlinePlus consumer website, through the Consumer Reports Medical Guide website and through ASHP's own safemedication.com website.

We were one of the first publishers to embed URLs in our CMI that would link directly to medication guides. But what we quickly discovered was that those URLs were not stable and we have since had to stop doing that. The URLs would change when the medication guide was revised. And a recommendation towards the end of my presentation will be that FDA

must establish stable identifiers for all of their documents if they expect people to be able to link to them in an easy and dependable way.

The issues with medication guide first is the current reliance on an outmoded reprinted leaflet solution and the cumbersome distribution mechanisms that we've heard described over the past day and a half.

Secondly, as part of a group of stakeholders that worked with FDA in an attempt to permit some exemptions to the formatting requirements so that in fact medication guides would get distributed electronically as part of the normal work flow, but FDA was unwilling to provide exemptions for those formatting requirements. And one of the ironies of that is that the regulation itself permits FDA to exempt those format requirements for the manufacturers. The manufacturers are not required to follow the format requirements, yet they were insisting that they be enforced in the retail pharmacy sector. As a result, there have been levels of distribution medication guide, there are gross under estimates of the burden of the regulation. If you read the 1998 *Federal Register* final regulation and the comments that go with it, you'll see that much of what

was predicted about the program is far different than what has actually materialized.

Another issue is the consumer confusion that exists with the array of documents that may be provided. The CMI, which is actually issued at a high percentage, medication guides which are not being distributed at a very high percentage, patient package inserts that the manufacturer may create and then FDA's latest risk communication documents, the patient information sheets.

One of our principal concerns is the lack of research concerning the role, scope and effects on patient understanding and behavior of the medication guide program. And one of our principal recommendations will be that we need to do research to define what will work best and is in the best interest of patients.

We've heard a lot about the distribution problems that currently exist with the tear pad approach. And I'm just going to skip by this and for the sake of time move on to some other issues. We've also heard about issues on whether or not pharmacists actually realize the federal requirements to distribute medication guides. The most recent information that I could find on the FDA's website was

the 2005 survey. And the key point in here is that only 20 percent of respondents, roughly 2500 pharmacists, knew that medication guides were required for all new and refill prescriptions. And I think that what we've heard over the past several days is that even if their knowledge of that requirement has increased, there still is a low level of providing that information which probably has to do a lot with the fact that we're relying on a preprinted tear pad distribution mechanism.

The gross underestimates, and I'm going to skip through these fairly quickly, too, because some of them have been alluded to, but I do want to make a couple of points.

If you look at the original medication guide regulations these are some of the estimates versus the realities. The original estimate was that it would effect roughly a million prescriptions a year. It's estimated that it actually affects almost 300 million prescriptions per year. There is an original estimate that it would take a pharmacist only five seconds to provide a medication guide to a patient. And there is substantial disruptions in electronic work flow that are resulting in this being an unlikely measure of time, particularly in a highly

automated environment and one of the Federal Government's own, the VA is a good place for the FDA to get some information. Conversations that we've had with them. Our preliminary estimates that it's decreasing their efficiency by about ten percent and they currently have pilot programs on the way to actually do a good study on the impact on their work environment of distributing these.

Firms were to ensure adequate supplies, and we've heard all of the problems in terms of that, one of which is FDA's failure to enforce that, in fact, they do get distributed.

Gross underestimates of the number of products per year that would be affected. And the key point I'll make here is that currently almost 10,000 NDCs are affected by medication guide. There's roughly 3,000 individual products and when you include the repackagers of those products which have unique NDCs, we're now approaching 10,000 NDCs. And even in an electronic world then all of those NDCs have to be linked to the specific medication guide that would need to be distributed.

The page length goals were two. I mean, currently it's roughly eight pages with a range of two to 31 pages. It originally was projected that they

would be required with the initial FDA approval of NDA, and in fact the ones that have the greatest impact are existing classes of drugs like the antidepressants, non-steroidals and drugs for ADHD.

And then finally that the manufacturers somehow would provide an electronic solution to the pharmacy departments and to the pharmacies. And that is not occurring as well. And as we just heard from Wolters Kluwer they have mechanisms in place to permit that.

Another problem deals with content. And just to reiterate, the focus of the current medication guides is on risks and the most recent ones typically are on one or two risks. There's little if any balance regarding the benefits of treatment. Antidepressants until recently had no information about the risk of untreated depression. That is finally going to be changed.

The non-steroidal medication guide is an interesting one. You have to get all the way to the end of it to find out that aspirin doesn't share the cardiovascular risk. But I would contend it should have been stated more positively that aspirin actually has lifesaving benefits in certain cardiovascular conditions.

And there could be unintended consequences. I don't know that there is any relationship, but people have certainly raised the question about a potential relationship between the decreased prescribing of antidepressants and the increased suicide rates in adolescents.

Highly variable content despite the general requirements. And the general requirements is really a misnomer. CMI has very specific guidelines as to what content must be included in them. And if you look at the regulations you might think that in fact medication guides have similar general requirements. The reality is that because of the exemption provision there's only two things that must appear in a medication guide. First, that it must be scientifically accurate, meaning that it can't disagree with the professional labeling. And then secondly, there has to be the title medication guide and that was approved by the U.S. Food and Drug Administration. None of the other requirements are in fact required.

The description of what the medication guide program was intended to do also says that it should include the information that is necessary for safe and effective use. And I think that the

medication guides are far too narrowly focused to really meet what is necessary for safe and effective use.

Issues for consumers. FDA again in the *Federal Register* said that lengthy information, that is by their definition information that exceeded a two page limit, could result in unnecessary or even dangerous barriers to effective communication of important concepts. Again, we've heard that the emphasis is on risk and that there is confusion about the information.

So what are our recommendations? First, we think the regulations have to be revisited. If they're inflexible in terms of allowing, for example, some resolution with the formatting problems that currently exist in pharmacies that would allow text documents to be printed until equipment and technology can come up to doing PDFs, then those things need to be fixed.

We also have to address the cost shift issues that have been described over the past day and a half.

We need to allow for innovative solutions that focus on electronic rather than print distribution of the information. We heard some

discussion of potentially merging private sector CMI and medication guide information. But the important issue is that we need to test which of these models is most effective in communicating the risk information that is intended for the patient to receive.

And then we also need to carefully evaluate the content that's in there. Why are certain medication guides written the way they are and others not? And I heard a suggestion earlier this morning for example of actually coming up with the clearer guidelines as to what the intent of the medication guide truly is.

We need adequate and well designed research to assess the useful and effectiveness of medication guide. We both have to evaluate them as stand alone documents and they also have to be evaluated in the context of other patient drug information that's being received.

We need to determine scientifically whether verbatim appendage of medication guide to CMI greatly enhances effectiveness in the communicating risk compared with contextual content integration into CMI and with reference to a medication guide, for example, that could be accessed electronically.

We also need to carefully assess the

balance of risk and benefit, and we should be doing that through some sort of an expert review process to determine whether or not there is a balance being provided. Whether or not patients can truly make an informed decision along with the health care provider about the risk verses potential benefits of the drugs. And if changes in FDA policy are needed to do that, they should be done. And we've heard a number of speakers talk about the need for patients to have not just risk information but also to have benefit information.

I'll skip by that.

The earlier slide where I said what the burdens were initially calculated at, we need to relook at those assumptions because there are costs associated with those and we need to figure out if there's going to be cost shifting, and there likely will be to the pharmacy departments, how will we deal with that cost shifting issue.

And then the final point that I'll make has to do with web access to the information. As a publisher I can tell you that it's extremely difficult to locate documents on FDA's website be it professional labeling or patient information.

It's not always readily apparent whether

you have the most up to date version of that information. I mentioned that the URLs are not stable so if you link to those documents in a piece of CMI today, it doesn't mean that it will link to that same piece of information a week from now.

There are websites that the FDA could currently take advantage of. MedlinePlus being one and DailyMed being another one.

And there must be an easy, timely and dependable method of notifying all interested stakeholders, publishers and health professionals about revisions to documents and how to obtain those documents.

Thank you.

DR. SELIGMAN: Thank you for your comments.

Any questions from members of the panel? Yes?

DR. BERNSTEIN: Thank you very much for these recommendations.

One of the recommendations that you made was, and we've heard this again and again over the last day and a half is merge the CMI and the medication guide. But you particularly said on the slide it said permit merging of CMI and medication

guides. And actually in retrospect I'm not sure how people, the ones that we've heard before, how they envision that merging of the information, whether it be something that FDA would do or allowing some third party to do it. Could you comment on that a little bit?

DR. McEVOY: Sure. I think that there are several options that can be explored. First, just appending the information. And I know in some early discussions with FDA there were concerns that the way that the information got appended may dilute the importance or the relative importance of the medication guide information compared to the CMI. So in its simplest form, that's one mechanism of merging it.

A second mechanism is that the CMI publishers currently are summarizing what's in a medication guide. It appears in a black box warning at the top of the CMI that they are publishing. And in our specific case we then provide advice on how to obtain the actual medication guide and electronically we would like to go back to including the specific link. We currently do include a link to CDER's website, but we would prefer to have it go directly to the document. So that's another approach that could

be followed where the patient could get the full detail, but the CMI that they have would be presenting the information in context. This is the context of this risk versus the other risks that apply to that drug.

The point is that we need to be creative and we need to study it. We can't just take the opinions of the assembled masses that have been testifying here. We need to engage the consumers. We need to create different versions of the same information and test it. And that's the only way that we're going to find out what the best way is to communicate this information.

The ultimate goal is medication safety from the consumer's perspective. And unfortunately we've got a program that was developed and implemented without testing the potential consequences of how the information is being provided.

So I think there are a variety of options that can be tested. And that's really what our recommendation is: Test alternative solutions.

DR. SELIGMAN: Thank you for your comments.

We'll take two additional questions from the panel.

Jason Woo?

DR. WOO: Yes. Thank you for your presentation and your comment about how to better inform pharmacists or providers.

We do have through the MedWatch system MedWatch Alerts subscriber system. I'm not sure how well it's used -- utilized by pharmacists. Can you speak to any ways to make pharmacists more knowledgeable or for them to access? Because we can't go and require people to sign up for their license, it's a voluntary process.

DR. McEVOY: Right. I can tell you what we do. In our professional information when a MedWatch notice becomes available, we immediately append that information at the very top of our monographs, our drug monographs and it provides them links to the additional detail that's on the FDA website.

We also reinforce what that MedWatch notice was in context within the document. So if it affected dosage, for example, or some other section.

We do the same thing for our CMI. When a MedWatch notice appears, we do append that and the links are also available to the MedWatch site. And last year, we added specific instructions on how patients can submit MedWatch reports, adverse reports

to the program as part of our CMI.

DR. WOO: Yes. Actually, I guess I was getting at how you provide all that information. Nevertheless, it still requires the pharmacists to either contact you or to sign into our system. Is there anyway to improve that type of participation?

DR. McEVOY: Well, I think part of the problem is just the general design of FDA's website. And the access points to find it. And I know that the agency is well aware of those issues. Resolving those issues, I think, will take a long step forward in perhaps bringing to people's attention some things like MedWatch program.

DR. SELIGMAN: I'm going to ask that we actually curtail questions for the moment in the interest of hearing from the other speakers. But, please save your questions so that if at the end of the panel, if we have time, we can return to those.

Thank you for your comments.

Our next speaker is Ms. Becky Snead from the National Alliance of State Pharmacy Associations.

MS. SNEAD: Thank you, and good afternoon.

My name is Becky Snead and I'm a pharmacist. I represent the National Alliance of State Pharmacy Associations which promotes leadership,

sharing, learning and policy exchange among pharmacy leaders in all 50 states as well as Washington, D.C.

NASPA appreciates the opportunity to comment. And our remarks will reflect a lot of the responses that you've heard. So on those items in which you've already heard about, we're going to omit out of my testimony this afternoon for an opportunity to have a dialogue, and also to reiterate some of the recommendations that we think are of are extreme importance.

This, as evidenced by the testimony that we've heard over the last day and a half, is an extremely important issue. And so I want to just once again thank you for the opportunity to convene this group and to have this discussion. Because the number one recommendation that NASPA and NASPA members provided to us was the importance of convening regular stakeholder forums. Great minds come up with great solutions, and if we keep the patient at the center of all of our discussions along with a strong commitment to a research agenda, we will at the end of the day make progress. And I think that that's what our expectation should be: We should all leave here with an expectation that we're going to make progress in this area.

Evaluation and reevaluation is necessary to analyze the outcomes. If it's important enough to do, it's important enough to measure. I can't underscore that enough.

We need to prompt increasing access points for medication guide information. The patient, the prescriber and the pharmacists triad implies that this information should be available directly to the patient at point of prescribing, directly to the patient through an electronic means, and then also from their pharmacist.

Included in our discussions around this, though, we also need to address the issues of sampling, prescription assistance programs and also nonpharmacy points of dispensing. Because they are a part of the comprehensive review that you need to take in order to be able to craft an appropriate solution.

Provider education is crucial. And you struck at the very heart of what state pharmacy associations spend a tremendous amount of time and energy on. I am given the opportunity and have the pleasure of serving as the Virginia Executive Director for the State of Virginia. And through that role, every year I go around to 14 different locations and do face-to-face education with pharmacists and student

pharmacists throughout the Commonwealth.

For the last four years, I have had a multitude of slides on medication guides. And I just completed my cycle just last month of my 14 location road show of updates of what people needed to know. And this year I got the blank stares: medication guides? I got the question: "You mean they need to be distributed with refills, too?" "You mean the antidepressant medication guides don't just need to go to adolescents and teenagers?" "Well, what do I do if the prescriber asks me not to distribute it or if the patient requests not to get it anymore because they've gotten it from me repeatedly." "Well, where do I get them?" "You know, I got a pad to begin with, but since that time I haven't gotten any more." "And I call the 800 number for the manufacturer, and they don't know what I'm talking about."

And so I don't think any of these comments are new comments. You've heard them from other presenters today. But I wanted to let you know that they're real and they're current. This system is unworkable and unsustainable at the rate of growth in which we've experienced. And so provider education is critical. And not only the education on the medication guides, but also the education about other

FDA resources that are available. We've included that in our programming and in our journals and in our e-alerts. But the reality of it is, and I would love to say that it was different but it's not, but only 30 percent of the practitioners belong to any professional group.

So we have a lot of work to do to get the masses to move along. And that's the reason why the stakeholder forum are so critical. That's why it's so important that you bring all of the people together. And we all work at this together. Because none of us alone can provide the solution.

I was struck by the fact that I consider myself after being a practicing pharmacist for over a decade and being in association management for the last 12 years, I thought I was pretty well connected. I provide a lot of educational programs about federal agencies and resources that pharmacists could have. And I left here yesterday having to Google and find out what DailyMed was. And I'm only admitting that to you to underscore the point that for a practicing pharmacist to be able to keep up and know all of the resources that are available to them and all of the things that they need to do to provide appropriate patient care is a tremendous challenge.

And I think that we've got one of our best kept secrets in some of the resources that are available from the FDA. And we need to do a better job of trying to do that. That's not a new concept. Many of the speakers have already attested to that. I just wanted to reenforce how important I felt that it was.

The flexibility in formatting so pharmacists can integrate printing of medication guides into their current systems is a reasonable and an immediate solution for some pharmacies. However, this will not be a solution for all pharmacies until their technology advances to a level where they can implement this option.

In addition, I would not say that that should be viewed as a long term solution.

Dispensing medication guides with new prescriptions and upon patient request I think is reasonable. I would say that dispensing medication guides with every new and refill is not. Three hundred million prescriptions and growing is not sustainable in a paper system as long as we're still in that paper system.

Allowing medication guides to be emailed to patients that choose to have them distributed in this fashion is a given. There's no reason why we

shouldn't proceed down that pathway.

And in addition, allowing patients to opt out of receiving medication guide is also reasonable. Right now when I have a patient that comes in and requests a nonsafety container because of their arthritis and they can't get the child proof cap off, they sign a waiver at the pharmacy and say please put my packaging for my prescription in a nonchild proof container. We could implement that system very easily for the patients that would like for us to not distribute the medication guide to them for that particular product. It would not be a blanket if there were other prescriptions that would be issued to them, but I think that that is very reasonable and doable and implementable solution to some of the burden that's being placed on the pharmacy profession.

Certainly, and I've already highlighted, the centralization of medication guide as well as information on how to obtain medication guide. Because not everybody is going to be able to print them or have the technology to integrate them. But having a centralized place that tells me where to call to even get them would be a huge step.

I indicated earlier that I provide a lot of education to pharmacists throughout the country,

and certainly in Virginia. And while preparing my testimony for this I went back to the FDA website. And I'm ashamed to say it took me five minutes to find the medication guide section, and I'm frequent user of the FDA website. You use search and you don't get it. And I guess I should have had it bookmarked by now, but I didn't, and so I fumbled and I finally found it. And if it's that difficult for me, then I wonder how we're ever going to be able to have that as a vehicle that's usable for our practitioners.

And then I believe eventually standardization of length and format is essential. Additional information that may be useful can be referenced and located on a centralized website. If they're alerted that there's more information if it's too detailed to include, then you can use that new robust siting, centralized website that you were going to build and have additional information for those that have the capacity and are wanting additional information, or they can ask their health care providers. It says here there's more information. I don't have access, but I really want it. The health care provider for that patient would be able to facilitate that request.

And then in closing, I believe that

written information alone is not the answer. Individual's health literacy levels, language barriers deter and demand that we require and find a health care model that supports face-to-face provider education on prescriptions, especially for medications that are deemed to pose serious and significant public health concerns. It's essential that we understand that this is part of what we need to be doing in conveying this information.

And one of the opportunities of being one of the last panels to present is to answer a question that was previously asked, and it was a concept that I had, and that was how are we going to drive the pharmacists to be more aware and more compliant in providing this information to our patients. And one very real and dynamic tool are the quality measures that are being developed by the Pharmacy Quality Alliance. I happen to have had the privilege of chairing the Patient Safety Workgroup. And one of the items that we added in as a starter measure for the Pharmacy Quality Alliance were contraindications in black box warnings. And while there are severe limitations currently within the implementation of those starter set of quality measures because they're all linked to drug claim data right now, it's not

integrated data for patient care, there are some drug claim data indicators that can be measured and monitored and pharmacies can receive feedback on how they're doing regarding adhering to the warnings that are on those black box warnings. And so I think that there is a pathway to drive compliance in the pharmacy community through the Pharmacy Quality Alliance and new and emerging quality standards that will be evolving.

We will have to test those, of course, and validate them. And then research them and then introduce them into the marketplace, which is exactly the process that I would suggest we use with medication guides.

Thank you for the opportunity. I'll be glad to answer any questions.

DR. SELIGMAN: Thank you for your comments.

Any questions from members of the panel? Yes, Ilisa Bernstein.

DR. BERNSTEIN: Can you just briefly expand a little bit on the quality measures?

MS. SNEAD: Sure. And I could spend two days because that's one of my recent passions.

CMS has been facilitating quality measure

implementation among various health disciplines, the Hospital Quality Alliance has hospital measures, the Ambulatory Quality Alliance has outpatient ambulatory care centers, physicians' offices that they are now collecting data on. And with Medicare's payment for prescriptions drugs, last April they formed the Pharmacy Quality Alliance, which was given the charge of developing a starter set of quality measures in which pharmacists and pharmacies would be measured on as it related to medication use. And to that end the Alliance has adopted 27 to 30 starter measures that are currently in the process of being tested and validated. Once they go through that process, they will then go into a demonstration project and then be implemented out into the payer community that chooses to adopt it. But certainly CMS is a willing partner through their Medicare Part D plans.

One of the areas that we identified that we needed to have quality measures in for pharmacy was around patient safety. And we divided up the different focal areas into what we called clusters. And so the patient safety cluster considered things like drugs to avoid in the elderly. They considered drug interactions. And then what we term our never never list of instances that should never occur. Now knowing

that there's always an exception, but if you have a patient with it by claim data, it would indicate they had a certain diagnoses and it was a black box warning that said that that patient shouldn't use it, then it would hit. And that would be, of course, taken into consideration and context of all the claims that were coming in for all the variables that would be there, but it would be a reportable event through claims data. And that that would be the foundation of assessing quality in pharmacy.

DR. SELIGMAN: Very good. Thank you for your comments.

Our next speaker is Bryan Ziegler from the National Community Pharmacists Association.

MR. ZIEGLER: Thank you for the opportunity to be here today. I represent the National Community Pharmacists Association. And we represent the 24,000 plus independent pharmacies in this country. And these independent pharmacies dispense nearly half of all the prescriptions in the retail setting in this country. And as an organization we do share the FDA's interest in making sure that patients utilize medication appropriately, have access to information so that they can make informed health care decisions.

These are the questions that we hope to address in a brief presentation here.

This slide here is just highlighting some of the current status of the medication guide situation today. And of these, I don't want to harp on them because we've gone through this the past day and a half, but there were two instances here that I think highlight some challenges specific to independent pharmacy. One of them is the PDF only format for the electronic versions. We've mentioned before that printer and computer issues have been a problem. But there are certain instances where another issue that if we do go to the electronic format, just to make the panel aware of, that many of the independent pharmacies in this country do satisfy the need in the rural community. Internet connection is sometimes not available. And if it is available in many of these areas, it is only on a dial-up basis.

So speaking with a member in a rural area his question to me was if there are medication guides out there that are 20 to 30 pages long, as Mr. McEvoy has pointed out in some of his research, how long would it take him to download that if he had to hand it out to a patient. Even if it was a two page document, how long would that take him and what

implications would that have on his daily work flow as far as distributing in electronic format for some patients.

The other point I wanted to highlight was the variable methods of informing the pharmacists of the medication guide requirement. The Board has had multiple questions about that particular aspect. I feel that the comments that I have received and the input from others at our staff, the pharmacists, there are many of them out there that are still unaware of the requirement. They're still unaware of which drugs need them. And as Becky pointed out, Becky Snead, the issue is current and we can confer with that. We feel the FDA could certainly improve their communication efforts with which pharmacies receive this information. We feel that utilizing the pharmacy trade organizations, some of the publications they have, state boards of pharmacy and yesterday it was mentioned increasing communications and relationships with the national association boards of pharmacy in the state level could be a very important valuable communication tool that you could utilize to get the word out to this particular population.

The medication distribution as far as the independent pharmacy community is concerned, these

were some of the more prominent ways in which they are finding out about medication guides. Trade organization magazines and publications. Their computer software vendors, some of them do have flagging systems in place, but this is not across the board or even a standard from what we have gathered. Drug representatives were mentioned as a method that these were being distributed to some of the pharmacies. So as they are coming in providing information about the products, they are actually leaving medication guides. Email notification and the word of mouth from other colleagues.

Yesterday, the National Association of Chain Drug Stores presented various mechanisms that manufacturers are sending the medication guides to pharmacies. I certainly don't want to revisit that, but we certainly agree with their assessment. And independent pharmacies are experiencing the same issues with the inconsistency in methods of obtaining the medication guides from the manufacturers.

Maintaining work flow was mentioned yesterday as well as an important component to safe medication delivery. Med guides have presented an impairment to the work flow of many pharmacies as many have to store the medication guides in locations

separate from the drug product itself. They have to hunt through medication guides in order to find the information they need to distribute to the patient or they possibly have to stop the dispensing process in order to download a medication guide from a website, which in some independents they mentioned they have their Internet connection on a separate computer from their dispensing computer. So in that instance they would literally walk away from one computer to another in order to get this information.

If pharmacies will be printing the medication guides, another concern is the cost of printing these medication guides. And certainly we feel that's the responsibility of the manufacturers and the panel has expressed that same comment yesterday.

This slide points out some of the challenges that independent pharmacies may face if the electronic distribution of the medication guide is considered a sole method of distribution. One comment on here is regarding the email delivery from the pharmacy to the patient, which is not necessarily pointed out as a sole method of delivery, but as a viable option. On behalf of the independent pharmacies, the technology that most of these

pharmacies have is not the same as the CVSs and the Walgreens. So therefore, it would certainly be a larger challenge and obstacle for these individuals to take on to incorporate email capabilities into their software systems.

Also, chaining emails is not considered a standard practice for many of these pharmacies. They would certainly have to implement that and start from scratch. Work flow interruption in order to send the emails. And also once again, we revisit the Internet connection problems they may have.

As far as electronic format for obtaining the medication guides and that way the pharmacy could print them out presents a challenge. As mentioned previously as far as pharmacists actually knowing which medication guides they need to actually be downloading and handing out to patients. Also, where in the world do they find them? That continues to be a common response that we are receiving as well.

If the electronic distribution is implemented, we do feel that paper medication guides still have a place in the regulation and should be continued. We think they should be done in a standardized distribution format, and that way pharmacies can have the choice to implement either the

electronic format or the paper format into their work flows so that they can choose which one works best.

Class medication guides, they certainly have their advantages and their disadvantages and we don't want to harp on that. But overall from the comments we've received from our members the class medication guides have been the most effective ones as far as getting them and distributing them. They seem to be the ones that folks are most familiar with. So overall we feel those were somewhat the most successful, even though the successes varied from store-to-store.

We think that if we can limit the number of different types of medication guides that would certainly improve effectiveness of the program.

Earlier there was discussion about the length and readability of the documents. We agree that some of these documents are too long, incomprehensible based on the reading level and that they should be addressed with further study. We also agree that the benefit information should be included with the risk information in the medication guide. If the ultimate goal is to provide valuable information to patients, then risk and benefit information is a key to a patient making a decision as to whether or not

take a medicine. How can they assess the risk and the benefit of the medication if they only have half of the story?

We also recommend altering the requirement to distribute the medication guide only with a new prescription and not for all refills. If patients coming in monthly, and in many cases pharmacists mention there are patients that are still without health insurance. They come in every single week to refill a prescription. Do those folks have to get a medication guide every seven days stating the same thing? That is an extreme example, but it does occur on a regular basis.

At this time, I just want to point out our recommendations that have been shared with us from members and also some ideas that we have come up that may be beneficial to the panel.

Number one, we feel that enforcement of the current FDA medication guide regulation holding manufacturers accountable for providing the medication guide is important. The FDA has the leverage to regulate the manufacturers.

And we recommend standardizing the printing distribution methods to those which pharmacists can implement easily into their work flow.

Successes so far has been unit of use products that have the medication guide implemented with the product:

Products that have been them attached to the drug bottle has been positive for pharmacists. That way they have them right with the product itself. Tear off sheets were beneficial for the class med guides.

We would recommend including an adequate amount of medication guides to the product for the pharmacy to have sufficient supplies. In these instances where some of them only have one medication guide, you know possibly have a set standard where there's a certain percentage extra on top that the manufacturers are required to include with the product.

We also recommend that the medication guide be easily retrievable from the other labeling and package information. In other words, no cutting, no tearing required to minimize the time spent for the pharmacist to actually hunt for this information. If the electronic format is utilized, we just need to create a place where these documents can be easily accessible.

The second recommendation is to revise the

medication guide regulation for three reasons:

One is to mandate product manufacturers to create electronic medication guides with access on an NDC on National Drug Code based database as well as providing the hard cop paper medication guides. This would allow pharmacies to once again introduce either format that they wish for their work flow means.

Second would be to allow the incorporation of the medication guides into their pharmacy management software. This would further implement the compliance of the medication guide distribution and, once again, linking with NDC links that product being dispensed with the medication guide that they should be giving out to the patient.

Lastly is combining brand and generic medication guides into one document.

The third recommendation is to implement a standard message system to inform pharmacists of new medication guide availability. Communication, once again, with trade organizations, state boards of pharmacy, software vendors are a valuable commodity here as well, et cetera, could be a very important key to success.

Fourth would be to create a standard ordering system or clearing house for ordering the

medication guides. Especially if they're going to continue to be printed and not necessarily included with the drug products.

The fifth recommendation: If pharmacy will be printing the guides allowing formatting changes of the medication guides that the pharmacies can print if they're unable to handle a PDF document could be valuable for these pharmacies to meet the compliance requirements

The sixth one is manufacturers must bear the direct and indirect costs of distribution and printing by pharmacies if they will be utilizing the electronic format.

This is just the end of my presentation. I just wanted to highlight the cost and the amount of paper associated with printing these medication guides at the pharmacy level. My numbers here represent that seven percent of all prescriptions which yesterday Mr. Coster highlighted that number is now based on 2000 numbers. Closer to ten percent or 300 million prescriptions. So we could just bump it up by another 20 million to get the numbers. But these are rough estimates highlighting that right now eight pages based on Mr. McEvoy's research is the average med guide. At 280 million prescriptions it comes to 2.24

trillion pages of paper. That number will continue to grow each year as we introduce more drugs and more medication guides.

Current cost if we figure the cost of the paper, the cost of the toner and then an administrative cost to the pharmacy actually obtaining and storing these supplies at about .04 cents a page, it's nearly $90 million worth of printing costs.

If we get it down to two pages, we're still talking about 560 million pages of paper and a cost of nearly $22.5 million.

Yesterday the panel raised the issue of how do pharmacies get reimbursed for this expense. This is certainly a topic that has no perfect answer and would require further discussion. But there is not necessarily an unsurmountable challenge that can't be crossed. A gentleman from CVS mentioned that there can certainly be some sort of a reimbursement system set up for pharmacies to submit invoices to a single entity the FDA can control where the manufacturers distribute pools of money to reimburse pharmacies for this. Our initial thoughts, and by no means would these be conclusive, but would be to allow the pharmacies to submit basically a number of prescriptions dispensed during a specific time period

that actually require medication guides. We know how many pages these medication guides would be, and therefore they could be receiving reimbursement for this printing cost.

The next slide just highlights where I came up with my .04 cents. An important thing to keep in mind is this does not incorporate the cost of actually purchasing a new printer. It doesn't incorporate the cost of any warranty. It's strictly paper, toner and the cost of obtaining these supplies.

And that's all I have. Thank you for the opportunity to be here. Any questions, I look forward to them.

DR. SELIGMAN: Thank you for your comments.

Any questions from the panel? Yes, Bob Temple?

DR. TEMPLE: Just one. This comes up a lot. How close do you think most pharmacies are to being able to print in the designated format? I mean that seems to be a big problem that we didn't allow people to use alternative formats. But things move. You got to think they must be fairly close to being able to do that. Do you have any view?

MR. ZIEGLER: From the comments I've

received from my members, I mean we'll certainly try and gather some more data on that if necessary. But it's a wide range as far as the technology that some of these stores have. In the rural areas, I would say that we're probably much further away than we are in some of the metropolitan areas. But I think it would depend on a store-by-store basis as far as what kind of technology that they currently have in place.

Yesterday we mentioned there are some pharmacies that still use dot matrix printers. That still occurs. So you think nowadays most folks would be using laser printers, but that's not necessarily true.

The software that they use for their dispensing management system, that would be something that the software vendors may be able to answer in more detail about where they stand as far as incorporating the formatting into the CMI that they utilize. So that may be a question that they further could give you detail into.

Personally it's one of those things where in my practice experience I've seen the CMI formatting that's come out with the prescriptions and I've seen the PDFs. And I think the big question is now is just how many of these pharmacies can download a PDF and

how we incorporate that. It just depends on software. Software travels so quickly in technology that it seems like it could be updated fairly easily if everyone's on the same page and we have a set of standards.

DR. SELIGMAN: Toni Piazza-Hepp.

DR. PIAZZA-HEPP: Yes. The regulations have been referred to a few times. I just wanted to clarify the portion of the regs and then I wanted to ask a question.

The section on exemptions and deferrals, I've heard that discussed a couple of times and I just wanted to make sure that's clear. The regulation on exemptions and deferrals first has a section directed toward the applicant, who is a manufacturer. And it says that there could be an exemption or deferral from particular required sections because there's different section headings that are the required sections. But they first -- it's not as just they have just a blanket okay to do anything they want. They develop the medication guide in the way they feel is appropriate for that product, and they submit that to the Food and Drug Administration. And then we review it. And actually we have a patient quality information specialist, two which are in the audience today, who

review it not only for the language, not only for patient friendly language, but we consider actually the format, the heading, the bolding, the chunking, all that to actually be -- you know, contribute to its patient friendliness and useability by consumers.

And so we determine what headings and what format and language are appropriate for that particular product. And that's discussed and reviewed quite a bit by our office, by the Office of New Drugs and the manufacturer until we all decide what the best way to go -- what the optimal medication guide for that particular product is. And perhaps we have some improvement to do based on the discussions, but we'll take that into consideration.

So that is the medication guide that we intend for the patients to receive. And so that's why we hesitate when we're asked if there could be exemption from formatting and this kind of thing. And actually the regulation doesn't really in that section, it doesn't really pertain to its production at the pharmacy and changing it -- you know, giving any kind of a blanket waiver to change it. So that one pharmacy gives it one format and pharmacy B gives it another format. That's been our hesitancy. Because what we've approved, we feel this is what we

want patients to have. And so that is our hesitancy on that.

So I wanted to make that clear.

And just as an aside, if a physician -- the regs also state if a physician specifically informs the dispenser they don't want the patient to have a medication guide, then the dispenser doesn't dispense it unless the patient asks for one, and then they give it to him. And that's part of the regs as well.

But my question is I've heard a couple of referrals to the regs having to be changed. And rulemaking, regulation making is not a small task nor is it a brief endeavor, okay. And so the way the regs are written right now, it never mentions the word paper, hardcopy or electronic. It talks about providing the means, providing to patients. And we try to write regs so they'll have some longevity. What is about the regs that is actually a showstopper to some of the efforts that we've been talking about? You know, is there anything really in the regs that would prevent us from going forward and improving the access distribution, et cetera, of medication guides?

MR. ZIEGLER: Gerry, do you have the information? I think Gerry may be able to answer that

question a little better than I could. So I'll defer to him to that, if that's okay.

DR. McEVOY: There has been a stakeholder group that has been meeting with FDA now for several years. NCPIE has been a facilitator in that process. And the obstacle that we keep meeting is that the format of the medication guide must be precisely the same format, i.e., a PDF version of it that a text rendition of that was not acceptable.

Now, if the agency has changed its position, we'd be all very happy with that. And that's really the examples that were provided by CVS and Walgreens, I think it's about two years ago now, and the agency was not willing to allow that as a solution. Again, we've had these conversations and we've never gotten a response indicating that FDA was willing to permit pharmacies to print off a version of it that was not the same as the approved format. And if that's changed, I'd be ecstatic.

DR. TEMPLE: Well, I suspect that hasn't changed. Because we've become believers in all of this stuff about how to communicate and how format matters and bullets matter. So since, we believe in it, we've tried to devise formats that would have those properties. So my guess is we're probably not,

but I'm sure that's something we'll discuss.

And I want to ask you the same question I asked before. Surely, most pharmacies, anyway, must be fairly close to being able to print out an exact copy of the required thing. And is this is a matter of another six months or are the rural places never going to be able to do it? Where is that at the moment? I mean, all these things march on. They must be getting fairly close to being able to do it.

DR. McEVOY: I think it's highly variable depending on the pharmacy or corporation involved, and in many cases it's a business decision.

I went home last night and looked at the CMI that I received from the pharmacy that I get. And it stops midstream whenever its allotted space of eight inches by 6 3/4 inches is filled. It doesn't matter what information I've received. If it's filled that space, it stops. And the patient doesn't even know what they're missing.

And, you know, the study that showed that problem, FDA's evaluation occurred six years ago. So here's a very large chain that I get my prescriptions filled with, they've made no progress in addressing an issue that was identified six years ago. Now extend that to the medication guide. And I think it really

is baffling to me, but I think a lot of it has to do just with the sheer expense of replacing that equipment, replacing the software that drives that equipment. And I'm not the best person to answer that question.

DR. TEMPLE: Right.

DR. McEVOY: Ray Bullman, I know, from NCPIE has been involved with the group. And maybe talk to him later and he'll give you some additional insights.

DR. SELIGMAN: John Jenkins, you had a question?

DR. JENKINS: So we can better understand the technology limitations of some of these smaller pharmacies, can you help us understand how do those pharmacies that have the limited Internet connection handle their insurance information? You know, when I go to my pharmacy, I'm assuming that they're connecting through the Internet to figure out whether my insurance is still valid to fill those prescriptions. Maybe I'm wrong. How are they also handling their CMI information? Do they have it all stored on their hard disk?

MR. ZIEGLER: They are using phone line technology for the claims transmission. And as far as

their CMI, some of them is coming directly from updates with their software vendor that provides their pharmacy management system. And those usually come in CD ROMs for those folks.

DR. JENKINS: Okay.

MR. ZIEGLER: Some that do have Internet connections can update on a regular basis via the Internet. But the other folks receive a frequent mailing of the information on a CD.

DR. JENKINS: So they can receive electronic information via CD. Then it would be a question of whether their printer can handle a PDF versus --

MR. ZIEGLER: And if it's compatible with the rest of their -- if it's compatible with the rest of their software and hardware, then they can handle CD.

DR. JENKINS: Okay. And say a little bit more about what you said they handle their claims via a phone line connection. Is that the same as like a dial up Internet?

MR. ZIEGLER: Quite possibly, yes. But telephone lines are much more frequent and more common than necessarily Internet service providers in some of these rural areas.

DR. JENKINS: Okay.

MR. ZIEGLER: So that's another key issue, especially in very, very small towns in this country still an issue.

DR. SELIGMAN: We'll need to move on at this point.

Our next speaker is Anita Ducca from the Healthcare Distribution Management Association.

MS. DUCCA: Good afternoon. I am Anita Ducca, the Senior Director for Regulatory Affairs and Healthcare Policy for the Healthcare Distribution Management Association. On behalf of HDMA, I commend the FDA for holding this important public meeting.

I am here today to represent approximately 40 primary full service health care distributors, including national, regional and small family owned businesses that comprise our membership. Each day HDMA member companies deliver 9 million prescription medicines and health care products to more than 144,000 pharmacies, hospitals, nursing homes and clinics across the United States.

HDMA thanks the FDA for seeking comment on ways to improve communications to patients who receive medication guides. Today I'll discuss the following:

How distributors use medication guides;

How distributors are informed that a medication guide is required for a specific medication;

How distributors receive medication guides;

Additional operational considerations, and;

Our recommendations for the program.

Although we are aware of the specifications under the regulations for providing medication guides or the means to produce them to the authorized dispenser, distributors do not use medication guides in any way. Medication guides contain patient information and HDMA's distributor members do not interact with patients. Our connection with pharmacies and other dispensers is through a business relationship. We provide a product to them at their request. Developing or interpreting medical or risk information contained the medication guide is the sole purview of the product manufacturer in conjunction with FDA, not the distributor.

Similarly, patient information is needed by the prescriber, pharmacist or similar health care practitioner, not the distributor.

There is no standard or formal method for

informing the distributor that a medication guide must be provided the drug. Typically, distributors are first informed that a drug has a medication guide because a shipment of them arrives at their distribution centers. And for those that aren't aware of our terminology, a distribution center is essentially a very large warehouse.

In most cases, the shipment of medication guides is the only alert that the distributor receives, and there are usually no accompanying instructions or other information about providing medication guides to customers.

Similarly, there is no standard way that a drug with a medication guide arrives at a distribution center. Some manufacturers attach the guides to their products in the same way they attach a package insert. Medication guides also may be appended to and included in the drug's package insert or glued to the drug's package or container. Other manufacturers put a few loose copies in the cases holding the product, or send distributors medication guides in a tear-off pad. Occasionally these tear-off pads are included in the shipping case, but usually manufacturers ship entire cases of tear-off pads separately from the drug.

Typically, medication guide tear-off pad shipments do not include instructions for connecting the medication guides with the appropriate drug products or customers.

For HDMA members medication guides that are already attached to the package or package inserts are easiest to manage. When they are attached, they are automatically included with the product when the product is ordered by the dispenser. However, under these conditions the medication guides are also the least likely to be evident when they are added to the bottom of the package insert, since distributors currently have no specific notice of the medication guide's presence.

Distributors do not open a product package or unfurl the product's package insert to determine if a medication guide is included, as we do not want to risk compromising the integrity of the product or the package insert.

It's especially confusing when we receive medication guides that arrive separately from the product itself.

None of these methods for supplying medication guides to us is very efficient. Providing medication guides to distributors in varying ways

creates substantial operational difficulties at the distribution center, undercuts attempts to streamline or standardize procedures for receiving and distributing medication guides to our customers, and results in additional staff time and cost to handle them.

Before I turn to specific recommendations, I would like to make an observation about the medication guide program from the distributor's perspective.

Pharmaceutical distributors' expertise, as well as our operations, distribution center layout, equipment, computer systems and staffing are all designed to move millions of drug and health care products per day through distribution centers to dispensers.

The medication guide program has superimposed an information transmission expectation onto this product distribution system. These are two very different types of businesses and require very different sets of internal operations, staff training, storage provisions, retrieval mechanisms as well as packing and shipping processes. This information transmission requirement adds operational costs and requires manual effort which can lead to a significant

increase in the worker head count to perform the process. Not only are additional staff and shipping processes are needed, these operational problems are mounting concurrently with the increasing number and length of the medication guides.

Inventory space is also becoming an issue for distributors. More medication guides take up more inventory space, turning revenue producing space into nonrevenue producing space which becomes a hidden but significant cost increase.

We share the concerns others have expressed about the growth in number and length of these documents as the accumulative impact of these factors escalates the difficulty of providing them. To put it simply, distributors have had to revise the picking, packing and shipping systems to transmit a form of information they do not need or use sent in a variety of ways, if at all, and without advance notification.

Further, distributors have been expected to do this while experiencing an exponential growth in the number of medication guides coming through distribution centers.

We urge FDA and other stakeholders to consider proposals for simplifying the system in light

of the operational impact on distributors that do not typically provide this service.

HDMA is familiar with the recommendations offered by pharmacy trade associations representing our customers who receive medication guides. We believe many of their recommendations merit full consideration, especially those designed to streamline the entire program.

We particularly want to emphasize the need for an electronic medication guide system that is easy to use at the dispensing site. We recommend that FDA require electronic versions of this information and eliminate the paper approach entirely. We believe this is the most efficient method for ensuring the information reaches patients.

It is our strong belief that if a paper system continues, in the interim, FDA and affected stakeholders should move very quickly to simplify the paper system.

First, we recommend having physicians and other providers give the medication guides directly to the patient at the time the prescription is being written. In the interest of time, I won't elaborate on that, but we do agree and we've heard that recommendation by others in the last two days.

We urge the agency to consider limiting the information contained on the medication guide by setting a page length maximum or other information limitation. A page limit could be coupled with an 800 number on the label or on the medication guide itself where patients or pharmacists obtain further information if they so desire.

We also recommend considering the use of an 800 number, website or fax on demand approach for pharmacists to order medication guides directly from the manufacturers. Such an approach would meet the requirements of the regulations as it would provide the means for authorized dispensers to make a medication guide available to each patient receiving a prescription.

Finally, we agree with recommendations we have heard for grouping medication guides into a class when the risks are the same among similarly acting drugs. This will limit the number of different pieces of paper that must be tracked by all parties involved from the manufacturer through to the patient.

I would like to make one final comment regarding repackaging operations, as this has not been an FDA focus so far. Many retail pharmaceutical and other health care entities rely on repackaged products

which can encompass many different forms. Should FDA dispense with paper medication guides and permit their distribution electronically, we ask that the agency clarify responsibilities for preparing and transmitting electronic medication guides for repackaged products.

Thank you for including pharmaceutical product distributors in the discussion today. I'll be happy to answer any questions.

DR. SELIGMAN: Thank you.

We'll take one question. You have a question, Jason?

DR. WOO: Yes. Thank you.

If you can help just clarify for me how you're distinguishing between the product versus the information transmission? Because to me the medication guide seems very much like a part of the labeling.

MS. DUCCA: Yes.

DR. WOO: And yet you define these two as two separate business functions.

MS. DUCCA: In terms of how operationally it works, they are distinct from each other.

In our distribution centers, we're used to receiving products of different sizes, different

shapes, you know, bottles, liquids, pills, you know packaged differently, different package shapes and configurations. And we're use to that and we're set up to handle that, and we do it very well.

For the different formats that the medication guides are coming in; sometimes in paper pads, sometimes in the bottom of the case, whatever, you're transmitting information. You're not transmitting a product, a pill, a hard product in the same way. And, therefore, the way in which we would have to set up computer systems to do inventory tracking, for example, the kinds of shelves and racks you would buy to store these things, the way in which you would flow the product through the system as you are collecting overnight all the orders that are being placed and collecting those products; all that would be different for transmitting information versus the products.

DR. SELIGMAN: John Jenkins?

DR. JENKINS: I'd like to ask one quick question of whether the panel members can help reconcile. We heard a recommendation in your presentation that we go completely electronic for distribution of these medication guides, and yet we hear that it's just not possible. So how do we

reconcile those competing recommendations?

MS. DUCCA: I think -- yes, that is a problem. I think we recognize that this is not the immediate solution, the electronic. It's probably more the long term solution.

I think that if you had -- some of the panelists have been recommending a single central location that you could call on the 800 number or whatever to order medication guides, that might be a good interim solution.

I think what is troubling everyone is the different formats and the different ways in which is comes in, and even from the different places that it comes in is what is becoming extremely troubling. So I think if we could get some interim solutions together until we get that ideal electronic system, I think that's where we're going.

I don't know if anybody else has any further comment on that.

DR. SELIGMAN: I will let other members of the panel cogitate while we hear from our last speaker and we can return to this question of reconciliation at the end if there are additional thoughts.

Our final speaker is Danielle Daignault from Gold Standard.

MS. DAIGNAULT: Good afternoon. My name is Danielle Daignault. I am a pharmacist at Gold Standard, a division of Elsevier Health. I am managing a patient education and clinical decision support modules for Alchemy, an integrated drug database.

Today, I would like to start off by discussing what is at the heart of the matter, which is the patient.

Medication guides were originally developed to provide risk and safety information to the patient so that they could be better informed about their medication. As the system stands today, many patients are not receiving medication guides when they are required. The patients that are receiving them are overwhelmed by the high literacy level of the documents and the amount of information provided to them, particularly at a time in the prescriptive process when they no longer have an opportunity for discourse with their prescriber.

Some of the medication guides are currently inclusive of information other than the risk. This information is already provided to the patient in the CMI document dispensed by the pharmacy.

At Gold Standard, we currently include

some of the risk information highlighted in the medication guide in our CMI materials and use a standardized statement that tells the patient that they will receive a medication guide with their first fill and also with refills. We encourage the patient to discuss the medication guide with the health care professional.

The literacy levels of the medication guides are not adherent to guidelines set forth by the CMI document, which are sixth to eighth grade reading levels. If it was determined that these reading levels should be the goal for CMI, should medication guides should have similar literacy goals applied to them.

The medication guides should compliment CMI and not attempt to duplicate it. A suggestion is that the FDA rethink the medication guide's content to focus on the original intent, which is risk information for the patient. If this was the case, the documents would be shorter and complimentary to the CMI documents received. This would benefit the patient in that they would have less duplicative materials to read and perhaps be more likely to read and understand the material. Yesterday this issue was addressed by Jeanine Best.

Some of the most recently approved

medication guides have been shorter and punchier. I commend this effort and think that we need to continue this in this direction.

I have discussed how to better medication guide content for patients who are receiving them. Now I would like to discuss issues around why many patients are not receiving them and offer possible solutions.

One reason patients are not getting medication guides is because pharmacies do not always have an ample supply to give out to patients. If the medication guide was to be made available in an electronic format that is printable, this would increase patient's access. As it stands today, with the current formatting requirements it is a challenge to print out the medication guide in accordance with the regulations. This poses a problem for database companies who wish to include these documents in their files in order to help find solutions and get these important documents to patients. One possible solution is to have manufacturers to provide files in several format to database companies so that pharmacies can print them out. I realize this brings up cost issues of printing for pharmacies. If you consider my previous point of shortening medication

guide to include only risk information, this would alleviate some of the costs associated with printing.

Electronic medication guides could be incorporated into the drug product files of information vendors. If the medication guides could be integrated into the pharmacy work flow, the pharmacist would receive a system flag at the time of dispensing that a medication guide is required to be given to the patient and would have immediate access to it. This would eliminate the lag time from the pharmacist learns of a new medication guide to when they receive it. Also, the patient would receive the most current required medication guide as soon as it was made available by the manufacturer.

Finally, this method is effective as the pharmacist no longer has to waste time looking for the correct medication guide to give to the patient as opposed today often difficult to locate or simply unavailable. The pharmacist can spend more time with the patient.

As drug information providers, we have a team of pharmacists that update our database several times a day on a daily basis as we are notified by manufacturers and other sources of drug information -- I'm sorry - of new product information or changes to

existing product information. This is what we and other database companies do to provide timely accurate drug information, and why it is so pertinent that we integrate medication guides into our systems.

Since each of our vendors also incorporate drug data files into their systems, it would behoove manufacturers to provide database companies with electronic medication guides. This way physicians would have access to the most current medication guides and could discuss them with their patients at the time of prescribing. The pharmacist could reiterate this information to the patient at the time of dispensing at the pharmacy.

Gold Standard would also like you to consider innovative methods to increase distribution of medication guides, all while providing multiple access options to patients. One consideration is to have an Internet URL to provide to the patient. This URL will contain the most current medication guide.

Another idea is to provide a 1-800 number top the patient that he or she can call to get the most current medication guide.

Another thought is emailing the patients the medication guides.

These ideas are cost effective in that

they do not increase printing costs for pharmacy. We realize that these considerations do not provide a solution for all patient populations, but they are steps in the right direction towards giving patients better access to medication guides. And isn't that why we are all here today? For the patient.

We look forward to collaborating with you to come up with better solutions to provide patients with the information about their medications.

I would also like to address the issue of notifying pharmacists and other health care professionals about medication guides. I know as a licensed pharmacist in two states, I am required to complete specific CE programs in order to renew my license. This could be a required CE about medication guides and how to discuss medication guides with the patient.

Thank you for your consideration.

DR. SELIGMAN: Thank you for your comments.

Do we have any additional or further questions from the panel? Jason Woo?

DR. WOO: Thank you.

Actually, my question is back to Mr. Ziegler. When Dr. Jenkins was discussing what

electronic information is available. Do you have a concept of what percent of the pharmacies you represent don't have access to either cellular or microwave technology? Because tele-medicine has really come a long way in ten years since I've been involved with it. And I don't think there's any part of the country that doesn't have at least access to microwave towers?

MR. ZIEGLER: I don't have that information today. We can certainly compile that.

DR. WOO: Yes.

MR. ZIEGLER: And try and gather it for our public comment. I'd certainly like to do that for you if we could.

DR. WOO: Because I think that type of information would be helpful. If we're going to move forward towards looking towards how quickly electronic means could be adopted, it's helpful to know how soon we'd be able to drop the paper system.

Please?

MS. SNEAD: Could I possibly have a follow-up to that?

DR. WOO: Sure.

MS. SNEAD: I think that the additional item of consideration is even if you can have the

Internet accessibility, it's the innerconnectivity to be able to actually print that document that comes. Because most of the pharmacies operate in an operating system that is very specific to the dispensing of the prescription and the printing of the existing CMI. So unless it can be integrated through the data company that's providing the pharmacy that, then having access to the Internet is not going to be helpful.

DR. WOO: Sure. And there's certainly more costs involved. But I think one of the things is you have to start looking at the pieces of the puzzle before you can put the whole together. So providing access or ensuring that everyone has access, how we pay for the compatibility of the system is another issue that would have to be addressed with that.

DR. SELIGMAN: Any additional questions or comments?

Well again, thank you to this panel for your insights and inputs.

We will reconvene at 2:40 for the final panel of the day.

Thank you.

(Whereupon, at 2:25 p.m. a recess until 2:42 p.m.)

DR. SELIGMAN: If everyone can have their

seat, please. And if the next panel would come forward, we would like to begin.

Our first speaker on the last panel, and I'd like to thank the members of the last panel for being here and staying until the end, is Dr. David Fassler from the American Academy of Child and Adolescent Psychiatry.

Dr. Fassler?

DR. FASSLER: Thank you very much.

My name is David Fassler, and I'm a board certified child and adolescent psychiatrist practicing in Burlington, Vermont. I'm also a clinical professor of psychiatry at the University of Vermont.

My comments today are on behalf of the American Academy of Child and Adolescent Psychiatry where I serve as Chair of the assembly of our regional organizations.

The Academy is a medical specialty society representing over 8,000 child and adolescent psychiatrists practicing in clinical, academic and administrative settings.

In 2004, I had the opportunity to testify at the FDA Advisory Committee hearings on the use of SSRI antidepressants in the treatment of children and adolescents. As you recall, the Committee ultimately

voted 15 to 8 to recommend the imposition of black box warnings on these medications. To this day, there is no data which demonstrates that SSRI antidepressants increase the actual risk of suicide for patients in any age group. Yet as a result of the FDA's decisions and the attendant media coverage we saw a precipitous reduction in the use of these medications in the treatment of children and adolescents.

Tragically, we've also seen the first increase in the actual adolescent suicide rate since the early 1990s. And this is an increase which represents the annual loss of approximately 250 additional young lives. While it's still premature to draw definitive conclusions regarding causality, the association is clearly disturbing and several FDA officials have expressed similar concerns.

We would encourage the agency to continue to monitor this issue closely and to set a specific date to review the previous regulatory decisions and actions.

Although the Advisory Committee met in September of 2004 and the FDA announced its decision approximately a month later, it took over two years before medication guides for the SSRIs were actually developed and released. From my perspective these

medication guides were relatively one-sided, addressing primarily the potential risks of treatment while minimizing the benefits.

In addition, they didn't adequately address the risks of not treating a person with a serious psychiatric disorder such as depression.

In addition, the medication guides recommended a monitoring schedule which was not based on research or data, and which had no demonstrated impact on safety or outcome. The monitoring schedule was also widely viewed as unrealistically and impractical further limiting access to necessary and appropriate treatment.

Overall, the Academy did not believe that these medication guides contained adequate or sufficient information for our patients and their parents.

From a clinical perspective, they didn't really answer the important questions people had as a result of the extensive and often contradictory media coverage of the hearings and related activities. To address this issue, the Academy worked collaboratively with a number of advocacy and professional organizations to develop a more comprehensive resource for parents which was made available on a dedicated

website at www.parentsmedguide.org. Our guide, which was written without funding or support from the pharmaceutical industry is set up to answer 14 specific questions which parents have actually asked about the use of these medications. It also provides references and resources where parents can obtain even more detailed information if they so desire.

To date, the parents medication guide site has received over a million hits.

In February of last year, I testified at the FDA Advisory Committee hearing on medications used to treat attention deficit hyperactivity disorder, ADHD. In this instance both the Pediatric Advisory Committee and the agency ultimately rejected the imposition of additional black box warnings. Instead, existing language was updated based on current research findings. Drafts of proposed medication guides were developed and made available online in February of this year, one year after the Advisory Committee hearing.

During the development process the Academy and other organizations were invited to provide input, feedback and suggestions. The resulting medication guides appear to provide a more balanced and accurate view of the relative risks and benefits associated

with these medications.

While these medication guides are a useful resource, the Academy is once again working with the American Psychiatric Association and several family organizations to develop a more extensive guide which will provide additional research-based information about the safe and appropriate use of these medications.

In summary, I'd like to offer the following specific suggestions for your consideration.

First, the Academy supports the continued development and distribution of medication guides which contain research-based information about specific medications. Parents, patients and family members need and deserve as much information as possible in order to make informed decisions about treatment options.

Med guides can also help reenforce realistic expectations regarding treatment which can enhance compliance, reduce side effects and improve outcome.

Second, medication guides should be developed and disseminated as quickly as possible.

Third, medication guides must accurately address both the risks and benefits of treatment as

well as the risks associated with not treating a particular condition.

Fourth, monitoring schedules for clinical practice should not be included in medication guides unless they are clearly supported by research findings.

And finally, medication guides should be reviewed and updated on a regular basis as additional research becomes available.

In closing, I'd like to thank you for the opportunity to share these observations and suggestions. The Academy appreciates the FDA's attention to our concerns and we're happy to participate in this important and ongong public dialogue.

Thank you, and I'd be happy to answer any questions.

DR. SELIGMAN: Dr. Fassler, thank you for your comments.

Any comments from members of the panel? Dr. Temple?

DR. TEMPLE: Well, I have one main question. This has come up before that we should try to point out that these drugs have benefits. But let me tell you what our problem in this case is. It's not

that we don't suspect that they have major benefits, too, but nobody's ever shown that any use of these drugs improve survival or anything like that. So here you have something you're worried about, which is that kids are thinking about suicide and you can say in the other part well it does treat acute depression. But we couldn't figure out how to say what we think everybody would really like to be able to say, which is probably long term of these drugs has an effect on outcome. But, of course, that's not documented in the way that we'd be comfortable putting in there.

Got any thoughts on that?

DR. FASSLER: Well, one thing we do have good data that -- if you want to talk specifically about the SSRIs, that the use of the SSRIs prevents relapse, reduces the risk of relapse in adolescents by approximately 50 percent. To me if I was a parent of a child with depression, that would be extremely significant data which I would want to have.

So I agree, certainly, we don't have all of the data or all of the information that we want and we need more funding and we need more long term studies. But we do have important data.

We can talk about bipolar disorder and lithium. Lithium reduces the death rate, the suicide

rate 50 percent in adolescents with bipolar disorder. Lithium is a drug with a lot of significant side effects. But if I was standing here talking about treatment of cancer and I told you I had a medication that would reduce the death rate by 50 percent, it would be front page news in the *New York Times*. So parents and physicians need this kind of information. They need it accurately. It needs to be clearly based on the research that we do have.

DR. TEMPLE: Well, I agree we have it for lithium. But in fact for pediatric antidepressants, we only have one drug that we thought has been shown to work now. We suspect others do, too.

I'm just pointing out it was hard for us to write the balance because what we believed didn't meet the test of having been well documented, which comes up with a lot of these things. We have a lot of views about control of, oh I don't know, control of diabetes but precious little documentation of some of those things.

DR. FASSLER: But it also speaks exactly to why it's important to review and update the medication guides as additional information becomes available.

DR. TEMPLE: Oh, totally agree.

DR. FASSLER: Thank you.

DR. SELIGMAN: Yes, Dr. Woo?

DR. WOO: Well, thank you.

We've heard from earlier panelists, particularly the consumer groups, how they feel that the medication guides are an important source of understanding the risks of medications when their providers haven't necessarily covered those with them or have in fact told them ignore anything that comes with the labeling because that will just scare you.

The medication guides, in that sense, have a very specific role of being able to arm the patient with a little bit more information to go back to the providers. I get the sense from your presentation that this is more of a hinderance or a problem in providing good care, and in that sense the medication guide should really have a very different role than what the consumers are --

DR. FASSLER: I fully support giving people as much information as possible and having medication guides and other resources to enhance the dialogue between patients, family members and physicians. And to give people the information to ask appropriate questions.

One of the positive outcomes of the past

couple of years is I think people are spending more time asking questions and talking about both the risks and benefits. But I do worry whether it's the medication guides or even more so, the media coverage. If the risks are being exaggerated or magnified particularly relative to the actual incidence -- I mean, we've seen approximately a 20 percent reduction in the use of SSRI antidepressants in kids under 18. And I'm not a psychiatrist who thinks all kids need to be on medication, and we can successfully treat a lot of kids with depression and other psychiatric disorders without medication. And if all of those 20 percent of those kids were getting appropriate intervention, were getting CBT, that not be a bad thing. But that's not happening.

And so I'm worried that what we're doing and how we're approaching this issue, a combination of the media coverage, the delay until the medication guides and then the medication guides focusing more on the risks is really creating an increasing reluctance and hesitancy to use some appropriate and effective interventions.

DR. SELIGMAN: Thank you.

DR. FASSLER: Thank you very much.

DR. SELIGMAN: Our next speaker is Dr.

Darrel Regier from the American Psychiatric Association.

DR. REGIER: Good afternoon. I'm Darrel Regier and representing the American Psychiatric Association where I'm Research Director and also the Executive Director of the APA's American Psychiatric Institute for Research and Education.

APA is a national medical specialty whose 38,000 physician members specialize in the diagnoses, treatment and prevention of mental illnesses, including substance use disorders.

I note that I am speaking on behalf of the APA with no pharmaceutical or other outside funds used in conjunction with my testimony to this Committee.

I first wish to commend the FDA for proposing to substantively revise the labeling requirements for antidepressant medications prescribed to children and young adults. Numerous analyses conducted over the three years since the agency mandated a black box warnings have consistently noted that untreated depression carries substantially greater risks of suicidality and completed suicide than do the medications used to treat depression in this population.

To repeat, the risks of the disorder left

untreated far outweigh the risks of appropriate treatment, which by definition includes systematic monitoring of a patient's response to treatment.

Depression can be lethal illness. FDA's recognition of this clinical reality is a major public health contribution to the health and well being of children and adolescents and young adults who have depression, and certainly is recognized in some for the revisions to the patient guidelines and other descriptive material now associated with these medications.

Equally important is FDA's proposal to delete what many researchers and clinicians alike recognized as a well intentioned but arbitrarily chosen schedule for mandated follow-up to initiation of treatment of children and youth with antidepressant medications. The seven visits and 12 week requirements that was imposed more than two years ago as part of the initial black box labeling language had no empirical basis, and it was simply a measurement protocol used in the NIMH funded treatment of adolescent depression study.

Since then the value of measurement based treatment approaches has been convincingly demonstrated in the NIMH STARD, Sequence Treatment and

Alternatives for Remission of Depression study. One specific assessment and monitoring instrument, the PHQ9 has been tested and used in a research project jointly conducted by the American Academy of Family Physicians, the American College of Physicians and the APA to monitor depression, treatment response and risks including suicidal ideation.

In that study, the real world practice in a range of care settings demonstrated that PHQ9 scores influence clinical decisions for 93 percent of patient contacts. The most common events recorded were changing the dose of the antidepressant or adding another medication followed by starting or increasing psychotherapy and switching or initiating antidepressants. In three percent of patient contacts recorded by this study, PHQ9 scores triggered additional suicide risk assessment.

We all agree that monitoring is vital. It is encouraging to see a consensus that it should be tailored to the severity and treatment needs of the patient whatever his or age for close observation of clinical worsening, suicidality or unusual changes in behavior.

Now as my colleague, Dr. Fassler, noted controversies indeed, serious scientific debate

associated with the meta-analyses that led to the Pediatric Drug Advisory Committee's split vote in favor a black box warning on the antidepressants for children and adolescents beginning in 2005 prompted the APA and the American Academy of Child and Adolescent Psychiatry in consultation with the National Coalition of Parents, Providers and Professional Associations to develop and disseminate a factsheet labeled "The Parents MedGuid" that we believe provided a balanced overview of the benefits as well as the risks of antidepressant use and of the decided risks of leaving depression untreated at any age.

More than a million visits over the past two years have been recorded to this website. And this attests to the need for a balanced reader friendly presentation of the complex research-based data that must inform clinical decision.

Effectively communicating the risks and benefits of any medical intervention is a challenging task. And for that reason our research staff at APA planned from the first issuance of The Parents MedGuide materials to evaluate how it was received and how we might improve it. And we are now collaborating with the Agency for Health Care Research and one of

their grantees to conduct an evaluation of the use and the benefits of this particular website information source. And doing it in comparison with some of the information that patients will receive from the medication guide that is issued by the FDA.

We would recommend that the FDA similarly support evaluations surveying both patients and physicians of medication guides that pharmacies hand out with prescriptions for the antidepressant medications.

The success of The Parents MedGuide prompted the APA to collaborate over the past year with the American College of Obstetricians and Gynecologists, otherwise known as ACOG, to develop a similar factsheet that summarizes an immense amount of research data pertinent to the interests of women who have depression in the context of pregnancy as well as providing information to their spouses or significant others.

Like the original Parents MedGuide, this new product will be accompanied by a somewhat more technical and fully referenced advisory prepared by physicians and other primarily health care personnel. These guidances are now undergoing a rigorous scientific review by both organizations, that is both

the APA and ACOG, prior to distribution later this summer.

And in closing, I would repeat a caveat that I made in my testimony before an FDA committee two years ago. A special collage confronts the review of research-based treatments for mental disorders that is not often experienced in research on other general medical surgical conditions. The FDA is under substantial pressure from individuals and organizations with an ideological belief system and bias which denies the existence of mental disorders altogether. Certainly if mental disorders did not exist, many of the issues addressed by this Committee would certainly be moot. Yet mental disorders are very real and only through the combined expertise of all parties involved in this discussion have we realized a scientific revolution in treatment of these disorders.

The decision facing the FDA are profound and have the potential to greatly improve our ability to accurately assess and understand both the risks and benefits of long term use of potentially lifesaving medications.

We certainly commend the exploration of the scientific treatment guidance questions raised in

this hearing with the hope that better and safer communication about treatments will emerge as a result.

And thank you. And I'd certainly welcome any questions.

DR. SELIGMAN: Thank you very much for your comments?

Any questions from members of the panel? No questions.

DR. REGIER: Thank you.

DR. SELIGMAN: Thank you again.

Our next speaker is Dr. Carol Watkins from CHADD.

Dr. Watkins?

DR. WATKINS: My name is Carol Watkins. I'm a children and adolescents and adult psychiatrist. I don't take money or office lunches from the pharmaceutical industry. I've been involved with CHADD, children and adolescents with attention deficit disorder for many years. I'm the mother of a 16 year old and 12 year old son who take Concerta and short acting methylphenidate for ADHD.

I brought my 12 year old son Adam with me. He recently read the medication guides for Concerta and for the antidepressants and he has some reactions

to them.

The guides are meant for adult consumers and parents, but children will be reading them and they're definitely at a reading level he could manage.

As a clinician, I recognize that when I give a diagnoses or discuss treatment recommendations initially, the patient and family can be in a highly emotional state. Sometimes this can be helpful. That emotional state may focus the family and motivate them to follow through on a treatment program. However, intense emotions can sometimes interfere with memory and make it difficult for patients and families to process complex discussions of risk and benefits, treatment plans and what to do if A doesn't work and B doesn't work and long term issues. And that's why sometimes having something in writing can be very helpful.

As a parent, I remember the intense emotions I experienced when my older son was first diagnosed with ADHD. Even though, I was a child psychiatrist at the time, worked a lot in the schools, it was difficult for me to hear and process what his teachers were saying to me. I wasn't the ideal parent hearing this.

The next time around with my younger son,

I was more relaxed about the diagnoses and treatment planning and was much better able to process what we planned for treatment. And was much better able to be a reasoned advocate. And I think this occurs for a lot of people, regardless of their educational level and their background.

We, as clinicians, do see patients and families with a wide variety of beliefs, emotional states and background knowledge. The detailed information that has been in the past included with medication so complex in detail that people tend to ignore it. On the other hand, some people read that and will get overwhelmed with it, too. However, so in principle I really welcome the plain language medication guides, and it's something that's been needed. There's really need for something written in plain English that explains risks, but also explains potential benefits of medications.

The current guides have some strong points, but do also show some need for improvement. I really appreciate that they're shorter, that the font is easier to read and that particularly they have instructions in how to take medications. That may be one of the reason they have so many different ones for the stimulants because there's some that says don't

cut them, others that says you can sprinkle them over applesauce. Things like that are really very helpful. I think that that is one of the really major strong points that I'm glad is in there.

However, the medication guides as currently published aren't really guides completely in that many of them are more focusing just on risk as opposed to what you're taking it for and what you might hope to see.

What I do when I'm working with patients is we go through and we pick out let's come up with some observable measurable things that we can look for. This is in addition to maybe checklists and other forms of measurements. I come up with their top three or four things that we would both like to see the medicine change. Something that means something to them and follow that.

And I think it would be nice if the guides did say a little bit more about what you would hope to see. Because you don't necessarily want to keep giving a medicine if it's not doing anything.

Now I think also the guides, they list the most severe side effects first. And it's good to have those in there, but the things that most people run into are the more annoying side effects. And a

lot of times those things may be the reason people change the meds on their own or stop them. And I would like it if they had the more common things first, because this is what a typical person is going to run into. Things like with the stimulants appetite issues or irritability. Well, they do irritability. But I mean minor irritability kinds of things, too.

It might also be useful to have side effects or to compare the incident to side effects to placebo. Some things like headaches you can get with the placebo also.

The guides should be coming out sooner. I think that's been mentioned. And changed more frequently to reflect new understandings of the medications, their indications and side effects.

I asked several of my patients what their thoughts were about the medication guides because a number of them have gotten them. And what they said was that they were somewhat frightening but that nobody's gone off them based on the medication guides because they said that I'd covered most of that stuff in the session, but I put it in the context of why we would give you something that has these potential side effects. So I think really it would be nice in a way of something like this were given out by physicians.

But if I were to give something like this out, I'd like to have -- and they take it home in writing and read it, that it have a lot of the benefits on what we should look for, too.

And some of them, such as the antidepressant ones, do say these are some things to look for in case this side effect might occur. The suicidal ideation. And it's nice if you could give some ideas of how you might assess for some of these things. What you could ask your doctor about doing for tests.

I would also like to see for some medications that come in liquid form that there be some sort of a guide, because I've had a number of patients where I've had to prescribe something in a liquid form and I had and or two people who came to me on a liquid medication where I cured their side effects by just getting it straight about how they're measuring the darn thing. Because people don't always get instructed. That's something pharmacists could help with, but physicians, too. Do you want to have an insulin syringe to measure it up. That the spoon in your kitchen cabinet isn't the same as a measuring spoon. And I would really like to see, you know, all liquid medications or at least many of them have some

sort of a guide that talks about accurate measuring. Because you'd be surprised how often this happens. I mean a great couple of my cures that I've done just by bringing in the spoon. But I'd like it if that didn't have to happen.

In addition to these guides, I'd like to see a different sort of guide directed at physicians. I think it would be helpful if the FDA sent the physicians lists of drugs in each category with their average wholesale or retail cost for people like who aren't using insurance.

We, as physicians, are inundated with pharmaceutical representatives who urge us to prescribe the newest and most expensive drugs. And when pharmaceutical costs rise, insurance companies then develop formularies which restrict our medication choices. Because there are sometimes when the most expensive drug is the best one, and you may not then be able to do it very easily. But there are many other times, we could get by with a less expensive one that isn't advertised as much.

And it used to be when you have a Pennsylvania license you would get that sort of thing. I don't think they do it anymore. But it would be nice if they had a national education program to

inform physicians of equivalent medications that were less expensive, we might able to achieve a voluntary cost savings and reduce some of the need for mandatory formulas.

In general, what I would like to see is more of the list of benefits of these medications and things we could look for to show that they're helping as to balance off the side effects, too.

Now my son Adam Brynes is 12 and just finished the sixth grade at Montessori School of Central Maryland. And I recently had him read some of the medication guides, the one on Concerta and the one on antidepressants in adolescents. And he had a few reactions to it.

ADAM BRYNES: Well, when I read the guide, I had already taken some of the meds that I was reading about, for several years. But had I been made to read this before starting on the medication, I would have been worried and pretty much it makes it look like there's a higher chance of the bad side effects than there is in reality. I mean, because it lists them first and doesn't for a lot of guides give the statistics or statistics that may necessarily apply.

I mean, if I had written it or could make

some changes, I would have pretty much said at the beginning and the end instead of just like in the middle maybe to -- if you have any questions, to consult your doctor or the person who prescribed it to you. Because, I mean I really think people, as my mother said, would be more worried -- should be more worried about the annoying ones rather than the downright dangerous ones, because those tend to be a lot more common. Like, I mean, such as blurred vision rather than sudden death or psychosis. I mean, or such as -- or like maybe they should be more read like decreased appetite.

So I-- in conclusion, I really just think that maybe there should be more stress in the medication guide on what to do if you are worried about it, more -- pretty much -- also to make sure that the studies are something that will not give people false beliefs about -- I mean, making them think that a drug is more dangerous than it truly is.

All right.

DR. SELIGMAN: Thank you for your comments.

Adam, I actually have a favor. Could you spell your last name for our transcriber.

MR. BRYNES: B-R-Y-N-E-S.

DR. SELIGMAN: Thank you very much.

MR. BRYNES: You're welcome.

DR. SELIGMAN: Any questions for either Dr. Watkins or for Adam? Questions, comments? Okay.

Thank you very much for your input. I appreciate it.

MR. BRYNES: You're welcome.

DR. SELIGMAN: Our next presenter is Mrs. Janet Sisk from the Juvenile Justice Foundation.

MS. VAN SYCKEL: Hi. I'm Lisa Van Syckel, I stepped in for Janet. She had a crisis down with one of our kids in South Carolina. So I'm going to read her statement.

And be patient, because I'm reading without my reading glasses.

DR. SELIGMAN: That's quite all right. Just repeat your name one more time again, please.

MS. VAN SYCKEL: Lisa Van Syckel, Capital V-A-N capital S-Y-C-K-E-L.

DR. SELIGMAN: Thank you very much.

MS. VAN SYCKEL: Okay. It says dear members of the FDA. Thank you for giving me the opportunity to speak at today's hearing. I would like the FDA panel to hear how the lack of research into the association of severe agitation, violence and

aggression are affecting our children. I believe without question, drug companies have known for many years that there is indeed an association of severe agitation, violence and aggression that can lead to the risk of harm to others.

There is data available today showing the link between SSRIs and violence associated with a small population taking antidepressants. And many drug companies have taken great care to keep those results secret.

Luvox and Effexor have now issued warnings of homicidal ideation as a rare side effect. These drugs carry the same warnings as does each every other SSRI on the market today. There are no comparable different between the side effects, therefore all SSRI medications should carry the possible harm to others or homicidal ideation as a rare side effect.

One has to only look at the long list of side effects listed on the medication guide inserts to see that harm to others is a real possibility when a child begins to show signs such as severe agitation, aggression and violence and the medical professional as well parents deserve to have this information in order to protect their patients and their children.

Pfizer Canada has issued a warning of harm

to one's self and harm to others saying that there are clinical trials and post-marketing reports with SSRIs and other newer antidepressants in both pediatrics and adults of severe agitation type adverse events coupled with self harm or harm to others. But in American Pfizer states there is no acceptable evidence that Zoloft causes such thoughts and behavior and there is no current and available data linking SSRIs to increased aggression or violence.

I ask you today, do American families not deserve to have the same information and warnings in order to take precautions to be aware of the violent changes that can occur from these medications? New studies and clinical trials are desperately needed today on the association into SSRIs and violence. It is reported that there are now 23 million Americans prescribed antidepressants with a population of four percent who will develop adverse reactions to these medications. This is one million time bombs ready to go off at any given time, many who are children and are prescribed antidepressant medications off label and not approved by the FDA.

As of today, the FDA has failed to take any action into this issue, given the American public the impression that the FDA cannot or will not act on

this danger to our children. The FDA must remember whose interest it is supposed to protect and to issue a warning of a possible risk of harm to others on medication inserts which will protect our children.

I hope when looking at this issue the FDA would err on the side of our children's safety.

I am also here today to speak on behalf of one child who may have survived the adverse reactions to SSRIs. One of many that want his story heard that want you, the FDA, to take the proper action required and include a warning on SSRI medications of a risk of a harm to others.

His name is Christopher Pittman, and he could be the poster child on the importance of including a medication guide insert of the risk of harm to others.

Christopher while being prescribed Paxil and Zoloft suffered adverse reactions and killed two people he loved the most, his grandparents. Christopher was only 12 years old at the time he was prescribed the medication off label and not approved the FDA.

Christopher's grandparents were handed free samples of a mind altering drug with only the instructions written on the outside of a brown paper

bag. Had they received a proper medication guide insert, they may have become aware of what was happening to Chris.

When he complained of how the medication was making him feel or that his skin felt as though it was on fire, Christopher's grandparents, Joy and Joe Pittman, could be alive today if only they had received the medication guide insert.

We must make sure all vital information is included in the medication inserts given to professionals and parents, vital information needed in order to avoid such tragedies as the Pittman family and the many more families suffering today.

So my suggestions to the FDA, so that other families are saved from the tragedy and heartbreak that Christopher Pittman and his family are enduring today, I urge you to create an independent research program and begin to collect and establish a separate database on adverse reactions consisting of severe agitation, aggression and violence. The American consumer needs to be aware that there is a place to report such events, therefore, I urge you to require all the drug ads to prominently display a 1-800 number where these violent side effects can be reported.

I also urge the FDA to require the drug medication inserts containing all side effects and adverse reactions be printed in a larger format so consumers will have every opportunity to educate themselves on the dangerous side effects that are possible with these drugs.

I urge the FDA to require that all medication inserts be distributed to all juvenile detention centers as well as mental institutions and adult prisons. Many children and adults in the criminal justice system are on SSRI medications and may be having adverse reactions. It is very important that those in charge of these children and adults be aware that their actions may be a symptom of an SSRI and not the child or adult himself. In order to achieve this, they too must have the information to offer the best solution to a child or adult in the criminal justice system.

I thank you.

Oh, and she also when I spoke to her last night wanted me to reiterate the prescribing of antipsychotics, which is up 117 percent in girls, and I believe it's 71 percent in boys. And she was concerned of the violence associated with antipsychotics. And also increased suicide.

Thank you.

DR. SELIGMAN: Thank you for your commentary. And please thank Janet Sisk as well. Appreciate it.

Are there any questions or comments? Yes, Dr. Woo?

DR. WOO: Yes, this is actually a question for Drs. Fassler, Regier, who you can help shed some light on them.

A colleague and I were discussing that this is the second presentation of a case where something was used off label or given as a sample. And I guess some of the recommendations I've been hearing is to try and balance what's on the medication guide with an indication or the benefits to it. But for off label uses, where the FDA would not have approved some of the uses, to what extent do you think that that would be a hindrance or a benefit to the use of the medications?

DR. SELIGMAN: Want to try the question again?

DR. WOO: Sure. I mean for some of these medications for behavioral disorders there's an approved version, and that's I think when you are promoting including more information on the medication

guides that discuss the benefits that that seems more reasonable. The difficulty comes with some of these uses when they're used off label for other indications.

A label that strictly restricts it to the benefits that have been approved would not have that information. So when the medication guide's given to a patient and he says well this is not the benefit that I'm using, therefore there's all this risk and the provider is actually using for that off label use, is that going to be a greater hindrance to addressing some of the conditions that you're concerned about?

DR. REGIER: Well, let me just speak to the problem of off label use. One of the great difficulties we have is that many of the known benefits of medications such as the reduction in suicide associated with lithium are actually not on label. There has been a request to really get the suicide reduction indication for lithium approved by the FDA, but the FDA has not taken it up because these are generic medications with no payment to the FDA for taking this particular indication up.

Likewise, one of the most common uses of imipramine, and another generic drug, is an antianxiety benefit, and that is not on any label.

It's not an indication because it's been generic for so long that no pharmaceutical company has bothered to try to get an indication for it.

So I think there is a problem of the inadequacy of the indications that are currently on a whole range of psychotropic medications as well as other medications.

Now the other issue I would mention about the antidepressants, certainly there have been studies now of the antidepressants that have included nondepression uses such as some of the antianxiety, the obsessive compulsive disorder indications. And what's striking is that there has not been the increase in suicidal ideation, for example, that was identified with the antidepressant trials.

So I think that one of the things that now particular series of -- that comparison of trials demonstrates is that suicidal risk is really inherent in the diagnoses of depression. And the greater risk of suicidality or violence in that case seems to be associated with the particular diagnoses as opposed to with the medication.

So I think that the medication guides certainly go out to anybody who gets a prescription for one of these medications. I think that they do

list the risks. I think that putting it in balance with the benefits for the known indications, you know, is very helpful to put some balance into it. Because certainly as Adam mentioned, to read some of these things just straight out about the risks only without having some balance with the benefits can cause kind of an alarmist reaction. And if there are no benefits, as I've mentioned before as some people believe there are no mental disorders, then anything that you say about the risks, you know, will be left out of balance.

DR. SELIGMAN: Yes, Dr. Temple?

DR. TEMPLE: I can't not say that we don't agree with the analysis that didn't find the increase suicidality in the other groups. It was there. The same direction was there. The same hazardous ratio was there. It's just that there were many fewer patients in it. So we actually tried to tell them that before they published it, but you can't know that it's not there. It looks like the same direction.

Can I just say one other thing? You're absolutely right about the lithium, and we are trying to look into seeing if there's a way to get that in. But you're right. If there's not an interested party like a company ready to look closely at the studies

and parse them out, it's very hard to get anybody to do it.

One of my favorite examples of this, it's not a psychiatric one, is spironolactone which is now absolutely part of the ordinary treatment of congestive heart failure is not labeled for that because the company wasn't interested in doing it. It's generic and they have a drug that's similar that isn't generic. So there it sits as standard therapy and it's not on the label.

The more troublesome, and there's no ready solution to this, is some of the new uses in children and psychotic drugs and all those other things that are being actively studied now, but it's not all in the label yet. To the extent they have been studied, they're not looking so bad. But there is that period of time when use is widespread before there's much in the label. And that is distressing. It's not clear what the remedy is.

DR. SELIGMAN: Dr. Fassler?

DR. FASSLER: You know, when you first asked -- I think it's a good, first of all. And I think what I don't want to have you do as a child psychiatrist, I don't want to create a back door for off label uses. I don't want to make it look like the

FDA is approving or endorsing specific uses that haven't been thoroughly reviewed. So I sort of hear that in your question. But on the other hand, one of the things that I am the most pleased with in recent years is the development and the expansion of the registry of clinical trials. So we already are creating a way for patients and physicians to get more information earlier.

I fully support in the medication guide for it to say this is an off label indication, but here is the information that we have now.

The goal of the medication guides should be to promote dialogue. And exactly the kind of dialogue that you've been hearing about so that people can have questions and come to their physician and have the discussion as why are you using this medication, which of these side effects should I be most concerned about.

I did want to make one comment in response to Dr. Temple's comments on the suicidality. Because I agree with you that the signal is there with anxiety disorders. But I would also point out what the medication guide doesn't say, you're right we have the two percent and four percent issues, but one adolescent in six thinks about suicide every year

according to the CDC. And these are kids without depression. So if I'm a parent and I'm reading that medication guide and it says two percent or four percent of kids had suicidal thoughts and it doesn't tell me that suicidal thoughts in adolescents who are not depressed is a common phenomenon, then it's misinformation. Then I'm confused. Because obviously a parent, any parent would be concerned if there is a risk of suicide. We don't know if there's a risk of suicide. We know that there's an increased reporting of suicidal thoughts or behavior. But when we ask kids in high school across the country, one adolescent in six thinks about suicide every year. And I need that information in order to accurately evaluate what these two percent and four percent numbers mean.

DR. SELIGMAN: Yes, Ms. Van Syckel.

MS. VAN SYCKEL: As a consumer of and also a child who attempted suicide twice while on the antidepressant Paxil and had self-mutilated, Michelle's diagnoses of depression and anorexia was incorrect. She had lyme disease. And she suffered horrific effects. And I'm not with any religious groups or -- I'm here on my own dime. And actually it was because of the wonderful research done by a psychiatrist at Columbia with the wonderful research

that he had, afforded me to know what was happening to my child. So in that respect, it was great.

Let's get back to the medication guide. I did see the Parent MedGuide.org and I looked at it. And it is lengthy.

I love the tear-off sheets. They're great. I said this to Congressman Ferguson back in 2005 when I saw them for the first time. And as far as benefits, efficacy has not been established with SSRIs in children. I make a correction, under the age of 18.

DR. SELIGMAN: Prozac, yes.

MS. VAN SYCKEL: Okay. Well, let's talk about the other ones then. But anyway, there's still a causal role of suicide. But as a parent who is going through as I was looking at that medication guide, had I had that knowledge, I could have sought the treatment, a hospital for my daughter without her having such a violent rage, a suicidal rage. And we wouldn't have had law enforcement at our home. She wouldn't have had a police record. Because that stays with a child.

Like I said, this medication guide, the tear-off is a wonderful piece of information as it is now. And please leave it alone. It's good.

DR. SELIGMAN: We'll take one other

comment and then I'd like to turn to the last speaker. But go ahead, Dr. Watkins.

DR. WATKINS: I think it is not a problem putting benefits of the FDA approved indications. I think that if we as physicians are using something in an off label use, which we sometimes do, we need to inform patients as such. And if you get a discussion of what this medicine is supposed to do and they see that and they're taking it for something else and aren't aware of it, then they're more likely to ask. If you don't really list too much about potential benefits, then there may be less awareness that something is an off label use.

DR. SELIGMAN: Good point. Thank you.

Our final speaker is Mrs. Susan Nelson.

MS. NELSON: Okay. My name is Susan Nelson and I am from Bainbridge Island, Washington.

I realize that I am the last speaker here today and not a professional, so please bear with me as what I have to say is very important.

I appreciate the opportunity to be in this forum to express my concerns regarding the serious and sometimes deadly side effects of statin drugs and also to stress the urgency of getting this information out to the prescribing doctors and patients.

I am a widow. My husband died at the age of 49, but not before suffering four years of very debilitating neurological side effects from the statin drug, Mevacor.

I'm a mother of three. Jake my middle son committed suicide after taking Lipitor, another statin, the world's biggest selling drug made by the biggest pharmaceutical company Pfizer.

I would like to focus today on the details of Jake's story regarding Lipitor.

Jake was prescribed Lipitor in March of 2001 at the age of 16. He had familial hypercholesterolemia. As soon as Jake began taking Lipitor, he began having violent nightmares of "guns and knives." One such nightmare caused him to jump out of a hotel window two stories up. He was injured but survived the fall. He happened to be in Nepal on a trek doing community service with his high school. He couldn't finish the trek on foot, but had to ride on a donkey.

For the next two and a half years of high school, Jake struggled with the inability to concentrate, read and focus. It was so frustrating that he begged me to take him to a doctor to get tested. We consulted five doctors. All of the doctors

knew that Jake was on Lipitor only, but not one made any association with any neurological side effects of Lipitor. Even the prescribing doctor, who is the head of the Northwest Lipid Clinic in Seattle admitted to not being aware of any such side effects. No one even bothered considering that Lipitor might be the culprit.

Jake was then put on a few anti-attention deficit drugs and antidepressants, but nothing affected his inability to focus.

Jake graduated from high school in June of 2003. He was voted the most beautiful eyes.

After graduation, Jake went on a six week trip with his friends to Europe. Jake left his Lipitor at home. He wanted to be free and not have to worry about pills. While he was gone, he had a wonderful time and even was able to read three books.

Upon his return, Jake began taking his Lipitor again. As soon as he started, so did the violent nightmares of guns and knives. He was very bothered by them and I felt helpless except to wonder what he had eaten or watched on television, never thinking that he began taking his Lipitor again and that could be it.

On August 10th, I went to the store and

while I was out Jake left too. He bought a gun and shot himself in the head.

Our island of over 20,000 was shocked and silenced. Jake Nelson had no psychological problems. He didn't fit anything close to a suicidal personality. He was a kind, generous, loving, loved, fun, funny, bright, athletic, class one gymnast, wonderful young man. He was the common bond and friend that tied many together. That's just his friends and the community. His brother and sister Sophie and Zackary and myself are left crushed and forever devastated. We were, and still are, in disbelief and complete shock forever mourning his loss.

I thought the cause of Jake's suicide must have been the stress of being 18, going off to college, life expectations, et cetera. Then in October, a few months after Jake's death, I suddenly recalled a study I'd read in the medical section of *Time* magazine many years back. The study was an alert stating that in some men, statins may cause violent behaviors such as homicide and suicide.

I began making phone calls and investigating. I found that there certainly was evidence of suicide and depression as side effects of statins. I found nine other people personally who had

either known of someone who had committed suicide on a statin or had themselves thought seriously about it. I found people who couldn't concentrate, were depressed, felt like they were in a fog, had nightmares and then people who were physically crippled from peripheral side effects. And yet, the doctors still continued to dismiss these complaints as unrelated to the statin because they aren't aware of them.

An important factor in this is that people don't make the association with a cholesterol drug and the brain. Antidepressants are directly related to depression, so it makes sense that one would look for these related risks. However, with statins we don't make the connection to the brain and neurology. Most think heart disease and maybe liver functions when they think of statins.

In my searching, I came upon Dr. Beatrice Golomb at the University of California, San Diego, who has authored many studies regarding the side effects of statins and was just in the middle of completing the first independently funded by the NIH study of the side effects of statins in the country when I first read about her.

She has encountered in her work patients who were suicidal and homicidal and could validate

Jake's experiences and suicide. And I was actually here in Senator Grassley's office a year ago with Dr. Golomb telling his top investigators our stories. Dr. Golomb was excited about my involvement in this forum today and wished she could herself attend.

I, too, as she has the scientific knowledge needed to alert and inform you. Dr. Golomb's work is extensively and extremely valuable. I would suggest that when considering unbiased statin side effect alerts that she be contacted for advice.

Another doctor with us here last year was Dr. Duane Graveline. Dr. Graveline is a retired physician, former NASA astronaut who has written two books on Lipitor. One is called *Lipitor, the Thief of Memory*. His books and research validate the very dangerous side effects of these powerful drugs. His personal transglobal amnesia events from Lipitor lead him to his research and then books.

Dr. Graveline emails a paper he wrote specifically for this forum entitled "Cholesterol Guidelines For Our Youth." I believe you should be able to access this important paper through the website associated with this meeting. And I strongly encourage you to do so. His unrelenting request for knowledge and new research regarding statins is

impressive, and his compassion to get the word out is unbeatable.

I have a box of scientific research relating to depression, suicide and cognitive impairment relating to statin drugs. I have piles of papers and books with information. I know many, many people who have and are suffering from debilitating side effects, yet there are no warnings. The doctors aren't cautioning patients because they aren't informed. The pharmacists certainly aren't informed. With this particular class of drugs, you need to start at the top with the pharmaceutical companies and the FDA. They need to step up to the plate and tell the truth about the risks and benefits.

There is a huge breakdown of trust. I think that the drug companies have to begin by trusting that doctors will prescribe drugs with known risks and that patients will still take their drugs, only now with the confidence that they are well informed and can trust the information they have gotten. I don't know about you, but Dr. Jarvik walking around the beach with his coffee and dog calmly assuring me that Lipitor is tested and trusted doesn't make me any more confident. It's irritating.

We have been brainwashed by the pervasive

advertising of drugs through the media. This is one very important reason that it is critical that objective risk benefit information get out to the public and doctors as soon as possible.

Please trust us with the truth and let us be informed. It's time that the drug companies and the FDA gain back the trust that they should have from the skeptical medical community and public. Help ease our worries and bring back confidence.

I cannot bring back the four horrific years my late husband lost, nor could I bring back my son Jake. But I am convinced that had we known of these side effects my son would be here today. He's not here for one reason, and that is to help enlighten millions of others who could be affected by the serious side effects of these powerful drugs.

I'm here today to alert you to the seriousness of communicating the side effects of the powerful statin drugs being prescribed to more people than any other drug on the market.

Thank you.

DR. SELIGMAN: Thank you for your testimony.

Are there any questions or comments for Mrs. Nelson?

With that then, let me just make some final remarks to close this meeting.

First of all, I want to thank all who have taken the time to testify at this meeting on medication guides for creating helpful and creative ideas on how best to use this public health tool.

We will be making a summary of this meeting and that summary will be available shortly on our website, followed by a full transcript of the meeting.

I want to take just a few quick moments as the presiding officer to summarize just some of the many valuable points that I have garnered during these two days, and then to give members of the panel as well an opportunity to make some additional final comments.

My list of comments is by no means complete, nor does it reflect all of the important points made at this meeting, nor is it in any particular order.

First we heard starting yesterday morning from Congressman Ferguson about the need for greater cooperation between states and national boards of pharmacy and other professional association and alliances and the FDA in ensuring that all parties

responsible for producing and distributing medication guides are meeting their regulatory and communication obligations.

We also heard that this information is critically important in patient decision making. We've heard personal testimony both yesterday and today of the consequences of not receiving such information.

We've also heard testimony about the potential public and clinical consequences of receiving information that may dissuade patients or clinicians from using medication if benefits are not adequately described and the conundrum that we sometimes face when such benefit information relative to risk is not readily apparent.

We've also heard very clearly that best practices in communication should be informed by science and research, and that our regulatory decisions on how best to communicate should be informed by such research. How information is displayed using, for example, things like chunking and layering and various alternative representations is important to make information cognitively accessible to a broad range of sophistication of consumers. And that such research really needs to focus on utility,

balance, comprehension as well as how to reach this broad range of consumers.

We've also heard very clearly that medication guides are a piece embedded in an overall health care delivery system.

We've heard about the importance of communicating to patients when prescribing decisions are made in a doctor's office and ways that the medication guide may be used to accomplish this end or the means of accomplishing this kind of communication. And that information not only needs to be available at the pharmacy, but as well at the doctor's office, as well as from various other sources.

We've also heard that the current system may not be serving all patients well and that there have been difficulties in implementation. Many have stated that two pieces of paper may be one too many and that lengthy medication guides have potentially too much information. And that due to their length, may provide information that as a result is not readily accessible because people either stop reading them or just don't read them.

That these medication guides are not regularly or uniformly received or distributed to pharmacies, and that there are considerable burdens in

the pharmacy and a pervasive sense as well as in data to indicate that the program, at least at the pharmacy level, may not be working well. And that we should reconsider the current requirement to distribute with every refill such a medication guide.

Clearly managing paper particularly in distributing them at the pharmacy and managing the paper and the distribution from sponsors to pharmacies in an electronic world is increasingly becoming or in many cases has become an anachronism and that really need to take a fresh look at our current regulations in light of CMI and the large number of medication guides as well as the current and evolving pharmacy practice.

There needs, I think at some point soon, some reconciliation between the provision of medication guides and other consumer medication information, and to make their provisions simpler and more manageable at the pharmacy.

We have heard during the course of these two days some electronic solutions to some of the distribution problems. I think these are definitely worth pursuing. And I think it's worth taking a close look at our medication guide tool which has now been in use for ten years to make sure that it indeed is

meeting our communication goals and is consistent with best communication practices.

Finally, I think it's critical and I think all would agree that a program of evaluation that looks at the various aspects of providing information that communication needs really does need to be done on a regular basis and built into any modifications that are made to our medication guide program. And that this effort should be part of an overall communication strategy.

In closing then, I want to thank all the persons who contributed to our meeting and to remind everyone that the docket to submit comments will remain open until July 12th. Following closure of the docket and our review of all the input, we plan to use the ensuing weeks and months to chart a path forward that will incorporate many of the lessons learned and directions proposed at this meeting.

With that, let me turn to the members on the panel and to inform as well members of the audience that we are going to engage many of the key stakeholders represented here in these last days as we attempt to reconcile many of the problems that have been identified in our current system. And, hopefully, we'll end up with an approach that works well for

patients and that can be executed well and in a consistent and in a sensible way at the point or points of delivery for such information.

So are there others of the panel who wish to make any final remarks? I know, Bob, would you like to say something?

DR. TEMPLE: Sure. I think you really covered everything, and I share your appreciation of all the people who came to tell us about their experience and suggestions.

Just a couple of thoughts that occurred to me. In figuring out how to revise physician labeling, we concluded that sometimes -- last at least in the beginning is more and endorsed an approach that emphasizes highlights at the beginning. It seems fairly obvious that if that's reasonable for the physicians, most of whom can read at above the sixth level, it's worth considering for the patient information also. Highlight followed by more details.

I'm not so confident that people are going to go to other websites, but I do think that people could read the next step. So that's certainly one thing that seems worth considering.

Just to state the obvious, usually medication guides are written in a high sense of

urgency and there's really little possibility that we're going to test them out too much before we implement them. But that doesn't mean we can't test them after we put them in place and see if they can be improved.

And then finally, it's a thorny problem to think about how to be sure that benefits are reflected. And remember one of the three reasons for having the medication guide is to help people weigh the benefits and risks to see if they want to be on the drug. Well, you can't really do that if there's nothing about benefits. The ones that are designed to help you avoid the problem, maybe they don't need it quite as much. But certainly one of the major reasons is to help patients understand all this. And you really can't do that if you have no idea what the drug is good for. That goes along, however, with the fact that some of the things we think they're good for aren't documented. So that's a thorny problem and we're going to have to deal with that.

But other than that, I think Paul summarized things very well.

DR. SELIGMAN: Mr. Woo?

DR. WOO: Yes. I think I'm just adding to your summary, but emphasizing that I think there's

been a good discussion that medication guides certainly aren't the end all and be all in patient communication. That they serve a particular role, but certainly as we get more into the practice of pharmacy of the practice of physician, we get farther from the regulatory authority that FDA actually has over those processes. So that doesn't mean we shouldn't be looking at trying to improve the way medication guides serve their purpose within that overall practice of communicating and informing the patient. And certainly that should be one of the ways at what electronic measures there are to try and facilitate that process, certainly for the patient but also for the other stakeholders involved, including the providers both physicians, pharmacists and the manufacturers of the drugs and the information.

DR. SELIGMAN: Any other comments?

Well, with that again I want to thank both FDA colleagues here at the table for taking the two days to carefully listen to all of the comments that we've received.

I want to particularly thank Mary Gross and Diane Ehrlich from our staff at the FDA for all their work in organizing this couple of days.

And with that, I would like to formally

adjourn this Part 15 hearing.

Thank you very much.

(Whereupon, at 3:50 p.m. the hearing was adjourned.)