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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TUESDAY, JUNE 12, 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.

FDA EXPERT PANEL MEMBERS:

PAUL SELIGMAN, M.D., M.P.H., Associate Director, Safety Policy and Communication Staff, CDER
ILISA BERNSTEIN, PharmD., J.D., Director, Office of Pharmacy, Office of Policy and Planning, Office of the Commissioner
JOHN JENKINS, M.D., Director, Office of New Drugs, CDER
LISA MATHIS, M.D., Associate Director, Pediatric and Maternal Health Staff, CDER
TONI PIAZZA-HEPP, PharmD., Deputy Director, Division of Surveillance, Research and Communication Support, Office of Surveillance and Epidemiology, CDER
ROBERT TEMPLE, M.D., Director, Office of Medical Policy
JASON J.Y. WOO, M.D., M.P.H., Associate Director, Scientific and Medical Affairs, Office of Compliance

CDER PARTICIPANTS:

JEANINE BEST, M.S.N.,R.N.,P.N.P., Patient Product Information Specialist, Division of Surveillance, Research and Communication Support
LILLIE GOLSON, R.Ph., M.S.A., Team Leader, Labeling Review Branch, Office of Generic Drugs
JANET NORDEN, M.S.N., R.N., Associate Director for Regulatory Affairs, Office of medical Policy
DAVE ROEDER, M.S., Associate Director of Regulatory Affairs, Office of Microbial Products, Office of New Drugs

PANEL 1
HONORABLE MIKE FERGUSON, U.S. House of Representatives
LISA VAN SYCKEL, Drugawareness
NICOLE CUMBER, Consumer
LAURIE YORKE, Consumer
ROBERT MANCIERO, Full Vision Productions

PANEL 2
NANCY ALLEN LaPOINTE, PharmD., Duke Clinical Research Institute
WILLIAM LANG, M.P.H., American Association of Colleges of Pharmacy
RUTH S. DAY, Duke University
MICHAEL S. WOLF, Ph.D., Northwestern University

PANEL 3
KIM WITCZAK, Consumer
VERA HASSNER SHARAV, Alliance for Human Research Protection
ELLEN LIVERSIDGE, Alliance for Human Research Protection
DIANE DORLESTER, Mental Health America
ANTHONY NG, M.D., Mental Health America

PANEL 4
TOM LAWLOR, R.Ph., Walgreen Company
THOMAS FLOTTMAN, Pharmaceutical Printed Literature Association
JOHN COSTER, Ph.D., R.Ph., National Association of Chain Drug Stores
RONNA HAUSER, R.Ph., National Association of Chain Drug Stores
STEVE HEIDENTHAL, R.Ph., CVS CareMark Corporation
BEN STONE, Pharmex

C-O-N-T-E-N-T-S

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

8:37 a.m.

DR. SELIGMAN: Good morning. We'll begin in about one minute. Good morning, and welcome to the Food and Drug Administration's Part 15 hearing on medication guides. Joining me this morning here at the rostrum to my right is Dr. Ilisa Bernstein, the Director of the Office of Pharmacy in the Office Policy and Planning with the Commissioner's Office at the FDA. Next to her is Toni Piazza-Hepp, the Deputy Director of the Division of Surveillance, Research and Communication Support for the Office of Surveillance and Epidemiology. To my immediate right is Dr. John Jenkins, the Director of the Office of New Drugs.

To my left is Dr. Robert Temple, the Director of Office of Medical Policy and to my far left is Dr. Jason Woo, the Associate Director for Scientific and Medical Affairs in the Office of Compliance at CDER. At the FDA table, we have starting at the far end, David Roeder, Assistant Director of Regulatory Affairs in the Office of Microbial Products in the Office of New Drugs. Next to him is Janet Norden, the Associate Director for Regulatory Affairs, Office of Medical Policy.

Next to her is Lillie Golson, the Team

Leader in the Labeling Review Branch in the Office of Generic Drugs and finally Jeanine Best, Patient Product Information Specialist with the Division of Surveillance, Research and Communication Support in the Office of Surveillance and Epidemiology in CDER.

Please note on the screen overhead that there's no food or drink allowed in the auditorium and again, so there's no confusion, FDA does not stand for no food or drink allowed, although they do look strikingly similar. Starting this morning's proceedings, let me welcome to the podium Susan Winkler, who is the Chief of Staff in the Office of the Commissioner to bring us greetings from the Commissioner of the FDA. Susan?

MS. WINKLER: Thank you, Paul, and good morning. I'm pleased to be here this morning to welcome you to this very important meeting. Patient information, as you know, is essential to the major challenge in the healthcare system which is securing the promise of medications, making sure that that risk and benefit that the agency carefully analyzes actually exists in the healthcare system by making sure that those medications are used appropriately, that they're used in the right way.

Today and tomorrow, we will hear many

different perspectives and that's very important. I think each of us brings many perspectives to the discussion of patient information and medication guides. For me personally, as a pharmacist, I see medication guides as very important in stimulating that conversation between the healthcare professional and the patient.

As a patient, I'll admit that perhaps I don't use medication guides in the way that they were intended in that they may end up in the place where we don't want them, which is not in my mind but in a garbage can. As a parent, however, I would devour the information, in making sure that I know precisely how something should be used as I'm deciding whether or not to give a medication to my daughter. And as a staff member at the FDA, this information is extraordinarily important because it's an attempt in very important and very specific situations to translate the volumes of information that we have at the agency about a specific drug into information that can help patients make the best use of that drug.

So there are many of us listening carefully to what it is that you have to say. I will acknowledge that there are certainly challenges to providing consumer information in the medication

guides and that's why we're here today, to figure out how we can improve this system. I'm also pleased that there are so many different perspectives that will be presented and know that the Commissioner is very pleased with that as well. As he and I discussed the agenda for the meeting, he was very interested in the fact that we would have such a broad range of individuals helping the agency do a better job, to help us understand how to bring the promise of these medications to people and to have medication guides deliver the information that we need.

So with that, I'll say welcome from the Commissioner, from the Commissioner's office and we're very interested in what you have to say in the discussion and we'll use that in our future consideration as we try to improve all of these processes, thank you.

(Applause)

DR. SELIGMAN: Thank you very much. The next speaker is Dr. Steven Galson, who is the Director for the Center for Drug Evaluation and Research. Dr. Galson?

DR. GALSON: Thank you, Paul and I'll continue this tradition of using the podium slightly strangely, but so we can see everybody. Thank you for

being here everybody. I want to thank the FDA organizers of this meeting, particularly Diane Ehrlich, Mary Gross and Ilisa Bernstein. A whole group of people have been planning this for many, many months and it wouldn't be so well organized if it wasn't for their efforts. Thanks to the FDA panelists who are going to be sitting here all day listening to the input that you're providing, and too, all of you in the audience who are participating in the panels during the day. It's really, really important that we get feedback; otherwise, we're just always talking to ourselves. So we appreciate your effort in preparing your remarks and giving them to us today.

As everybody in this room knows, CDER and the Agency have been focusing hard on improving our drug safety processes and activities over the last few years. In January, we announced a comprehensive response to the Institute of Medicine report that we received last year. And the response included dozens of actions on individual projects across the center and the agency to improve our drug safety system. Many of these actions include components that are related to how we communicate to the public.

As you also know, there's legislation on Capitol Hill covering PUDFA and drug safety that is

certainly going to give the Agency new resources and perhaps, give us new authorities that are related to what we're talking about today as well. So this is a time of great change and progress in all of our activities surrounding drug safety.

How we communicate about drugs is absolutely critical to ensuring the proper balance of benefits and risks for the products that we regulate. Communication between FDA and healthcare providers and consumers is also in a state of flux. With the rapid adoption of internet-based methods of communication, changes to the pharmacy industry, the proliferation of large healthcare provider organizations, and increasing sophistication of the medical consumer, our traditional methods of communicating, including medication guides are looking more and more antiquated.

We need to keep up with these changes in information technology in the pharmacy world, in the healthcare world, by looking carefully at our medication guide program and this Part 15 Hearing today is going to help us to do that. Although I can't stay for the meeting, I really look forward to hearing the feedback from the FDA staff. We're going to be taking notes and listening carefully to the

input from the panelists. So I wanted to thank you again for being here and at this point turn it back over to Dr. Seligman. Thank you, sir.

DR. SELIGMAN: Thank you, Dr. Galson. We've also been joined here on the podium by Dr. Lisa Mathis, who is the Associate Director for the Pediatric and Maternal Health Staff. In case any of you are wondering, my name is Paul Seligman, I'm the Associate Director for Safety Policy and Communication in the Center for Drug Evaluation and Research.

With those opening remarks and the introduction of the panel members, let me take a few minutes before we proceed with the agenda, to make a few remarks regarding medication guides and provide a historical perspective. Communicating information about medicines effectively is essential to their appropriate use and has been, is and will continue to be a challenge to regulators, healthcare providers, product manufacturers, consumer organizations and all those involved in the creation and distribution of such information. Today and tomorrow, we are seeking feedback on that portion of FDA's regulations that provides for medication guides for patients for prescription drug products as found in the Code of Federal Regulations Title 21, Part 208.

In doing so, we are seeking ways to improve patient communications consistent with this Part that makes the Medication Guide a part of the FDA approved labeling for a product. The Medication Guide is considered when one or more of the following circumstances occurs. First, the drug product is one for which patient labeling could help prevent serious adverse effects. Second, the drug product has serious risks relative to the benefits of which patients should be aware in making decisions to use or continue to use a product. And finally, where it is crucial to a drug's effectiveness, that the patient adhere closely to the directions for use.

When the regulation came into being approximately 10 years ago, it was thought that medication guides would be developed only for a handful of products a year. But over the last two to three years, the medication guides issued for two widely used drug classes, the NSAIDs and the antidepressants, the number of medication guides required to be distributed has increased substantially.

FDA's website lists 65 drug names that have medication guides. In a March 2006 issue of the Pharmacist's Letter/Prescriber's Letter, there's a

list of over 240 individual and combination drug products for which there are medication guides. In discussing the production and distribution of these medication guides, it is impossible to ignore other important forms of mandated consumer medication information currently being distributed. After almost two decades where FDA sought to require sponsors to produce and distribute agency reviewed and approved information for consumers, Congress enacted Public Law 104-180 in 1996. The law established a private sector process to develop an action plan to achieve usefulness and distribution goals specified in that statute.

Public Law 104-180 charged the private sector, in particular pharmacies, with the responsibility to make sure that such consumer medication information or CMI was made available to patients with the dispensing of each new prescription. Importantly, the new law enjoined FDA from taking further regulatory steps specifying uniform content or format if these product sector initiatives met the goals of the plan within the specified time frame. FDA's defined role was to monitor the progress of the private sector in meeting the goals laid out in the legislation.

According to the law, by 2006, this past calendar year, 95 percent of prescriptions dispensed to patients in the United States must be accompanied by useful medication information. A survey conducted by the FDA in 2001/2002 found that although distribution of written prescription drug information has increased, the usefulness of this information varied widely. This year, FDA will be conducting a final assessment to determine whether the private sector initiative has satisfactorily met the goals of the public law.

We are keenly aware of the challenges presented by medication guides both as a stand-alone communication tool, as well as in the context of other consumer information. We are aware of the challenges that stocking and distributing medication guides has placed on pharmacies, particularly in the context of their additional responsibilities to distribute information. We appreciate the potential problem of information overload for patients with the provision of both CMI and a medication guide for some prescriptions.

And we are particularly interested in hearing how to make medication guides a useful, integral part of patient communications in light of

other mandated information. How can we meet this need in a way that is practical and sustainable for all parts of the information production and distribution system?

On the other end of the spectrum, we are also aware that sometimes medication guides are not getting into the hands of patients as intended. A 2004 FDA study of 5,000 randomly selected pharmacists examining their knowledge of risk minimization tools, found that 29 percent of pharmacists were not familiar with medication guides.

In December 2005, in this very room, FDA held a meeting on risk communication and whether FDA materials were actually finding their way to patients. Testimony and study results presented at that hearing documented circumstances where medication guides were not being distributed. Comprehensibility and ease of understanding of medication guides is essential to their success and I'm glad today that we have experts in evaluation of these tools who will help explore these issues during their testimony.

So what do we hope to get out of this hearing? Primarily, we are looking for creative solutions to an important communication issue that greatly impacts on public health. We know that all

drugs have benefits and risks and that every drug comes with side effects. It's important that patients have a clear picture of how the drug can help them or in select cases, how the drug may harm them. It is doubly important that patients understand the risks and benefits of drug products coupled with medication guides since FDA has determined that these drugs carry special risks.

We have listed questions for specific groups in the Federal Register notice that should be part of your packets, but here is what we want to hear back. From consumers, we're eager to learn how best to serve their information needs into the future, what their experience has been with medication guides to date and what can be done to improve both the physical as well as cognitive accessibility of these guides.

Since pharmacies play such a critical role in providing written information, we look forward to their creative and constructive ideas on how to improve all aspects of medication guides from their receipt from manufactures to their distribution to patients. Since manufacturers are required to produce and make available to pharmacies the medication guide, knowing the problems they face, and the concerns they have in producing and supplying these

guides, and ideas that they have that take advantage of other electronic initiatives will be of keen interest to us.

From information vendors and wholesalers, again, creative ideas on how to offer electronic versions of medication guides and the appropriate format and with other consumer information will be sought. And finally, from academicians who do research in this field, learning how to best apply the science and evidence to make communications the very best that they can be will help guide us in considering what modifications should be made to reach the intended audience, the consumer.

We are all too familiar with many of the problems associated with the distribution of medication guides. We know the problems. What we are eager to hear are creative ideas and solutions. We recognize that successful communication to consumers involves collaboration and cooperation among the drug sponsor, practitioners, pharmacies, healthcare institutions, academicians and consumers in a sensible regulatory and legal environment.

With that perspective and charge to today's speakers, let me go over a few housekeeping rules before we turn to the first panel. As you'll

note in the agenda, we have structured the panels and questions in order to help focus on roles, responsibilities and challenges for each of these groups. We have a very packed agenda. So in deference to all of the participants, we ask each speaker to observe the time limits for testimony. We have a signaling device on the podium and at one minute a yellow light will flash and asking the speaker to sum up.

This is a public hearing that is being held in accordance with Part 15. As such, this hearing is an informal one and the rules of evidence do not apply. We ask that no participant interrupt the presentation of another participant and only the presiding officer, that's me, and the FDA panel, may question presenters during or at the conclusion of each presentation. We have allowed interested persons in the audience who are attending the hearing but have not signed up in advance to make oral presentations at the conclusion of this meeting, if time permits. If you are so interested, please check with the registration desk.

Finally, written comments on this topic may be submitted to FDA's Division of Dockets Management by July 12th of this year. A transcript of

the hearing proceedings will be made available on the Internet within 30 days after the hearing and again, please see the Federal Register notice in the blue folder for the appropriate web link.

Please, before we begin today, turn off all of your cell phones, pagers, blackberries, and any other noise generating devices while we are conducting these proceedings. Our hosts, the National Transportation Safety Board, requests that no food or drink be brought into this auditorium. If you need to eat or drink during these proceedings, there is a room immediately to your right as you exit where you can actually listen to and watch these proceedings through a glass partition and you can, in that room partake of any beverages or foods that you wish.

With that introduction, I would like to call the first panel to the table, to include the Honorable Mike Ferguson, from the House of Representatives, Ms. Lisa Van Syckel, Ms. Nicole Cumber, Ms. Laurie Yorke and Mr. Robert Monciero. The first reading is from Congressman Ferguson.

What better way to start this hearing but to hear from the Honorable Mike Ferguson, the Congressman from New Jersey, who has provided many thoughtful and challenging questions to the FDA on

this topic. I'm confident that he will set the right tone for this hearing by providing his thoughts and some creative ideas of his own on how best to affect communication with consumers. So Congressman Ferguson, if you'd like you can either do it from the table or you can take the podium, whatever suits you. Thank you.

CONGRESSMAN FERGUSON: Is this on? Is that working? How is that, better? Thank you, good morning. I'll just sit here if that's all right. I'm really pleased to be with you this morning. I appreciate the opportunity to present some thoughts. I'm trying to figure out the significance of being at the NTSB here, but I haven't figured that one out yet. I also must tell you that I am going to have to leave at the conclusion of my remarks. We have a hearing, as many of you know, on PDUFA this morning. So until I figure out a way to bi-locate, I'm not going to be able to stay for the remainder of the presentations this morning or the questions. But if anybody does have any questions that you'd like me to address, I'd be happy to do that, if you'd let my office know.

Today's hearing, I think, is very, very important and I'm pleased that there will be a wide variety of folks who will be able to present concerns

and thoughts on really what I believe is a potentially alarming situation in which young patients and their parents may not be receiving the information that they need to make fully informed decisions about certain prescription medications. Specifically, I want to register my concerns that FDA approved medication guides are not being distributed to patients and parents when antidepressant medications are being prescribed.

This matter was brought to my attention by constituents of mine from New Jersey and I'm joined by some of them here today, Lisa Van Syckel, Laurie Yorke and Nicole Cumber. I know that they plan on relating their experiences and concerns today and I'm pleased to be able to present with them, at their side today. They've been touched by traumatic events stemming from adverse reactions to antidepressants and have dedicated their time to ensuring that people receive the information they need to make fully informed decisions.

We're all aware that the use of antidepressant medication is controversial, particularly by children and adolescents. In September 2004, I participated in hearings conducted by our House Energy and Commerce Committee's Oversight

and Investigation Subcommittee concerning the pediatric use of antidepressants. At that hearing, I strongly advocated that the FDA issue black box warnings, the highest FDA warning on prescription drug labels regarding the potential serious side effects of the pediatric use of antidepressants.

Later that month, at the FDA's Psychopharmacologic Drugs Advisory Committee and Pediatric Drugs Advisory Committee discussed and ultimately issued recommendations concerning these drugs and their use by children and adolescents which included the black box warnings. The FDA, on October 15th, 2004, echoed the Advisory Committee's recommendations and issued a public health advisory announcing a multi-pronged strategy to warn the public about the increased risk of suicidal thoughts and behavior in children and adolescents being treated with antidepressant medications. The strategy's main components were the issuance of the black box warning, the creation of a medication guide to be distributed with each prescription dispensed to a child or adolescent and the formation -- formulation of a unit of use packaging for ease in disseminating information. As a part of the oversight responsibility of the FDA by the House Energy and

Commerce Committee, I have maintained strong interest in issues concerning these drugs and their use by children and adolescents.

It was my belief in 2004 during the congressional hearings and it remains so now that these drugs must be administered to children and adolescents under the strictest scrutiny. I believe that medication guides are a vital component to the overall strategy of ensuring that fully informed decisions are made by parents before their child begins a regiment of antidepressant medications. That's why I was greatly concerned when constituents of mine informed me that the FDA required medication guides were not being distributed when antidepressant medications are dispensed, even though such distribution is required under a regulation introduced by your agency on October 15th, 2004 and finalized on February 3, 2005.

This information prompted me to engage in a thorough examination of the government regulation and private distribution of medication guides to patients and parents and guardians. Over the course of the last year, my staff and I have spoken to and engaged in written correspondence with FDA officials and representatives of the National Association of

Chain Drug Stores, the National Association -- the National Community Pharmacists Association, the New Jersey Pharmacists Association, the New Jersey Board of Pharmacy, and four manufacturers of antidepressant medications.

The pharmaceutical manufacturers I contacted insisted that they adhere to their requirement and that they provided documentation -- and they were provided documentation on the steps taken to fulfill their obligations, including when the production and initial distribution to pharmacists of the medication guides are outsourced to third party vendors. Pharmacists' professional associations I contacted insisted that their members distribute the medication guides to patients, though some pharmacists' professional associations did say that their members do not always receive adequate numbers of medication guides from the pharmaceutical manufacturers or their third party vendors.

In their written responses to me the organizations each pointed to the regulatory responsibilities of the State Boards of Pharmacy and the importance of continuing education received by pharmacists to update them on requirements. In addition a representative of the National Association

of Chain Drug Stores mentioned a number of proactive steps their organization and member companies were taking to make it easier for pharmacies to provide medication guides to patients but also pointed to a perceived lack of cooperation by the FDA as a hindrance to their effort to improve the distribution system of medication guides.

I applaud the NACDS for their diligence in trying to work with the FDA to streamline the medication distribution system to make it easier for pharmacists to distribute Med Guides to patients and parents. Most telling was my correspondence with the FDA and the New Jersey State Board of Pharmacy about the regulatory environment governing the distribution of Medication Guides. I have in my hand letters I sent to the FDA dated August 31st, 2006 and December 11, 2006. The FDA responded to those letters on October 6th, 2006 and March 20, 2007 respectively.

My letter correspondence and staff level conversations between my office and FDA officials uncovered a significant breakdown occurring between the FDA and state regulatory authorities, a breakdown that deprived parents of children whom antidepressant medications are prescribed of their ability to make fully informed decisions. I found that it was

impossible to determine with certainty that the medication guides were, in fact, being distributed with the prescribed antidepressant medications because regulatory authorities at the federal and state levels were simply not enforcing the FDA's stated protocol on Medication Guides.

According to the Medication Guide final rule, published in the Federal Register, it states, quote, "Each authorized dispenser of a prescription drug product for which a Medication Guide is required under this part shall, when the product is dispensed to a patient or to a patient's agent provide a Medication Guide directly to each patient or to the patient's agent unless an exemption applies under 208.26", close quote.

Although the FDA had the authority to issue the above regulation, I learned from the FDA that it does not have the authority to enforce the regulation and that the oversight of pharmacists falls to each individual state's Board of Pharmacy. These bodies currently have jurisdiction over all the pharmacies.

On September 5, 2006, I wrote my home state Board of Pharmacy in New Jersey to inquire about that body's jurisdictional ability to enforce the

FDA's regulation on Medication Guides. In response to my letter, Joanne Boyer, Executive Director of the New Jersey State Board of Pharmacy, wrote in a letter dated September 25, 2006 and I quote, "The Board of Pharmacy reviewed your correspondence regarding Medication Guidelines at the September 13, 2006 Board meeting. The Board does have authority to enforce the Federal Regulation regarding the distribution of these guides.

An overview of this Federal Regulation will be included in the Board of Pharmacy Newsletter with a statement addressing the need to be compliant and the fact that our inspectors will be including this item in their normal inspection routines. I will provide the inspectors with all necessary information regarding medication guidelines and instruct them to assure compliance when they perform their inspections in our retail pharmacies. Those pharmacies identified as being non-compliant will be brought to the Board's attention for review and action which may include financial penalties", close quote.

In my letter dated December 11, 2006, I strongly urged the FDA to use its authority to contact all State Boards of Pharmacy to bring to their attention the Medication Guides requirement and ask

that they follow New Jersey's example and secure commitments in writing to enforce the Medication Guide regulations in CFR 208.24, distributing and dispensing a Medication Guide. In the FDA's letter dated March 20, 2007, the Agency stated and I quote, "In an effort to better understand the problem, whether it is a systematic issue or just related to specific products, we're seeking the help of the State Pharmacy Boards to ask pharmacists to report to FDA's MedWatch Program when they do not receive Medication Guides in sufficient numbers or the means to produce Medication Guides in sufficient numbers to permit their requisite delivery to patients".

I continue to quote, "We recently worked with the National Association of Boards of Pharmacy which has kindly agreed to publish an article in its newsletter asking state boards to let pharmacists know about MedWatch reporting for Medication Guide problems. We are also asking pharmacists and pharmacy organizations to reach out to their members to report problems they encounter related to Medication Guides", close quote.

I believe that this is a significant step in the right direction but it does not fully solve the problem. I believe that one component of a solution

is consistent dialogue between the FDA, the National Association of Boards of Pharmacy, individual State Boards of Pharmacy and National and State Pharmacists Organizations. This dialogue must be established and maintained so that pharmacists are always current on their duties in distributing Medication Guides. Additionally, I believe that the FDA can itself take positive steps under existing authority and budgets toward ensuring the proper dissemination of Medication Guides to patients and parents.

In addition to the October 6th, 2006 response to my letter, the FDA stated that it has been engaged with pharmacists organizations and other concerned parties about streamlining Medication Guide distribution by allowing them to produce medication guides from an electronic source in their pharmacy. I strongly support electronic distribution of Medication Guides and hope that this meeting helps encourage the FDA to establish guidance on how pharmacists can receive and print Med Guides electronically.

In addition, I support other proposals such as waiving current Med Guide formatting requirements to aid in the ability of pharmacists to print out Med Guides with other printed materials generated at the pharmacy. The FDA has not been

willing to waive these requirements even though it would significantly enhance the distribution of Med Guides.

Additionally, when appropriate, pharmacists should be permitted to use single quote "class" Med Guides. In cases where Med Guide is required to be dispensed with a brand name drug that has a generic version or where a therapeutic class of drugs has a similar risk warnings, FDA should use a single uniform Med Guide rather than have each individual manufacturer produce their own Med Guide. This would mean the pharmacy would have to obtain and stock only one Med Guide for each class rather than one for each drug in the class or their generic alternatives.

This would make it easier for pharmacies to obtain and distribute these Med Guides to patients where we frequently hear about the simple problem of shelf space in a pharmacy. Additionally, there should be other steps taken to make it easier for pharmacists to receive and restock Medication Guides, possibly a 1-800 number connected to a clearing house for pharmacists who can't print them electronically to request new Med Guides.

In conclusion, I believe it's our shared

goal to ensure that all patients, including children, and their parents have access to the safest and most effective therapies including as appropriate antidepressant medication. But taking that into consideration, the FDA has rightly implemented strict requirements on the prescribing of these drugs by issuing black box warnings and requiring medication guides. Those and other requirements are necessary to ensure that the people to whom the antidepressant medications are prescribed, including the parents of children and adolescents, that they have the information they need to make fully informed decisions.

If these needed requirements are not being fully implemented however, the public cannot make fully informed decisions and therefore, may be placed at greater risk. It may well be that many, perhaps the overwhelming majority of antidepressant medications dispensed include the Medication Guides, but it cannot be said with certainty that the Medication Guides reached parents 100 percent of the time. And if that's the case, the regulation is broken and public safety is jeopardized. If even one parent failed to receive the required Medication Guide, and I say this as a father of four young

children, if even one parent failed to receive that required Medication Guide, that parent, through no fault of their own, cannot make a fully informed decision about whether antidepressant medications are appropriate for their child. And that the consequences of a less than fully informed decision could be very dangerous.

I want to just finish by thanking the FDA and thanking the extraordinarily good work that you do and the extraordinarily difficult task that you have in ensuring the safety and efficacy of our drug supply. I realize you face many, many difficult decisions and the consequences of your decisions are great and I certainly appreciate the work that you do and I appreciate your having this meeting today to give me and others an opportunity to present our thoughts and concerns with you here today.

DR. SELIGMAN: Congressman, thank you very much for your remarks. Do you have a moment? Are there any questions from the panel for Congressman Ferguson? Yes, Dr. Temple?

DR. TEMPLE: One of the things you mentioned was the suggestion that we provide some flexibility on what electronic versions of these things would look like. One of the reasons we don't,

of course, is that we've seen what comes out attached to your prescription all the time is in minute print. I just wondered if you had any thoughts on the tension between something that looks good and is informative and the convenience of it. That's been our problem, that's why there's a format for those things.

CONGRESSMAN FERGUSON: As you know, I'm not a doctor nor a pharmacist. I'm a parent and a concerned policymaker, but the great thing about Medication Guides is they're in plain English. Somebody like me can actually understand them. And that's the whole point. Much of what we're given when our child, you know, and believe me with four little kids you're at the pharmacy a lot. When we get prescriptions for our kids, most of that stuff is unintelligible to a layperson like me or my wife.

The great thing about a Med Guide is it's in English and that probably is far more useful than anything else the pharmacist gives to the parent. So you know, I'm certainly not going to be the one you want writing these things, but you know, people like me could certainly be helpful in telling you whether they're decipherable or not. And if the question is really a question of access right now, and one of the

problems with access is you know, we've got many different drugs and their generic equivalent in some cases, all requiring a different one, perhaps it might make sense for experts like yourselves and others to be able to look at this and say, "Do you know what, maybe a little bit more flexibility here will not jeopardize public health but will, in fact, make it easier to get these things -- the practicality of getting these things in parent's hands, maybe that will help us get these Med Guides in more parent's hands more easily, more effectively and will not -- you know, will not result in -- will not result from a dumbing down of the information but will simply provide the same information but in a more effective way. Does that address your question?

DR. TEMPLE: Yes, and we're going to -- I notice Dr. Day is on the program later and she will tell us things about whether if you lost the white space and the format and the size, that would be more trouble than it's worth, but one of our reasons has been that, well, as you know, the stuff you get that you described is not very useful, among other things, is minute and we -- there's a font size requirement for Med Guides.

And one of the reasons -- now, other

people, I'm sure, will tell us, I don't see why that's an electronic challenge either. I don't see why it can't print it out in a proper format. I guess the one other thing I'd say is we have used common med guides for a couple of classes. I think the NSAIDs and the antidepressants use the common Med Guides. So we share that concern of having 50 of them is too much for every pharmacist to be able to manage.

CONGRESSMAN FERGUSON: Well, again, using -- continuing to use the large font, the large print that, you know, people can read, most people are probably like me, they see tiny print and they read the first sentence and they realize it's some sort of medical gobbilty-gook and the rest of that is not going to get read. If it's in larger font and the first sentence reads in English, you say, I could read this whole thing and I think those types of guidelines certainly ought to be maintained and not sort of sticking them on the back page of the gobbilty-gook, that is probably not the way to go. It's just my -- one person's view.

DR. SELIGMAN: Let's just take one more question. I don't want to keep you from PDUFA reauthorization. Dr. Woo?

DR. WOO: Congressman Ferguson, thank you

very much for your presentation. Just a question regarding your dialogue with this New Jersey State Board of Pharmacy. In addition to further dialogue with the FDA, were there other issues that they identified as part of the problem? For example, was there a lack of cooperation with the FDA in particular with enforcement strategies or ensuring that the Med Guides are getting to patients?

CONGRESSMAN FERGUSON: I don't want to characterize the relationship as a lack of cooperation from the FDA. It's really a lack of communication from both sides. It was sort of a classic case of federal and state government needing to work together if this was going to happen effectively and not having the communication. It was really, from our estimation, a total lack of communication. And here you had the FDA issuing a regulation, but not having the authority to enforce.

The folks who had the authority to enforce are on the state level and not even, perhaps, in some cases, knowing that this was something they needed to be enforcing. So it's just sort of a classic breakdown but unfortunately for this one, it's not just one we should chalk up to sort of bureaucratic problems. We're talking about the health and safety

of children and adolescents who have a serious medical condition that -- which could be made better or, frankly, could be made worse if the medications that they're being prescribed are not -- are not taken and sort of all of the consequences of that are not known by their parents.

I mean, ultimately, the parent is the person responsible for the health and safety of that child, not the pharmacist, not the doctor, not the FDA. But a parent is powerless without information and that is the role of the doctor, the pharmacist, the FDA and others is giving that information to the parent. And if that information is not getting to the parent, I'm sure many of you are parents, you know what that feels like. My gosh, if we don't have the information we need to do what's best for our children, it is frustrating to say the least and potentially tragic in worst case scenario. So it was really a real utter lack of communication.

My hope is that in New Jersey the work that we've done has helped to foster that communication. I appreciate the FDA's work in working toward better communication and I appreciate the FDA taking the steps that I mentioned to encourage that kind of communication in other states as well. That

really has to be a key to moving forward, is fostering more of that communication to make sure that those developing the regulations and those enforcing the regulations and in this case, unfortunately, it's two different sets of folks, are communicating every step of the way.

DR. SELIGMAN: Congressman, again, thank you very much for being with us this morning and for your very helpful and insightful comments and we look forward, again, to continuing to work with you on this matter.

CONGRESSMAN FERGUSON: Thanks very much.

DR. SELIGMAN: Our next speaker is Ms. Lisa Van Syckel from Drug Awareness. Ms. Van Syckel, if you can again, either address the panel from there or if you wish to use the podium.

MS. VAN SYCKEL: I think I'm going to do both. I had a DVD or a clip that we're going to show first.

(Video played.)

I want to thank all of you for holding this vital important meeting. And I want to thank Congressman Mike Ferguson for being a champion for the children and adolescents of the 7th District in the State of New Jersey. Mike has heard from many parents

since the 2004 hearings. Parents are not receiving the Medication Guides. Doctors are telling patients and parents that this isn't a serious issue and it's very rare. We know that to be different. You hear an actual suicide attempt occurring.

My concern is with the Medication Guides and I've spoken to the pharmacist prior to coming and he was kind enough to give me a sample of the Medication Guides. I'm very concerned with this because you're talking about depression and parents are being confused. They just want the facts.

And the other thing that concerns me is the new CDC analysis where they state that -- if we can put up the first PowerPoint, okay, this is the most recent Medco analysis of 370,000 prescriptions and most recently in the Libby study, where they're also stating that the black box warning has increased the risk of suicide. As you can see with this chart, they cherry picked out of approximately, I believe 65 to 67,000 prescriptions. Here we have the increase of ADD drugs, which carry psychiatric side effects up 74 percent for girls, 37 percent for boys. And I think what I find most astonishing is in the Libby study they stated that the prescribing of anti-psychotics has leveled off during the time when the FDA issued

its black box warnings.

You can see the anti-psychotic use is up 117 percent in girls, 64 percent in boys. This is absolutely devastating. Why are we giving these drugs that also have a causal role of suicide? Okay, and this is another issue that concerns me because it's in the Med Guide and it's being reported in the media as an increased risk. This is the editorial from Dr. Pfeffer, who was a part of the PDAC in 2004 and this is her editorial of June 2007. And it says, "The committee concluded that a causal link" -- it's not an increased link -- "a causal link exists between antidepressant treatments and pediatric suicidality and advised that policies be implemented for pediatric use of antidepressants."

On October 15th, 2004, the FDA mandated that the pharmaceutical companies add a black box warning to the labeling of all antidepressants used with pediatric patients with a Med Guide. And we've also heard Dr. Mann and many others within the American Psychiatric Association that upon autopsies of adolescents they don't find antidepressant medications in their system. And this is SSRIs more likely in suicides than other young deaths. I also have an autopsy report here with me that shows from a

15-year old from the New Jersey District who was taking the proper dose and upon her death of cardiac arrest, there was toxic levels of Prozac in her system.

This is another very important issue. This was reported in the Newark Star Ledger in the State of New Jersey, "Sales reps told not to divulge Paxil data. In a memo last September GlaxoSmithKline provided an update on concerns over it's Paxil medicine, including study results showing a high incidence of suicide and hostility but instructed its sales representatives in bold letters not to discuss the contents with the doctors".

If the sales representatives are carrying these type of documents around, they are fully capable of bringing Medication Guides to the physicians' office. It's not that difficult. There the doctor could provide the Medication Guide to the parent, to the child, prior to prescribing the medication. As you can see, sales representatives can bring risperdal legos to the doctor's office, let's see if they can bring some Med Guides. This, I'm sorry, is disgusting.

Here we have our sales representative bringing a candy bucket and butter up the docs with

risperdal popcorn.

You're going to have individuals from CHADD, the APA and Dr. Fassler from the Child and Adolescent Psychiatry Groups. They're going to come and tell you that you should repeal the black box warning for antidepressants in children and adolescents. I encourage you, do not remove the black box warning. It is a vital piece of information. These drugs cause suicide. They also cause self-mutilation, which is the first sign of a toxic effect of the drugs. And I implore the FDA to please put the self-mutilation side effect back into the Med Guide. It's important. It will save lives. The self-mutilation is a precursor to suicide. You all know that.

And during the -- on May 9th, I testified before the Subcommittee on Health concerning the safety of our nation's drug supply and here, this is a statement that was made in response to Congressman Ferguson's question to Dr. Galson concerning the changing of the wording of the Med Guide and it says, "The psychiatrist community". The American Psychiatric Association has been very, very angry with the FDA because they think that telling people about these risks is dissuading people who really need these

drugs for depression from taking them and therefore, contributing to the number of people that are expressing suicidal activity.

Ladies and gentlemen of the FDA, I wouldn't worry about the APA being angry at you. You'd better worry about the anger of the American parent because it is our children. We monitor our children 24/7. These side effects can be deadly. And like I said, we are monitoring the children and I'm asking the FDA to take the issue of Med Guides out of the hands of the pharmacists, put it in the doctor's office where it belongs, so that the physician can sit with the mom and the child or the adolescent, go over the side effects, prepare us for what could or could not happen so we are able to monitor our children. Children are still dying from the side effect of antidepressants and I cannot express this to you strongly enough.

I hear two to three times a week of another child dying. And these prescriptions are not just being prescribed for depression and that's what I find alarming. They're still prescribing them for migraine headaches. They're prescribing them for your menstrual cycle. I'm very, very concerned. Again, in the State of New Jersey, we have A4245 which is

legislation that will make it mandatory for the physician to provide the Medication Guide to the parents and receive informed consent before the prescription is written and I would appreciate it if the FDA could also consider doing that, making it mandatory so parents have that information.

And I thank you.

DR. SELIGMAN: Thank you for your comments. The next speaker is Ms. Nicole Cumber.

MS. CUMBER: Hello, my name is Nicole and I'm 19 years old. November 2005 when I was 17 I was prescribed Prozac. I never received a Medication Guide. At the time I did not know even one existed and I did not know about the black box warnings for people of my age. My mom heard about the risk of suicide with the medication and she asked the doctor. The doctor said it was rare and that I was being put on a low dose so there wasn't any need for concern. A day later I started to self-mutilate. I was cutting hundreds and hundreds of times in just one day.

I could not go a day without doing it. I started carving die and death in my arms and legs. A couple of days later, I started to have suicidal thoughts. They were really intense. I wanted to crash my car into a tree. I had multiple suicide

attempts while on the medication that ranged from trying to overdose to trying to cut my wrists and I also suffered from homicidal thoughts. I would have thoughts to cut people's wrists and watch them bleed.

My mom would visit me in the hospital. I would sit there and trace her veins with my fingers and not even realizing I was doing it. The medication also made me hear voices. The voices would tell me to cut myself to try and kill myself or even try to kill someone else. I was out of control in the hospital and there were many times I had to be put into a quiet room or in four-point restraints to keep myself from harming myself.

Along with Prozac I was also put on other medications, including a few anti-psychotics which also have black box warnings as well, which I never received a Medication Guide for. The doctors kept on increasing and lowering my medications and giving me more instead of removing them. Every time they did, I would end up back into the hospital because of withdrawal. After five months on Prozac and other drugs, my mom called Lisa Van Syckel. My family was at their wits end and had no idea where to turn. The child that they knew before these medications was gone. Lisa has been a family friend since I was four

and my mom knew she was involved with this particular situation since her daughter went through it as well. Lisa met me for dinner and we sat down and talked about what I was going through. She told me about the side effects and she gave me a Medication Guide.

The whole time I thought I was actually crazy but it was the meds the whole time. I was horrified that doctors would do something like this to me. I thought I could trust them. If Lisa never told me and my family about the side effects, I'd probably be dead right now. The same month I was put into another hospital. The doctor had to drop me cold turkey off my Prozac because there was toxic levels in my blood. He dropped the medications I was on and put me on three anti-psychotics and again, I didn't receive a Medication Guide. Since I knew by then that the medication was causing my problems, I started to refuse it. The doctor told me he had the right to override my decision and force me to take it. He did exactly that.

At each med time, he would put me in four-point restraints or have security guards hold me down and he would inject me with meds against my will. I was hospitalized 10 times and not once did I receive a

Medication Guide. Neither my psychiatrist in my outpatient programs did not give me one. My last couple of hospital stays, they tried giving me medications but I refused it. They did not hand out a Med Guide so I went to a nurse and asked for one to see if they had them handy.

Well, they did not. She had to go onto the computer and go to the internet and even then she didn't print me out a Medication Guide. She printed me out a handout you can find on the internet. If I was given a Medication Guide and was properly informed about the drugs, I would not have taken them. It's been a year off the drugs, but I'm still suffering even today. I was a straight A student in high school and was going to college on an early scholars program while in my senior year.

After being put on the medication, I was no longer able to attend school or college. I ended up failing a class because no one told me how to withdraw from the class. After all this, I was still able to graduate with a 3.5 GPA even though I was only in my senior year of high school for four months. I missed out on applying for four-year schools as well as scholarships because of my hospitalizations. Now I can't concentrate in college because I have short-term

memory loss and I received failing grades in two subjects because of this.

I suffer from constant flashbacks and have nightmares of my hospital stays. I just wanted to say to the FDA that Prozac ruined my life. Before all these medications, I was looking forward to going to college and starting a new life outside of high school. I want to become an adolescent psychologist to help other children, listen to them and not let them endure what I've been through. I'm here today to ask each and every one of you to please, please get out the Medication Guides to the patients and their families and listen to what the children tell you, so they can make an informed decision, so they don't have to suffer the horrific of the side effects that I did.

DR. SELIGMAN: Thank you for your comments. The next speaker is Ms. Laurie Yorke. Ms. Yorke?

MS. YORKE: Thank you for the opportunity to be here. I can come at this -- the information from three different aspects. I'm a registered nurse, I'm a member of the general public and I'm also a mom who's had a child affected by adverse reactions to an antidepressant. But first the nurse aspect. Patient education is something that I do every single day.

Over and over thousands of times, I've probably educated more people than most of the people in this room. One of the basic tenants of educating a patient on drug use on a surgical procedure, on a radiological procedure, is that the patient is to be made aware of every risk that could possibly happen despite the numbers.

If a patient is going for surgery and they're going for an appendectomy, the risk of dying from an appendectomy is relatively small. That doesn't mean that the surgeon cannot warn the patient about that risk. It must be included on the informed consent.

The risk of suicide, homicidal thoughts, aggression, anxiety, increased anxiety with antidepressants is not that small; yet, we're prescribing them every single day and sending these drugs out into the community, out into our homes with our children without the information that they need to be properly monitored.

One of the big concerns of the American Psychiatric Association is that if we tell people what the risks are, they will not take the drug. Just because someone is depressed or anxious, does not mean they are stupid. They have the right to have all the

information that is available. They have the right to have it unwatered down in pure language and have it exactly laid out as the risks are known.

One of the aspects of my job is education at work. We've now -- the new Joint Commission standard, in addition to the original five rights of medication administration, the right route, the right dose, the right patient, the right time, we have now -- have a new Joint Commission standard that is the eighth right of medication administration and that is the patient's right to education. What we are doing now is not educating the patients. I did an informal survey at work and I can tell you that 99 percent of the nurses the I surveyed had never heard of a Medication Guide.

Ninety-five percent of the nurses that I surveyed had never heard of the MedWatch program. Hard to believe, but five years ago, I was in that exact same situation. I had no idea what a Med Guide was, didn't even know there was a way to report an adverse reaction to the FDA until I had to face it with my child.

The other aspect is from the general public. I have a website for antidepressant withdrawal. I talk to thousands and thousands of

people every single day who are going through antidepressant withdrawal, also known as discontinuation syndrome by the pharmaceutical industry. These patients are angry. They come to the board. They post their first initial message which is 99 percent of the time, "Why didn't my doctor tell me this could happen"?

These are people that were probably having adverse reactions after the first two or three doses. That adverse reaction was denied by their physician and subsequently doses of the drug that caused the adverse reaction were increased. One of the most stunning examples is a gentleman who came to the site 48 hours ago. He was started on Lexapro for depression. He was not given any information regarding suicidality, homicidality or any of the adverse reactions that are potential problems with the antidepressant group.

After one week on the Lexapro at a 10 milligram dose, he went into a flying rage in his family. The family was scared. They called the psychiatrist. That reaction was treated with an increase in dose to 20 milligrams. Twenty milligrams is the recommended dose for Lexapro use. By the time he got to my board and talked to other antidepressant

survivors and other members of the board who are going through antidepressant withdrawal, the rage had happened so often over the previous year that he was up to a Lexapro dose of 60 milligrams a day. That is a toxic overdose.

His doctor was treating the adverse reaction from the Lexapro with more Lexapro. Once we pointed it out to him, we pointed to the FDA information on the website, he was appalled. This is what the general public is dealing with. Without concise, clear and honest information about a drug's adverse reactions, they're not getting it from their physicians. I asked some of the people on the board to give me some statements that they had received from their doctors regarding Paxil and antidepressant withdrawal and antidepressant adverse reactions as a whole. The misconceptions were stunning.

One patient, when asking about trying to come off Paxil specifically in this case, he was told by his doctor that quote, "It has a fairly long half life, you can just quit taking it". As you know, cold turkey off of these drugs is not recommended and is highly dangerous and results in many of the suicidal and homicidal acts that we see.

We have another woman who, when she was

cold turkeyed off her Paxil went back to the doctor with the obvious adverse reactions from the cold turkeying off. Her doctor's response was, "After they tried to do the return of original symptoms crap, I had to remind him I was put on this garbage for irritable bowel syndrome". She was never placed on it for a psychiatric diagnosis but yet, was now extremely suicidal. When she pointed this out to her doctor, the response was, "I don't know what to tell you".

One of the other patients who had cold turkeyed off at the recommendation of his doctor and reinstated the antidepressant 12 hours later on his own, explained to the doctor that the symptoms had gone away after reinstating the drug. The doctor's response to him was, "You are only having these suicidal thoughts because you read the warning. If you would stop reading the labels, you wouldn't feel that way and the drug would start working again".

This is what the general public is getting. They are not getting the honest answers. They are not getting the honest potential reactions regardless of how low that risk is. It is a risk, they have a right to know. The risk is not predictable. This happens across the diagnosis spectrum. The suicidal risk is not limited to

depression which is another misconception that is out in the public. People will come to the website and say, "I would never be suicidal, I wasn't put on this for depression". That's why we need to have the causal role reinstated back into the Medication Guide because right now everyone is confused. The patients are not getting the correct information. These drugs have caused suicides in people who have not been placed on them for a psychiatric diagnosis. That is a causal role.

The last aspect that I can address is as a mother. My son is now 19 years old and is a Paxil survivor. He was put on Paxil initially for an anxiety attack and over the course of the next 14 months, since the information at the time that he was put on, in 2001, was not available. We did not know what we know now. His adverse reactions were also treated with increasing, ever increasing doses of Paxil. He went from 12.5 milligrams to an all time high of 50 milligrams. He was 15 at the time.

His outbursts of rage, his aggression, his impulsivity, his chronic pot smoking, obsessively pot smoking, his thoughts of homicide, his thoughts of violence, his actually being -- I discovered him researching bomb making on the internet. He was going

to blow up his school as an overreaction to a slight by another child.

At the 14-month period, we -- after continuously asking his doctor what was going on, his doctor never mentioned the possibility that the antidepressant could be causing it. At 14 months I had hit the internet because I had learned at that point that my best medical resource was Google. At that time I found his story was stunningly similar to thousands of other people out there. We attempted to wean, following his psychiatrist's advice which I now know was a drastically rapid wean. After his first wean, he attempted suicide twice in 12 hours.

It was then that I took over with help from other antidepressant survivors, not from his doctor, who at that point had refused to take him back as a patient after the suicide attempts. His doctor to this day, continues to deny that antidepressants have any adverse reactions. The only one he will ever admit to and has ever admitted to myself when my son was there and to future patients or current patients that he's treating that I have now talked to is, "You'll have a little bit of diarrhea. There's nothing else, there's no other side effect to this drug." This is what the public is being told.

My son's reaction could have been prevented because the signs were there. Every sign that is listed in the medication guide was there. We didn't know what we were looking for. It's my responsibility as his parent, to know what to look for when my son starts a drug. It's the doctor's responsibility as the doctor, to let me know what I'm supposed to be looking for. These were out of character responses by him that the doctor kept writing off as teenage angst. As we now know, he is now 19 years old. He is fully off of Paxil. He's been off now for three years.

He is emotionally wonderful; no anxiety, no panic, no depression but what he suffers from now three years being off antidepressant -- off of Paxil is a pseudo-Parkinsonism that comes and goes with unpredictability. He has myoclonic twitches that are totally unpredictable that in some cases have actually raised him off the couch. He is unable to attend college at this point. He is unable to drive. He did have to withdraw from high school because of the withdrawal of Paxil. I would not let him out of my sight.

He has now successfully completed his GED and is awaiting the neurological symptoms to hopefully

slow down. We should have been warned. Every parent has the right to be warned. It is never medically ethical to withhold disclosure of a potentially deadly risk to increase compliance by a patient, never. We're not talking nausea and vomiting. We're talking suicide and every patient has the right to know that that is a possibility regardless of how small the risk is and regardless of if that will make them compliant with drug use.

If they choose not to take it, that is their choice, that is their right. Thank you.

DR. SELIGMAN: Thank you for your comments. Our final speaker is Mr. Robert Manciero from Full Vision Productions.

MR. MONCIERO: Thank you. I come here as a film maker and commercial director from Los Angeles, California and if someone told me two years ago, I'd be sitting on this panel I would have told them they were crazy. Two years ago I set out to make a documentary film about children, teenagers on antidepressant medications who have committed suicide or have attempted to commit suicide. At that time, I did not know what an antidepressant was or an SSRI. I was just inspired by an article I read in the LA Times about a family who lost their 15-year old son to

Zoloft and he hung himself and he didn't have depression, he had anxiety.

The film, which I will show you a clip from, allows these families to speak and tell their story from their heart. I come here today as not a promoter of this film but as a voice of the family and the kids to show you real life what's going on out there without statistics, without graphs, but to put a face to these numbers that everybody talks about. So if we can please roll, I have a couple of edited clips from the film.

(Video played)

Sitting down eye-to-eye with these families for over a year, there was one common thread amongst all of them, and that was that, "We were never told the danger or side effects of these drugs". You know, it amazes me in this technological age that we can jump on the internet, I can search for a new car, find out all the safety features, find out if it's safe or not, yet, you cannot go on the internet and find out if a drug is safe. You know, we screened this across the country so many times and every time I get the opportunity to go out to a screening and meet family members and I hear the same story, just the names change, just the locations change. When we

first released the film, the first two weeks I got bombarded with literally hundreds of e-mails from across the country and around the world and there's two actually I wanted to share with you very quickly.

This one says, "On June 11th, 2004 our 15-year old son Brett committed suicide. He had been diagnosed with social anxiety and his doctor prescribed Zoloft. When I questioned her about the safety of this drug, she told me not to worry about it, the media has a tendency to centralize these issues."

Here's another one, "My 15-year old daughter hung herself while taking Zoloft almost two years ago. Shortly after she died, we found that there was a controversy about the safeties of these drugs. We were so stupid, we didn't even know that the drug wasn't approved for children and thus, was prescribed off-label. We were never told by our doctor".

The question I ask is why, just simply why? Why aren't physicians, pharmacists, anybody who prescribes this drug sitting down with these parents with a checklist and telling them the side effects so they can make a decision? This borders on a criminal offense and I hope that you listen to these family

members because you just saw three out of hundreds that have the same story. Thank you for your attention and thank you for allowing me to state this.

DR. SELIGMAN: Thank you, and thank you all members of the panel. Did you have an additional comment?

MS. VAN SYCKEL: Yes, I do, thank you.

DR. SELIGMAN: Ms. Van Syckel.

MS. VAN SYCKEL: Dr. Seligman and Dr. Temple, would it be possible to please put the self-injury behavior back into the Medication Guide. It's vitally important. What I've heard from numerous parents across the United States is, they said, "If we could know, if we were told about the self-mutilation, tragedy could have been prevented". It was in the original Medication Guide, the proposed Medication Guide back in 2004 and I'm begging you to please put it back.

DR. TEMPLE: I'd have to look to see why it was removed. I don't remember that.

MS. VAN SYCKEL: It's my understanding that it was negotiated with the pharmaceutical industry. I realize that you negotiate the labels, but when it comes to the self-mutilation, you can actually see the scars on Nicole's arms, those are

permanent scars. It's vitally important to put that back there. That is the first sign, a pre-cursor to the suicide and we can have them hospitalized. We can seek medical attention and tragedy can be averted.

And also, and I know this is really going out on a limb, is make it mandatory for the physicians to distribute and not the pharmacy, because that's where this information belongs, in the doctor's office with the patient, with the mom, the dad, the child or the adolescent and the doctor and go over this vital lifesaving information. As you all know, there is no greater pain on the face of this earth than the loss of a child. And I thank you very much.

DR. TEMPLE: Just one thing on that, we certainly like the idea of physicians handing them out also. I think one of the thoughts was that someone other than the physician ought to make sure that the patient gets this piece of information because, among other things, the physician having decided to prescribe it, might be more reassuring than this document. So, I don't think anybody thinks it wouldn't be a good thing if the doctor talked about all these things before it was prescribed, but I do think an independent source is considered a good thing, too.

MS. VAN SYCKEL: In our case with -- well, my children are now adults, Michelle will be 22 next month and is doing beautifully and of course, my son is 19, but their pediatrician -- I provided the Medication Guides to their pediatric group, to the local school system and our local law enforcement, and they were grateful to have the Medication Guides, and they do discuss the Medication Guide with their patients.

So I think all doctors, if they care about their patient, they'll be more than happy to share this information. Thank you.

DR. SELIGMAN: Any questions from members of the panel? Dr. Woo?

DR. WOO: Yes, thank you to all the panelists for their presentation. Actually, this is a fairly general question. Ms. Yorke, you actually referenced Google as one of your sources of information. I think certainly one of the challenges is balancing the different sources that you have, be it a physician or a pharmacist or what the FDA puts out. I would just be interested in your perspective on what might make the information source that the FDA does have, including our internet site, more accessible or more informative to you in addressing

some of these risks.

MS. YORKE: Well, I can tell you that the way the FDA site is set up right now, it's not user friendly. I mean, I'll be perfectly honest, I steal information from your site and put it on mine, you know, so that people can actually find it. You know, we put up a lot of links to the FDA site but the majority of people that come to my site, I've got 4,000 registered members. I have over 120,000 individual IP addresses and we're now getting 3.2 million hits a month from all over the world who are Googling antidepressant withdrawal.

You know, we can show them where the information is, but your site is horrible to search. You know, I tend to be a bit of a geek and can kind of find my way around but you know, I have women that are 65 years old, you know, that, number one, if they do have a computer, they don't know beyond the basic search engine and your search feature, you know, if you had one place. You say you have 65 drugs, I believe, that have black box warnings or that carry Medication Guide requirements. You know, put that in one place.

You know, right now, they're scattered. If you do a search, they're scattered all over the

place. If you put that in one place, and make them printable from that one location, now you have a situation where if a doctor chooses to give the Medication Guide, which in my opinion, they should be giving the Medication Guide, now it's a one-stop shopping. You know, now they go to their computer in their office. They have the FDA Medication Guide site bookmarked and it's two clicks and a print and now the information is there for the patient.

I love my pharmacist. The pharmacists have been amazing with working with us and working with Congressman Ferguson to get this information out there, but the bottom line is, this is too important to be in the bottom of the pharmacy bag with the toilet paper. It really should be coming from the doctors and if the FDA site was set up to be much more user friendly, with a single bold heading, "Medication Guides for These Drugs", the doctor or the psychiatrist who prescribes only psychiatric drugs, he knows which drugs have a Medication Guide. It's not asking the doctor, you know, to go out of his way to click twice.

The other thing is the MedWatch program, that's just a joke. I've walked more people through that process to file their MedWatch, their adverse

reaction. It is the most unuser friendly site. That needs to be addressed because right now you're not getting the true number of adverse reactions. It's estimated that you're getting about 10 percent of what's actually happening and I would probably venture a guess that it's probably less than that.

I can tell you that there are 4,000 people that have now put their MedWatches up because we actually walked them through the process of how to put it in, because prior to that, they didn't understand what they were supposed to be doing. So if you could get those two aspects of your site more user friendly, the MedWatch program plus the medication guide, to make it printable and make is accessible, and you know, bold these two things out on the FDA site so that you didn't have to search, you know, in little, you know, eight point font to find out what you're looking for. Make it bold, make it simple, make it point and click, and you're going to have people who Google for their medical advice, which is a lot of us, you know, even me as a nurse, you know, I have lost a bit of faith in the medical profession in the last five years and I tend to Google a lot and I interpret clinical trials and read clinical trials, and, you know, have learned a lot over the years but patients,

you know, they can Google and get at least the FDA warnings, that may stimulate them to research further and that could stimulate more conversation with their doctors. At the least, it will give them an idea of what to look for in the adverse reactions.

DR. SELIGMAN: Additional comments, questions from members of the panel? Again, thank you all for your comments and input. They are very important and valuable to us. At this time I'd like to take a 20-minute break and we will reconvene at 10:30 with the next panel. Thank you.

(A brief recess was taken.)

DR. SELIGMAN: If I may, let's everyone please find your seats so we can begin the second panel. May I call the members of the second panel to the table including Dr. Nancy Allen LaPointe, Mr. Allen Lang, Dr. Ruth Day and Dr. Michael Wolf. Please find whatever chair you like, make yourself comfortable and we'll begin in just a moment.

Our first speaker on the second panel is Dr. Nancy Allen LaPointe from the Duke Clinical Research Institute. Dr. LaPointe?

DR. LaPOINTE: Thank you for the opportunity to speak today. My comments will be focused on a research study that was evaluating

patient receipt and understanding of written information provided with isotretinoin prescriptions.

DR. SELIGMAN: Could you get a little closer to the mike or speak up a little bit?

DR. LaPOINTE: Okay.

DR. SELIGMAN: Thank you.

DR. LaPOINTE: By way of background, this research study was conducted in 2004 to 2005 to assess receipt and understanding of isotretinoin Medication Guides and estrogen mandatory patient packets inserts. Because the focus of this meeting or hearing today is on Medication Guides, I'm going to focus my comments predominantly on the component with regards to the isotretinoin Medication Guide.

And the reason this particular drug was selected in this study was because at the time the study was conceived in 2002/2003, this drug was actually, of the drugs that had Medication Guides, was probably one of the drugs that was most commonly used. Obviously, nowadays, that's not necessarily the case. This study was funded by AHRQ and the FDA and partial results have been previously published. The purpose was three-fold. One was to assess the receipt of Medication Guides by patients receiving prescriptions for isotretinoin and at the time we looked at all

marketed products of isotretinoin or all brand name products. We also assessed how thoroughly patients read the material and then conducted a preliminary evaluation of patient understanding of key risks associated with isotretinoin as was described in the Medication Guide.

So first, this was a patient survey study and the goal was to attain a sample size of 200 isotretinoin patients. The attempt was to balance the number of participants with different marketed brands and at the time, there were three marketed brands of isotretinoin. This was one of the reasons why our survey took a little bit longer as we wanted equal numbers of each of those brand products just in case we were to find a difference between them.

Also, as I mentioned, the study was conducted from February 2004 through January 2005, so this actually predated the current isotretinoin I Pledge Risk Management Program. Okay, adult patients with isotretinoin prescriptions were identified using claims data from a pharmacy benefits manager. Claims were reviewed every two weeks and patients were only eligible once during the study period so no patient would be asked to participate more than one time. Patients were contacted by telephone within 24 days of

prescription fill or refill for participation in this survey and they gave informed consent for participation.

The survey was designed, as I said, to assess receipt of the Medication Guide with not only the most recent prescription but also there were questions related to past receipt of Medication Guide with past prescriptions. We also made a concerted effort to try to differentiate the Medication Guide from all other written information that a patient may receive. As you well know, patients are many times bombarded by multiple different types of written medication information at the time they receive their prescriptions and we made a very detailed description of the Medication Guide to try to differentiate it from the other information that they may have received.

There was a maximum of 11 questions for any given patient on the survey; however, not all patients answered the same questions because they did not receive the current Medication Guide or did not receive the Medication Guide with their current isotretinoin prescription, we skipped to talking to about past prescriptions for example. The survey was administered by interviewer.

Okay, this is the breakdown basically of how we arrived at our 200 participants, and actually we need to start at the bottom. We had 1747 isotretinoin prescription claims that were required to be evaluated to arrive at our 200 participants. Of those 1747, there were only accurate telephone information on about half of those or 936 and of those only about half could be reached by telephone within 24 days, 498 and of those, about half were willing to even get through listening to the consent -- informed consent when we were reading it to them over the telephone. So of the 254, 229 were identified as English speakers and of those 200 agreed to participate in this study.

This is just a quick breakdown of some of the very basic information that we collected on participants as well as non-participants. You can see the median age of the participants was 30; 69 percent were female and they were predominantly from the Northeast Region of the United States and that was related to the Pharmacy Benefits Manager that we selected and the clients that that PBM serves.

The quarter and the year, you can see the distribution of patients who were included in the survey based on quarter and year and obviously, they

were fairly well distributed except for the third quarter of 2004. So the first set of results I want to talk about is confidence and receipt of a Medication Guide. The first issue with the confidence was actually the first question on the survey asking them how confident they were in their knowledge of their drug, in this case isotretinoin's risk so that they could safely take it.

This was the first question that we asked because we didn't want to get into all the questions about the medication guide and written information before we asked this. We actually found that 172 or 86 percent of patients ranked their confidence in their knowledge of their drug as very confident or confident. We also found that 186 of the 200 or 93 percent of patients stated that they did receive the Medication Guide with the most recent prescription. I think it's very worthy to note that for isotretinoin, the Medication Guide is enclosed within the product packaging. So we, in fact, know unless someone tampered with the packaging that 100 percent of these patients actually did receive the Medication Guide. This was another one of the reasons why we selected this drug for this study.

We saw different results with our estrogen

evaluation where we selected a product in which the mandatory patient package insert was included in the product packaging in one brand and not in another and actually did see a difference in patients' recall of receipt of that. So I think it's important to realize that this is not necessarily that they received it but they recalled receiving the Medication Guide.

Okay, the other important note here is that prescription fill and refill is not the only time in which the Medication Guide can be distributed in the case of isotretinoin. This is encompassed within an entire risk management program and there are many other places in which the patient can receive the Medication Guide. So the 93 percent, although it sounds quite good, there are a lot of mechanisms for patients to have received this besides the prescription refill point and we, in fact, know that the Medication Guide was enclosed in the product packaging.

We did find that there was a difference in level of confidence among those who receive versus not receiving the Medication Guide. Eighty-eight percent versus 64 percent were very confident versus confident. The next set of results I want to present to you are extent of reading of the Medication Guide

and this is with the most recent prescription we asked these questions. We only found that about 41 percent of patients said that they read completely the Medication Guide with their most recent prescription. Sixteen percent said they read more than one section completely. Less than one percent read only one section completely. Fifteen percent skimmed it, 26 percent said they didn't read it at all and about a little less than one percent said they don't remember.

So we tried to drill down a little bit more on this particular issue to find out the extent of reading the Medication Guide among those who did not completely read it with that most recent prescription. So of the 109 who didn't completely read the Med Guide with the most recent prescription, 25 percent said they completely read it in the past but if you look, another 75 percent of patients either didn't read it completely at any point in time of had never received the Medication Guide on isotretinoin before. So that means that 75 percent of the patients who didn't read it this time, never read it before either.

Of the 49 patients who didn't read the Medication Guide at all with the most recent prescription, 20 percent didn't read it at all before

and 39 percent either didn't receive the Med Guide for isotretinoin before, so it demonstrates a substantial number of patients who did not read the Medication Guide. Then the question of patient understanding and in our study, we did just basically a very high level assessment of patient understanding with this one particular question. Dr. Ruth Day will present some additional information that was done in looking in more depth as to patient comprehension of the medication guide materials. I am now going to read to you five different statements, "Without looking at any other medication information that you may have received with your Accutane, for example, please tell me which of the following statements, if any, are true for Accutane". And the two that are in yellow are the two that appear in the Medication Guide; so, "Accutane may cause birth defects, and Accutane may cause mental problems or suicide". These were yes, no, don't know, questions for each of these five, so they should have answered yes to the two in yellow and no to the two in white.

I know this is very difficult to see, but this is a reprint of the Medication Guide for isotretinoin which basically shows us is the front -- first page where these particular severe adverse

reactions show up on this page and the wording that is used on the Medication Guide that we used in developing this particular question. So the results were that if you look at birth defects, 96 percent of patients acknowledge that birth defects were a potential risk with their medication and 84.4 percent recognize that mental problems were a potential problem. If you look at those in which they should have said no, you'll see a little bit different responses. There was a little more uncertainty as to whether or not some of those were true adverse effects with their medication or not. I think the most important thing that we found was that if you look at of the 115 women who are age 18 to 45 and thus, we're presuming of child-bearing potential, four of them or 3.5 percent reported no or don't know to the birth defects question. So that still meant that there were some women who were at potential risk who were not aware of that risk.

If you look at this another way, we looked at mean score on those five questions and what we found was the mean number of correct responses was 3.1 out of 5 and this was only slightly better than would be expected from someone who is guessing. Another way we looked at this was a propensity weighted score

model in which we looked at factors that might predict a better score out of five on this particular survey question. And we found that patients who had high confidence levels or patients who had recently completely read the Medication Guide were more likely to do -- were more likely to do better on those five questions. As we mentioned earlier, there did appear to be a direct association between confidence and reading the Medication Guide.

So in summary, if I had to sum up our results from this particular study, I think I would do it in the following way, in sort of a report card style fashion and if I looked at receipt, I guess I would score it as good because I think that even though we had 93 percent of patients reporting that they received it, we know essentially 100 percent did. So we know that there still could be improvement in the way in which this information is given to patients so that they really truly do receive the information.

Reading, I would rate as poor, I think based on the fact that we found so many patients who did receive it, but actually never completely read the information and thus, cannot gain the potential benefit from the information contained within the Medication Guide if they don't actually read it.

And then understanding, I would rate as fair. Again, we found some areas, especially with birth defects where there is a high proportion of patients who recognize that but still found patients at potential risk. So in summary, I would say that the bottom line really indicates that I think we need to find better ways to communicate risk to patients.

DR. SELIGMAN: Thank you. Before we go on, are there any questions from members of the panel for Dr. LaPointe? Yes, Dr. Temple.

DR. TEMPLE: I guess on the understanding, I would have said that they did better than you suggest. They got the things that were true, which is, after all, the purpose of this and what they didn't feel sure of was what was not there. But you know, you or Ruth might want to address this. I would say most people don't know what's not in something. That's a hard question, but they did get the things you wanted them to get, didn't they?

DR. LaPOINTE: Yes, that's true. They got the birth defects questions which I think was key. Except, I think, given, though, if you think about it, isotretinoin Medication Guide is not the same as many of the other Medication Guides in the fact that it's encompassed by an entire risk management program as

well. So you could argue that this is like the best case scenario that we have available is a Medication Guide in -- you know, surrounded by a whole risk management program and you still only have 96 percent of patients who are aware of the birth defects risk.

I mean, one could argue that you'll never reach 100 percent, which I understand, but there still obviously are people at risk. I think the mental health issue was a little bit more concerning where you had only 84 percent aware and that's a very prominent adverse effect in the Medication Guide but is somewhat overshadowed, I think, by the birth defects piece. And so people, especially the male population, you would think, since they may not pay any attention to the birth defects part, would pay more attention to that one but may not be doing it.

DR. TEMPLE: I guess the concept of only 96 percent is unusual.

DR. LaPOINTE: Yes.

DR. SELIGMAN: Any other questions or comments? Yes, Janet Norden.

MS. NORDEN: I just wanted to ask if you had any research on why people don't read this information.

DR. LaPOINTE: That's an excellent

question. Actually, the survey was designed to really just start to scratch the surface with receipt, reading and understanding. And so we really didn't know what we were going to find in terms of whether or not people were reading them or not and so the survey was not designed to dig any deeper into that. There, I think, a lot of people have tried to make educated guesses as to why that may be, that people don't read them. I think Ruth has some information to present in terms of, you know, how people understand and retain the information within them that may be helpful, but unfortunately our study was not designed to dig any deeper into that. But that's a critical piece, I think, that needs to be done in order to figure out better ways to communicate to patients.

DR. SELIGMAN: John Jenkins?

DR. JENKINS: One way to try to improve the distribution of the Medication Guide is to have it attached to the packaging, the unit of use packaging that you're describing for isotretinoin. There are pros and cons to that on multiple levels. I'm interested, do you have any thoughts about whether people who receive it as part of unit of use packaging are more likely to read it than people who receive it handed to them by the pharmacist. So we might

achieve 100 percent distribution of unit of use packaging but is that a good way to get people to actually read the information?

DR. LaPOINTE: I don't have any information to that effect. I think that in this study we were just trying to figure out if they recalled receiving it in the first place and one of the difficulties is differentiating it from all the other written information someone may get. And so even if you have it included within the packaging, more than likely, that patient will also receive pharmacy leaflets that will be thrown in the prescription bag as well. And so, it's unclear, I have not seen a lot of research on whether or not which do patients preferentially choose to look at. Do they look at their pharmacy leaflet? Will they look at the materials that are laid in the box or the packaging or something that their physician perhaps gave them?

And so I think there is additional need for looking into what is it that draws the patient to read or look at a particular piece of information preferentially over the other, that is if they look at any of them in the first place.

DR. SELIGMAN: Thank you. Our next

speaker is Mr. William Lang from the American Association of Colleges of Pharmacy. Mr. Lang.

MR. LANG: Good morning. Today you've heard and will continue to hear recommendations for improving the Food and Drug Administration's Med Guide Program. We share the concerns voiced by others that the constraints reflected in the current implementation of Med Guides fail to address substantial public health concerns related to risk communication and effective medication management. The American Association of Colleges of Pharmacy appreciates the opportunity to publicly state our interest in working with the FDA to improve risk/benefit communication to consumers of prescription drugs.

Improving the quality of healthcare interventions, especially those involving prescription drug use and management is dependent on effective communication among patients and their healthcare providers. The Institute of Medicine's 2006 report preventing medication errors include strong and targeted recommendations that health professionals improve communication among themselves and directly with their patients. The report also indicates that improving patient safety can best be accomplished by

placing the patient in the center of the decision-making process.

Shrank and Avorn write that Medication Use Guides need to be standardized to improve patient medication use. Perhaps, it is the regulatory need to overly standardize the material as published in current Med Guides that minimizes their effectiveness. Communication research emphasizes the importance of communicating with healthcare consumers at literacy levels and in language they can understand. AACP believes this is fertile ground for deeper exploration. The many stakeholders here today are providing a significant number of potentially valuable recommendations for improving medication safety through use of Med Guides and other tools.

AACP is aware that most of these recommendations are not fully tested and may just reflect hypotheses that relate to how consumers really make decisions about prescription drug use. It is obvious that the status quo in terms of risk management and consumer education is not working well, but how do we know that the recommendations presented here today all offered in good faith, will lead to the improvements we so desperately need in our medication safety system.

Academic Pharmacy stands ready to work with FDA to develop and test new approaches to improving medication safety through risk benefit analysis and communication. Our researchers currently participate in the research programs of every federal public health agency. Academic Pharmacy should be considered as a strong partner in the FDA's efforts to improve the science knowledge of the agency. The three-pronged mission of higher education; research, teaching and service, provides the FDA with a breadth and depth of experiences in which to test and develop evidence-based practice -- best practices in the area of risk/benefit communication.

I will expand briefly on each of these and then end with a proposal for the agency's consideration. Research, Academic Pharmacy provides the FDA with a research framework that ranges from the molecular to populations. The research capabilities embodied in our membership create essentially opportunities for evaluation and analysis of product risk, intervention programs, patient care services and adult learning. Faculty at our nation's colleges and schools of pharmacy are engaged in a broad array of research activities. These activities include the scholarship of teaching, the diversity of patient

populations and the diversity of medications and biologics available to those populations pose a growing challenge in regard to the best patient provider communication strategies.

In response to this challenge, the Academy has focused its attention on improving the teaching of communication skills throughout the course of a pharmacist's education. This attention in improvement and communication skills of students is reflected in articles assessing student communication skills including those associated with non-prescription drug use and utilizing e-mail to communicate with patients.

Teaching; pharmacy education took the leadership position in the last decade that all pharmacists must be educated at the doctoral level to increase the profession's capacity for patient education and care management. Our commitment to the expanded role of pharmacists as patient centered care providers, extends to current practitioners through our schools' work and continuous professional development. The competency map for contemporary pharmacist education includes numerous references to the acquisition and use of communication skills broadly defined and emphasizes the importance of providing culturally and linguistically appropriate

services to diverse patient populations.

There are competencies as well related to understanding risk benefits of drug therapy, monitoring patient's reaction to medications, and providing risk surveillance information to appropriate parties. Further, pharmacy faculty can contribute significantly to other health profession students and providers education by sharing their knowledge as medication use experts.

Service, strong community campus relationships developed and maintained by pharmacy faculty and students provide the FDA with direct connections to diverse populations with unique needs and responses related to medication use. These populations and communities can be defined by a particular disease state, cultural, ethnic or socioeconomic background. This diversity creates the optimal situation for community based decision making regarding what works best for them in terms of risk benefit communication.

The Academic Pharmacy community is prepared to partner with the FDA to facilitate access to diverse populations and strengthen risk assessment. Engagement with the community is providing Academic Pharmacy with partnerships well-suited to address

community determined needs including provider patient communications, targeted to the health literacy levels of individuals.

Utilization of evidence based culturally sensitive communication efforts can significantly improve individual and community health outcomes. The diversity of these community campus relationships provides the FDA with a rich environment of placing valuable medication use and management information in the hands of those that need it most, the patients, while at the same time providing them with faculty and provider support that is essential for sustainable improvements and analysis of the information's impact.

The opportunity; I will close by sharing an exciting and very real possibility of a partnership between pharmacy educators, students, AACP and the FDA to enhance the evidence based supporting risk surveillance and communication. All pharmacy students must spend a considerable amount of their educational program in the clinical setting under the supervision of faculty and practicing pharmacists. This begins in the first year of the academic program and continues through graduation with a doctor of pharmacy degree. At any given time, somewhere between 12,000 and 20,000 PharmD students are in patient care environments, a

significant number of which are in the ambulatory and community settings. AACP proposes a new model of drug risk surveillance and communication assessment, deploying this army of developing professionals whose education uniquely equips them to communicate with the public regarding medications, their risks and their benefits.

These students are also required to gain insights into adverse event reporting, outcomes monitoring and documentation. With proper training, and with coordination provided by AACP in partnership with the FDA, we can imagine a revolutionary model of risk evaluation and communication assessment that responds to many of the concerns voiced today and previously about the constraints of today's models of risk management.

AACP would appreciate the opportunity to share more about this proposed model with FDA and other interested stakeholders and very much appreciates being asked to participate in today's panel to express our absolute commitment to bring the strengths of Academic Pharmacy into alignment with the needs of society for safer medication use and more effective risk communications. Thank you.

DR. SELIGMAN: Thank you, Mr. Lang. We'll

take you up on your offer.

MR. LANG: Thank you. Look forward to that.

DR. SELIGMAN: We never turn down an army. Are there others in the panel that wish to comment?

Yes, Ilisa?

DR. BERNSTEIN: Early on in your remarks you said that there's a regulatory need to over-standardize the Medication Guides and that may be reducing the effectiveness. Can you elaborate a little bit more? Is there research there or is that a hypothesis?

MR. LANG: I'm referring to an article in -- relatively, I don't have my reference list with me, but I think it's a recent article in the New England Journal of Medicine by Shrank and Avorn talking about the risk communication and Med Guides in particular and they think that they need to be standardized and my comment was that they may need to be standardized to a certain degree but that actually may reduce their effectiveness in the communication that we're trying to get with patients. Standard -- a minimum amount of standardization is probably necessary but there's a lot of other aspects of communication that need to be reflected in that

activity.

DR. SELIGMAN: Toni Piazza-Hepp?

DR. PIAZZA-HEPP: Just a follow-on to Ilisa's question, and then I had a completely separate question. Right, the way the Medication Guide regs are written is they do have some standardization which are standardized headings and we do encourage that and apply that, you know, to most products because we think it's important to have some consistency so patients know where to find the information that they need. However, the regs are also written so that there's some flexibility so they have certain headers don't apply to a particular product. Those do not have to be included.

And on the other hand, if additional headers need to be added, then that can occur as well. And so you know, the Medication Guides, believe it or not, were written with a little flexibility in mind because products certainly are not created equal. But actually, my question is, I'm a pharmacist, I went to pharmacy school quite a while ago, and it wasn't until I was on the job that I really was exposed to learning about how to communicate with patients. I didn't recall any didactic teaching of that nature. So my question to you and I'm very happy to see you here

today, is are accredited schools of pharmacy required to include a course or courses that focuses on health literacy or communicating with patients?

MR. LANG: As far as the accreditation standards that are -- that address the curricular aspects, I don't have those with me. I'll be glad to share those with you. This has been a significant growing focus of the Academy to make sure that our students graduate with the communication skills necessary to engage in diverse patient population. And we've helped both our faculty and our -- the leadership to understand the importance of this through seminars and programming and to provide that information to people in a culturally competent, culturally diverse way and you probably -- if you didn't go to school within the last few years where this has become even a more, much more recognized important activity of the professional upon graduation, and not after you get out into the workplace, you probably didn't get a lot of that because we have tried now to integrate this across the entire curriculum, that this isn't just an add-on responsibility of the pharmacist, that is somebody that is accessible in a community setting sometimes 365 days a year, that we need to make sure that the

people -- those professionals are competent to deliver these types of communications upon graduation.

DR. SELIGMAN: Dr. Woo?

DR. WOO: Yes, again, thank you for your presentation and I want to follow up with Ilisa's question and perhaps being a little bit more blunt. What I was hearing, what I thought I heard was that the Medication Guides are actually a hindrance to what the Academic Pharmacist world would be promoting for improving patient understanding and communication. I think the Medication Guides that exist sort of provide a baseline standard for the type of information that we, the agency feel is important to get to patients. We wouldn't want that to be perceived as interrupting the practice of medicine either by a physician or a pharmacist in their role in determining the way to get that information best communicated to the patient.

So I just want to be clear, is the perception that the guide is -- the Medication Guides are seen as being inhibitory to that relationship and that communication within the practice of pharmacy?

MR. LANG: No, I did not mean to intend that they are -- they inhibit communication. My point is that we don't really know whether that's the best way to communicate with patients in regard to the

medications that they're taking. And I think that Dr. LaPointe's presentation shows that Med Guides can be somewhat problematic and there needs to be the communities that are -- prescribe these medications that in this instance, that require a Med Guide might be the community that you talk to, how best to get them the type of risk benefit communication that they will read, that they will take advantage of, that they will be able to develop questions around and be active participants in their care.

DR. WOO: Sure. I guess I'm just concerned that -- and again, we're trying to establish a baseline and I certainly think certainly in a nation as diverse as we are in terms of the different cultural and educational levels that we certainly can't do it ourselves. We certainly appreciate the help of everyone else who participates in that. But recognize, I think, that we're not trying to be the end all and be all solution.

MR. LANG: Exactly. And that's why I'm here today to see what other opportunities that might avail themselves.

DR. SELIGMAN: Our next speaker is Dr. Ruth Day from Duke University.

DR. DAY: Good morning. The topic of my

talk is mandatory drug risk information, how much information is too much. First of all, I'd like to acknowledge the assistance of some wonderful research assistants and funding from AHRQ and FDA. The basic question is, how do people understand risk information? And the answer of course, is with difficulty.

Why is that? Well, there's a heavy information load, there's complex and technical information et cetera, but today I would like to focus on the problem of cognitive inaccessibility. Cognitive accessibility is the ease with which people can find, understand, remember and use drug information and hopefully in a safe and effective manner. Cognitive inaccessibility occurs whenever anyone has problems doing any of these things.

Research in my lab is on a variety of drug information sources from the TV ads and internet to hard copy and we're just focusing on one type of hard copy that we study today Medication Guides. The basic approach is first to do some cognitive analyses of the information sources. We obtain quantitative measures and calculate cognitive accessibility. We then develop enhanced displays on exactly the same information based on cognitive principles to make the

information more accessible. Then we perform cognitive experiments to test the effects on people's attention, comprehension, memory, problem solving, decision making, behavior and ultimately health outcomes.

Many cognitive principles underlie this research program and today we'll be focusing on the ones in red. So here are the project goals. We wanted to evaluate current versions of Medication Guides for their cognitive accessibility, especially for the benefits and risks, determine what is working well and what is not, design alternative representations to enhance cognitive accessibility, to recruit participants with relevant health status and test the effects of the original and enhanced representations on comprehension, memory and problem solving and to determine whether we can actually improve performance with various enhancements.

We had two documents in this study, two types of mandatory drug information. One was on isotretinoin and that was the Accutane Medication Guide. The other was on estrogens and for this we used the Premarin mandatory patient package insert and they are really equivalent types of documents. This morning you heard about the phone survey conducted by

the Duke CERTs and at the same time in the same funding arm, we were conducting the laboratory experiments over in my medical cognition lab. I will only be presenting results from the laboratory experiments where we met face-to-face with participants for an hour.

So let's now talk about load. When we think about the load of risk information we're giving people and we ask how much is too much, we often just think of information load, the number of words or the number of pages. Even more important though, is cognitive load. How much mental work has to take place in order for people to understand, remember and use the information? So let's look first of all at the information load for these two documents. The number of pages as you can see, ranged from something like almost five to almost seven and Accutane had more pages. And in terms of number of words, Accutane had more than twice the number of words as the Premarin document.

So therefore we see each, compare these two, for the Premarin there was a lighter information load and Accutane heavier. And so there's an obvious prediction that performance on Premarin should be better than on Accutane because there's less

information. All right, the participants, the Premarin participants were to be female, age 40 or older, interested in information about hormone replacement. There were no gender restrictions on the Accutane recruiting. They were just to be age 18 or older and interested in information about acne treatments.

There were 78 in each group for a total of 156. However, we conducted multiple experiments and obtained multiple measures with these people so the total number of observations was over 87,000. And here the actual ages of the participants, the Premarin participants were in their early fifties and the Accutane in their mid-twenties. And there's a breakdown by gender.

Basic methods went like this: they studied the information so we knew that they had adequate time to study the one document and then we tested them on all the content, using multiple tasks. Sample results, first of all, from both drugs. We did ask them about their general views about the document just as a preliminary warmup and we did this twice, both before we tested them and after we tested them, pre-test and post-test. One of the questions was, how easy was it to understand the information in the

leaflet and they gave us their responses on a one to five scale. And here you see what it was for understanding for the two drugs and as you can see, they thought it was pretty easy to understand but that dropped off after we actually tested them.

And when we asked them how easy would it be to remember the information in the leaflet, again you find that fall-off, that they thought it was moderately going to be easy to remember but then they were less convinced of that after we actually tested them and asked them things they didn't know. When we asked how helpful was the leaflet, we got very high scores, did not differ by drug or by pre or post-test. So in conclusion about the general views they had, people over-estimated how much they knew and understand -- stood after reading and then after testing they realized they knew less than they thought and then I'll show you in a moment they actually knew far less than that in many parts of it. Nevertheless, they still found the documents helpful.

All right, contraindications and predictions. For contraindications, we said, "You should not start taking this medicine if you have certain conditions. What are these conditions"? For precautions we said, "What did you tell your health

care provider before using this medicine", and we'll plot the results in terms of percent correct. First of all, for Premarin and those are kind of light bars, but you can see they're pretty low. Performance was below 20 percent on both contraindications and precautions. The same for Accutane and you will notice no difference between the two documents despite their differences in information load.

Side effects; many tasks here, one was the number estimation task. We simply asked people, "About how many side effects were on the leaflet", just to see if they had a ball park understanding. We're plotting the number that they estimated and before I show you the results, I would like to tell you that for Premarin there were 33 side effects throughout the leaflet, the Medication Guide, excuse me, the PPI, mandatory PPI, and for Accutane, there were 108. So there were over three times as many for Accutane and now here are the results.

They thought there were about the same number 12 to 14 side effects. We find this consistency from TV ads to CMI to Medication Guides to other studies we've done. People dramatically under-estimate the number of side effects and there was no difference in these two drugs independent of their

information load differences.

Other tasks I will show you now, one type of task called free report, we just say, "What were those side effects", and there are the results. They could not tell us many. Another task is what's called recognition. We gave people one side effect at a time and asked, "Was this on the leaflet", and they answered yes or no and there are the results. A couple things to note, the dashed red lines show chance level performance. Since it was a yes/no task, chance is 50/50 and they were up around 75 percent. So they knew more or it looked like they knew more as a function of how we asked. So the nature of the cognitive task is really important in terms of what we think people know.

Another point here is that there was no difference in overall percent correct between the two drugs despite their difference in information load on side effects. So the original prediction was the performance on Premarin should be much better than on Accutane was not supported. It was comparable in terms of the measures I presented so far. Let's focus now for the rest of the time just on Accutane the Medication Guide. Some of the key educational messages have to do -- well, we asked them, "What is

the most important information I should know about Accutane"? This is actually on the Medication Guide. And we asked them about this and there were a number of things about pregnancy. And when people reported, 96 percent knew and mentioned that you should not take it if you are pregnant, about half if you plan to get pregnant and no one mentioned that if you get pregnant while taking it, you should stop taking it and see your physician. So the question for that last one is why?

Well, if you go back to the original document, you'll see where the red arrow is there. It says you should not take Accutane and there is some information there, I'll now blow up and it does say all three of those things. However, we made an enhanced version of the document and we kept everything that's in the original Medication Guide, including the questions but we added titling and we made two time zones, before taking Accutane and while taking because a cognitive state could be in a different place after they're on something.

And you'll notice that the become pregnant is really functionally in the Medication Guide up in the before taking and it's okay to leave it there but I think that putting it down below in while taking,

would be a useful help. So we did make alternative representations for both of these drugs, Premarin and Accutane and again, just focusing on Accutane, I want to show you some sample pages.

First of all, here's the original Medication Guide, that's page 1, 2, 3, and so forth, and without trying to read that, you can see that all the pages look kind of similar. There's low visual distinctiveness. This does not encourage attention and other kinds of positive cognitive acts as much as more distinctive representations. Let's look now at the enhanced representation that we made. I'm not recommending this is the way to do it, but we were testing certain features.

For this we retained the exact same content as the original and then we added chunking. Chunking means first of all, put similar information together and then separate it spatially from other surrounding information. Coding means adding clear cues as to what this information is about, such as before taking and after taking and so forth or after you're on it, and then we did various enhancements on the side effects.

Here is the enhanced version for the Accutane Medication Guide, page 1, page 2. If you

just take -- if I take this page away, and just let you glimpse at this one quickly, even if you only spent five nanoseconds on it, you know, there's two topics, mental problems and about Accutane, so that you can get more at a glance. Let's do a head-to-head comparison, page 1 of the original versus the enhanced. Page 1, 2, 3, excuse me, so does it make a difference? All right, so we asked people about the leaflet sections. We said the leaflet is divided into several major sections. What are the titles of the sections? Why is this interesting? Well, do they know what's in the document? Would they look for information if needed and where would they look for it?

So in terms of the most important information shown on the screen, people didn't do very well when they studied the original representation. When they got our enhanced representation they all improved. So all of these circled portions say people did better in knowing this information. Final part of the study that I'll talk about today is the test, retest. Everything I've shown you so far is the original testing. We added a retest at the end. People studied again but we snipped away all the information except for the side effects and it was in

either the original or the enhanced version and then we tested them on the side effects. So I'm going to be calling these Test 1 and Test 2. It's the same people.

For Test 1, if they studied the original in terms of side effects percent correct report, they didn't get very much of the information, something like seven to eight percent and if we retested them, does it make a difference if they read it again? And the answer is, yes, they improve by 50 percent. But what happened if, on a random basis, they got the information in the enhanced version, did they improve? And the answer is yes, they improved by 300 percent, quite a difference.

So there are many results here that have been reported at professional meetings 2004, `05, et cetera, including a presentation to the FDA and other organizations and since then the new version of the Accutane Medication Guide has come out and I'm delighted to see that many of the things that we found in our study have been put to use. On the left is the one we use in the lab. On the right is the one that's out there now and you can see more chunking and other things going on. And so remember the lab original version had low visual distinctiveness and

now it's getting better as well as other features.

There are other findings but I'm almost out of time so I won't present them today. But I will present my conclusions. We can present information so it is there. It's physically present and I think the Medication Guides do a very good job of that. However, a lot of it is still functionally absent. If people cannot find, understand and remember the information and use it, what's the point? However, we can make the information more functionally useful and the more recent Medication Guides are doing a better job of that. How can we do this, by increasing cognitive accessibility. Thank you very much.

DR. SELIGMAN: Thank you, Dr. Day. Any questions, Jason Woo?

DR. WOO: Yes, again, thank you. I guess I'm just wondering what might be a better -- is there a standard to compare to, because even when we look at the enhanced version, we're still looking at only a 24 percent correctness? Please?

DR. DAY: I knew someone was going to say that. I thought it was going to come from Dr. Temple. Yes, there is one slide that I showed you where there's a dramatic increase of 300 percent but the absolute value is low. Since I've so much data here,

it was very difficult to decide what to pick out. I didn't show you the effects on the task which is just being able to estimate the number of risks that are on the Medication Guide. And that goes from very low, that dramatic under-estimation of thinking there's only seven, eight, nine, 12 or whatever it was, it goes up to 100 percent accuracy with the new representation, so that people are coming away knowing much better about how many side effects there are so that they could be aware of these and watch for them.

And so I should have included that slide, so that would be more encouraging. So it is -- you both want to see what is the baseline, what they're getting and then if you do an enhancement, what is the percent increase, but you're absolutely right, we have to see then what is the absolute value relative to the information there? Is it 100 percent correct, and there are some tasks where it goes up to 100 percent correct.

DR. SELIGMAN: Jeanine Best.

MS. BEST: Yes, Dr. Day, thank you, and we did much appreciate your comments on the Accutane Med Guide because we took them to heart when we reviewed and revised that Med Guide.

DR. DAY: It definitely shows, thank you.

MS. BEST: A comment I have is, we've had comments from numerous stakeholders to waive formatting requirements and this would get rid of bullets, white space. What would your reply to that be?

DR. DAY: I understand what drives that request, being able to print out the Medication Guides in the pharmacies is a formidable problem. Many still have dot matrix printers and so on. I think that's an issue that could be addressed by the pharmacy organizations. If I had my way, I would require every pharmacy to have a laser printer that could print things with formatting but I know that that's -- there's a lot of complication in doing that. I understand what drives that, but I think it's an absolutely horrible idea to get rid of the white space and so on.

Dr. Allen LaPointe was asked, "Well, why don't people read it, why don't people read these things more"? If it looks like it's a big block of print, people don't want to read it and say, "I'll read it later", and they set it aside and it disappears. It's got to be visually attractive so you can see something at a glance.

The Congressman this morning was talking

about if the first sentence is good, then you know to keep reading. Before you get to the first sentence, what does it look like? Okay, and if I just take a five-nanosecond glance, can I get anything out of it and you can see with the enhanced formats that do this spacing and so on, you can see what it's about and if you know what it's about, you would know, "I'd better save this and I'll come back to it later", or maybe I'll even read it now.

So I think that there are difficulties in getting these into the hands of everyone but it's not the way to go. You could get it physically into their hands and functionally they would get very little of the information.

MS. BEST: Thank you.

DR. SELIGMAN: Bob Temple?

DR. TEMPLE: Over the years Ruth, you've taught us a lot about this. I'm positive I've never heard about chunking till you taught us about it. So even asking this of you feels somewhat impertinent, but even the improved format with more space, more chunking, et cetera, looks pretty daunting still. Have you ever looked at the possibility that right at the beginning, you know, you'd put things like birth defects, mental problems and about five dark words and

then you'd get to read all the rest to draw attention? Is that silly?

DR. DAY: No, no, no, I've been playing with ideas about, say for the professional labeling, the up-front highlight section or something like that, and I've developed -- I have done experiments on about a dozen alternative representations for side effects and some of them worked really well. And I think that there can be an addition of what might be called a wall chart within it. Do what you're doing within the Medication Guide and then one of my representations that shows very clearly what they are and which are most serious and so forth and the ones that are more mild might go away with continued use and so on, and have it as an addendum and a tear-out sheet that a person could put on his or her wall to look at.

So I think that we need to have things that are more -- sometimes it's called graphic but what I mean is not a -- more spatially laid out, putting together the ones that are most serious and mild and so on. And I have some alternative representations for that. So I think this could be an addendum and then, of course, going back to how you print this out and all, I'm experimenting with ways to get this to happen within just regular word processing

systems and so forth and they can be objects. And the memorability and the understanding goes way up.

And by the way, I just conducted a study not only with consumers but with physicians at a professional organization and I have these physicians with permission and IRB approval and so forth, study the side effects for a drug that they regularly prescribe. I didn't tell them what it was, and then I test them in the same way that I do the consumers and they were just as bad at the tasks that I've shown you today about knowing about the side effects.

They did not get the complete label or Medication Guide or anything. They got one piece of paper and if it was the original way the side effects are usually shown, they dramatically under-estimated. They couldn't remember them, et cetera. On a random basis, half of them got one of my enhanced versions and they went way up. And so, it isn't just your knowledge and experience and expertise. It's the cognitive accessibility issue. We all are cognitive beings and our mental processes work in certain ways and if we present information that makes it hard for us to do it, everybody is going to be hurt.

DR. SELIGMAN: Ilisa Bernstein?

DR. BERNSTEIN: Thank you very much. This

morning on the first panel we heard a number of speakers saying that information should be presented by the doctor at the time the drug is prescribed. I'm just wondering in any of these research, you had a number of variables here that you looked at in terms of cognition and whether timing, where you looked at the timing and how that affected some of the things that you showed us.

DR. DAY: I think that would be great if they were given out in physicians' offices. I think physicians do not have the time to go through this. Maybe a staff person, but I think multiple times they must be given out in pharmacies because it is mandated that they be given every time the prescription is filled. It's not just a start-off document. And so that's the sense in which it's mandatory. So the more different places, but that wall chart that I was suggesting would be a nice way for a staff person to say you know, "The physician has recommended this for you and thinks it's good for you and you should know about the benefits and the side effects". And I've also worked on new representations for the benefits.

And so without trying to scare the patients only telling the risks say, "Here are the benefits" in the way that we know they will know and

understand and remember, and same for the side effects, "And so you should know about both". So I don't think there's only one place to do it. I think that in the physician's office that's a great additional place. I think that it has to be reiterated and in many places that they can find.

DR. SELIGMAN: Thank you, Dr. Day. One final question, Janet Norden?

MS. NORDEN: I'm going to go back to a little bit about formatting. Do you have any research about length in terms of how long is a good length for the patients? Your research showed that based on two different ones that had different lengths information load, people seemed to perform similarly on cognitive tasks, but we've heard a lot that people aren't going to read past one page or people aren't going to read past one paragraph and whether you had done any research on that.

DR. DAY: That's a really good question. It's not how many pages, it's what's on the pages and how it's provided. And we do have different studies which taken together show that there are some longer documents that people understand, remember better than the shorter ones because they were more cognitively accessible to begin with. So what we really need to

do is to take the same drug, and I'm trying to get some funding to do this, to take the same drug where you have longer and shorter versions of it and then higher and lower cognitive accessibility and then do a complete two-way head-to-head -- I should say hear-to-head-to-head-to-head.

DR. SELIGMAN: John Jenkins?

DR. JENKINS: Dr. Day, I notice in your enhanced version of the isotretinoin, one of the things you added was the star as well as a box. I'm wondering what are your thoughts about the use of more graphics in these medication guides. For example, if you're talking about you know, you shouldn't be pregnant while you're taking this drug, a graphic about avoiding pregnancy. We don't include graphics in these documents now. You included a star and a box to highlight some of these things. What do you think of that approach?

DR. DAY: Well, the star I'm a little bit embarrassed about in a way, you know, every time I look at it, but just something signaling. We did get enhanced comprehension and memory from doing that. I think more graphics would be helpful but I am worried about the printouts in the pharmacy. As for all of the ways to signal pregnancy, when I was doing a study

funded by the USP some years ago, they have their whole library of pictograms and so on and we found that people looked at those pictograms and sometimes had the right interpretation, sometimes had the wrong interpretation.

And curiously, one of the drugs in that study was also Premarin and there was a picture of a pregnant woman with a question mark over her head, and that was supposed to signal, "Are you pregnant, if so, you know, tell your doctor", or something of the sort. And the interpretations we got from people were don't take it, let's see, take it in order to get pregnant, she's wondering if she should tell her boyfriend, et cetera. So I think that we need to have all the research about pictograms before we do that.

But to get back to your question, do I think there should be more graphic elements, if we can solve the printout problems, absolutely, but they don't have to be cutesy pictures. There are spacial layout things with joining lines that helps people understand and absolutely that would be my strong recommendation if we can work it out but it's got to be the right kind of thing. Too many little graphics that aren't semantically sound can just confuse people.

DR. SELIGMAN: Thank you, Dr. Day. Our next speaker is Dr. Michael Wolf from Northwestern University.

DR. WOLF: Am I on now? Okay. I'd like to thank actually specifically Dr. Alistair Wood, one of my colleagues for giving me this great title, "Can we confuse patients less", and what I'm going to be talking about this morning is both hopefully not too redundant but even more of a 30,000 foot view from what has been presented by Dr. Allen LaPointe and Dr. Day. On behalf of both, at Northwestern University, our Health Literacy and Learning Program which is a joint venture of the Medical School and the School of Education's policy in their Learning and Cognitive Sciences Division, but also that research is done with my colleagues Dr. Ruth Parker, Will Shrank and Terry Davis in which a lot of our research over the past several years has been looking at health literacy concerns over drug labeling.

But also, I want to present some of the findings and recommendations from a recent report that I want to make the FDA more aware of from the American College of Physicians Foundation which is being reviewed by the Institute of Medicine Roundtable on Health Literacy later this fall and a publication that

could merge both the concerns of health literacy and medication safety together.

So the question we've been asking ourselves for the past few years is exactly where do patients get information about their prescription medications. We view this to be a horrible problem that in reality, there are very few good sources of information available to patients right now to help better inform them on how to safely use prescription medications. And just to think about it, we started kind of sketching out, where exactly do patients get information and how do Med Guides actually fit into this cycle.

So starting at the point of prescribing, you have the physician who is supposed to be communicating information, counseling patients on a newly prescribed medicine. And we know from countless studies as early as late summer of last fall, the Tarn study in Archives of Internal Medicine showing that patients are missing opportunities to adequately counsel patients on newly prescribed meds but also that was in Metley as well a year before in the Journal of the American Geriatric Society. The prescription pad information is clearly not information available to patients. That is a

communication between patients and providers. And then you have the pharmacist who also has been found in prior studies not to be communicating information orally to patients and prescription drug labels are not conducive for patients to understand. We've done countless studies as recent as last fall in the Annals of Internal Medicine showing that nearly half of patients could not comprehend seemingly simple dosage instructions on prescription bottles, as well as on the warning labels. Excuse me, my timing is a little bit fast here, but as well as the warning labels, which in December of 2005 we reported to the FDA in this very room, the problems that patients don't understand the warnings, anything that's attached to the bottle and Med Guides. In a moment, I'll talk about from some recent studies that we did last fall, how they fit in as a valuable resource for patients to understand some of the risks.

Then you get to the more informal sources, like direct to consumer advertising from PhRMA. You've got where patients might be actually relying -- some of the patients we've talked to in numerous studies have shown that that is a source of information for many of them. Websites that often times are very confusing and difficult for patients to

navigate. God forbid, patients go to a PDR to look at the prescriber insert information, where they have to navigate information like the chemical structure of the drug, and then you've got resources that may be very questionable on their reliability like family and friends as far as information about risks and warnings and safe use of medications. So we started to think about how patients can -- how can all of this be standardized and integrated into a valuable source of information for patients? How can we make sure that the information that's provided at the point of prescribing is equally conveyed at the point of dispensing of medications?

This has been an issue that has been raised in two reports by the Institute of Medicine in 2006, one the Preventing Medication Error in July 2006 and then in September, The Future of Drug Safety. And in these, they explicitly state that with over half a million adverse drug events occurring in outpatient settings, where one of the leading root causes of error, is the fact that patients misuse prescription drugs in how they administer the medication. We need to improve consumer directed information and this includes the importance of the provider/patient relationship as well.

So looking at Med Guides, we thought this is a valuable source because it's truly the only print resource for patients that can be viewed as regulated by the FDA that patients will receive, that will be guaranteed to have available to them taking not into account patient package inserts which are in the same line. We looked in April 2006 at the 40 current Med Guides and examined them through lexile analysis which is a rigorous readability reading difficulty form, similar to Flesch-Kincaid or PIMOs or PIKERs but we had found in prior studies using it as a quantitative co-variate in a data set that it actually is the most predictive variable for us to document patient comprehension and that was from the Journal of General Medicine Study.

We noted that the average reading difficulty was at a high school graduate level for all documents across the board. That ranged from the lowest few were from like the ninth or 10th grade all the way up through college graduate level. We also did a suitability assessment of materials which incorporates and analyzes documents based on the use of many of the cognitive and learning principles mentioned by Dr. Day that is done by Doak, Doak and Root and has been around since 1993. It's viewed as a

valuable health literacy resource, and found that rating these document, these Med Guides, by the Suitability Assessment of Materials or the SAM, around 22 criteria that ranged from literacy demand to use of graphics to cultural appropriateness, that we found none were deemed adequate for patients with limited literacy skills.

And in that study, we used three masters levels adult educators from three different states to independently review the materials and they were trained by the Suitability Assessment Materials method. The problems that we specifically targeted were that there were no content -- that there were inadequate content summaries, there was not a limited scope of information and the use of graphics was inappropriate.

In a second study -- I mean, in a second study as part of the same publication, we actually did a prospective survey of 251 patients at one public hospital clinic, in a primary care clinic. Twenty-three percent of these patients reported having never looked at Med Guides or any accompanying patient information materials coming from the pharmacy and we found that limited literacy skills, that being patients reading at a sixth grade level or below,

which represented over a third of the patients, that lower literate patients were less likely to review these materials.

There is a second study that is in press right now at Archives of Internal Medicine of which I'm a co-author. The first author, Dr. Will Shrank, at Brigham is not here today. The study involved administering four prescriptions filled at 96 pharmacies in four cities; Boston, Chicago, Los Angeles and Austin, and these prescriptions were given to these different pharmacies and filled and we documented what was basically returned to us. One prescription that required the distribution of Med Guides, that was a 200 milligram tablet ibuprofen, and it should be noted that none of the prescriptions were dispensed with the Med Guides at any of the pharmacies that we attended.

So when you introduced this hearing this morning, I know that these are problems that you're well aware of, that the issue of both distribution and also access at the point of information from the patient once they review the materials if they were to get the information, could they use that information to support their safe and effective use of the prescribed drug?

And I think listening to Dr. Day and having heard her speak before, I'm very well aware that there's clearly evidence out there that -- to improve how these materials are out there and actually, the FDA currently provides a lot of guidance already, I think I would say very explicit guidance to the industry as to how to develop these materials and correct me if I'm wrong, but I think the process is that in fact, the industry generates these materials following FDA guidelines and then gives them back to the FDA to review these materials and maybe in your comments you can tell me if that is incorrect.

It just does not seem clear through our assessment of the materials that were currently to date of April 2006 that these guidelines were being adhered to properly. That -- and part of the issue may also be that there's almost too much guidance. That there needs to be more standardization and I would -- I agree with some concerns that there's the possibility that if you provide such standard information your risk the possibility of them being ignored because patient expectations that this is something that always comes with the guides but I don't think that there's evidence to suggest that.

What we have shown or at least what we're

working towards right now is some of the basic principles from health literacy. Materials need to be simplified. NIH and many government institutions have been recommending six to eighth grade reading level. I think that is probably realistic. Limiting and layering the information, not doing away with information but providing a layering effect and a lot of these issues right here, cognitive chunking, the avoidance of distracters which we found more of an issue on prescription drug bottles where you have to navigate issues of pharmacy codes and logos and so forth with the patient friendly information.

Providing context and being more explicit, we're dealing with information to make instructions for patients, what are they supposed to do with this information? Is this a decision aid or is this just meant to inform consumers? I think it has to be explicit, what are they doing with this material? Why is it given? And again, using a patient schema, we found that a lot of times we've discovered that health education materials in general, not just for prescription medications, are not developed with the patient in mind and patients are -- in fact, we did a literature review for the Foundation for Medical Decision Making and found very few health education

materials state that they incorporated consumers in the development process. So I think that just is a very key common sense thing that needs to be brought into the picture.

The final few minutes that I have, I just wanted to bring about that we do have this White Paper that is now in its almost near availability as it's being reviewed by the Institute of Medicine, from the American College of Physicians Foundation which we have stakeholders from academia, Agency for Healthcare Research and Quality, the FDA, the Institute of Medicine, and Institute for Healthcare Improvement and the US Pharmacopeia are all on our advisory board at the moment and we've pieced together a paper draft that should be released this fall.

Some of the main objectives were to consolidate an understanding of the broad problem of inadequate patient medication information but also to identify a specific course of action to improve drug labeling in the United States. I'll hone on mostly the ones that I think are relevant for Med Guides, but again, this idea that there's a lack of universal standards and regulations for med labeling in general is viewed as a root cause of medication error. There is a problem and patients must be able to learn how to

use and recognize labels both on the container and on the accompanying medicines is one of the first key findings that there is a need for an evidenced based set of practices to guide label content and format and content should be minimized.

Standardized dosage usage instructions is another issue that is probably less pertinent here, but improving labeling beyond the container such as Med Guides and patient information leaflets addresses the concerns of how much information is a patient actually getting at the point of dispensing? Are they getting a Med Guide and a patient information leaflet? Is there a way to integrate these sources? Is there a way -- we've been talking about this idea of giving medication guides at the point of prescribing but not just at prescribing. Can there be a way to integrate it because there needs to be some synergy between what is happening at prescribing with the physician and what's happening, as far as counseling that might be happening at the point of dispensing where you really have healthcare professionals, who may have more training in pharmacology and having the ability to counsel patients and the desire to counsel patients at the point of dispensing than you do have at the point of prescribing.

We also need to address communication by physicians, nurses, pharmacists. This is the issue where there needs to be concern over what is orally communicated as well. Some of the things that we're talking about at Northwestern is the idea of using electronic medical record to provide some sort of content to be dispensed with a prescription for patients so the material -- like a Med Guide could be generated through an electronic medical record at the point of prescribing, so issues of e-prescribing may allow some information, maybe not the full Med Guide, but some of that content to happen right up front.

And again, researcher support is needed to move labeling efforts towards an integrated enhanced approach, so we can find that patients can have multiple access points for the information that might be contained on Med Guides. Thank you.

DR. SELIGMAN: Thank you, Dr. Wolf. Any questions from members of the panel either for Dr. Wolf or others?

DR. TEMPLE: I think my question is about something you called layering but I'm not sure. One of the things that comes up all the time is what level of language is going to be used and when you try to get things down to a sixth grade level you end up not

being able to describe a lot of the things you want to describe. It's always seemed at least possible to go in two phases though. That you present in a fairly simplified way a little introduction of the most important things which is then followed by more detail.

We, in fact, did that or something like that with the oral contraceptives 25 years ago when we first had labeling. It wasn't simple enough. It wasn't sixth grade, but it was an overview that was relatively simple, followed by something you needed a PhD to read. Does the fact that there's a lot of information following the early information, defeat the purpose of presenting it in a simplified way or is that something we should be thinking of, that is two layers?

I think -- I'm asking because I think the idea that you could get it all into that -- into sixth grade language is not going to be possible and it will be considered unacceptable because it will leave too much stuff out. But that doesn't mean you couldn't have a simpler version at the beginning.

DR. WOLF: Well, I agree. I mean, I think that first off, that you need -- I think one of the things we've been discussing is the possibility that

you need to provide a lot of the best points, the greatest hits kind of thing up front. So because there's no confirmation that patients will turn to the second page regardless, but if they get the information up well -- I mean, I like a lot of the elements that were in Dr. Day's form. We along with our research team, have been toying with a lot of different ideas for language as far as providing explicit versus less explicit information, for dosage instructions to warning information and I think given maybe a greatest hits, this is just a thought up front that making sure is very clear and concise that it's actionable information or information that can support the decision to take the medicine at that point. For a Med Guide, that could be up front and then you can provide more information because let's face it, there are some people who -- you know, and some people who will be very, very attuned to this and wanting everything. There are some patients who can't be bothered, but if they notice something that does catch their eye, it does seem simple, that warns them of an indication, something that they have to be careful of, maybe they'll read that but they're not going to go back to the later pages. I think that's one of the things we talk about with layering.

Layering can also be an issue where you may not be able to get a 10-page document stapled to a white paper bag at a pharmacy and so maybe you need to provide them access points where they can go, there's an 800 number to call. There's a website that they can go to, to get more detailed information and that may be another possibility. These are things that we're just talking about, but we don't have evidence to support that. In fact, patients would never use a 1-800 number or a web link if you took some of that information away. And again, we view Med Guides from the standpoint that they're also -- I appreciate the comment made by Dr. Woo that you know, these are -- it's a baseline.

It's also -- it's something that it's a good source, a print source but it's not -- should not be the only source for patients learning about some of these informations. It's a travesty that counseling is not happening at a greater rate and I think that's both for physicians and pharmacists. And I think we need to appreciate that system constraints or the environmental restraints on that and trying to figure out how we can get that information more into it, and that's why we're talking about electronic medical record and which is, you know, increasing in its use,

even at federally qualified heath centers.

DR. SELIGMAN: Jason Woo?

DR. WOO: Yes, again, thank you for the presentation. Sir, in reviewing the different objectives, I think in some of the discussion this morning about Med Guides almost being an alternative source of information. When we look at the level that we're trying to achieve in patient understanding, and integrating all those different needs of perhaps providing the physician -- having a source of information that the physician can provide or the pharmacist can provide, I'm wondering if there's some type of research that looks at what helps achieve the better balance of where Med Guides should fit as we begin to talk about how it forms as just part of the standard, I'm sorry, part of the information that's available to the patients.

Is there a concept of how Med Guides might best fit into that overall environment of patient education?

DR. WOLF: Well, I think that's a great question. I mean, one thing is what content is on a Med Guide? So if you think of it as, you know, an expansion of the limited real estate on a container label, that you'd want it -- that it would support how

patients use the information, then maybe that -- I mean, that might be one thing versus if it's information to support the decision making to actually taking the medicine. I thought some of the commentary this morning on the first panel was very -- you know, I mean, this is information that would have helped, you know, maybe support the decision for these patients and these families to actually decide whether or not they'd want to be on the medicine, and that would clearly then suggest the Med Guide would be at the point of prescribing. And if it's the latter, if it's information that you might refer to as, you know, warnings and auxiliary instructions for a drug that are also included then that information might want to be at both prescribing and dispensing. I don't know if that answers your question.

DR. WOO: I raise it just because I think there are a lot of good questions about how to best improve the patient understanding and helping gauge it to the patient, but as I mentioned earlier, we don't expect to be the only source of information in perhaps better understanding how folks use the Med Guides or what might be the most perfect -- now, obviously, I don't think we can get one straight answer across the board, but your comments help sort of put that into

perspective.

DR. WOLF: Just a comment earlier that was made by the panel in front of me is, and Dr. Day's research might support this, but we have a study that's coming out this fall -- we had 400 patients in Harlem, Chicago and in Shreveport, Louisiana that we interviewed and we came up with this idea of how patients approach prescription drug taking in general, which might provide some insight into why patients throw out the Med Guide or a patient information leaflet. And I think some of it is that medication use taking a medicine, taking a pill is viewed by patients as a very seemingly simple act and that the consequences of its misuse may not be adequately appreciated.

It's something that's done quickly and a lot of times, we've found medication mistakes and how patients would take a medicine were simply because they just didn't take the time to slow down and look at the materials. That they just quickly processed it and you get mistakes that -- you know, for instance, whether it be in the dosage instruction or recall of whether or not there was an auxiliary warning message or something on the bottle or in the supplementary materials, is just because they're just not attentive.

DR. SELIGMAN: Any further questions either for Dr. Wolf or for any other members of the panel? Just one final question, I guess from myself is, in looking at your data in the presentation, it seems like the simple act of receiving this information is in itself a major problem. We've spent a lot of time, of course, talking about cognitive accessibility and the ways to present the information but at least in your small study, the implication is that there's still a major problem with just the mere transmission of that piece of paper to the patient. Do you want to comment on that?

DR. WOLF: You know, I've spoken with a few in industry and I'm understanding a little bit more about some of the barriers. For instance, even with chain drug stores where you have -- if you do not have the Med Guide integrated into the system, that it becomes just an extra task for the pharmacist and that was probably one of the mistakes that we were hearing where sometimes just to be able to have to recall from the provider's side what drugs have a Med Guide attached to them if it's not something already linked into a pharmacy database and generated with the prescription labeling, then it's just one extra act. So I know some pharmacies are going ahead and starting

to try to integrate that so it will come out and it should eliminate a lot of those errors, but I don't know what happens with some of the smaller pharmacies if it remains to be kind of a second behavior that they have to pull the Med Guide. That probably is my only comment on it. I was alarmed when I saw that finding because that was not what we were targeting at and we were more looking at the variability in the dosage instructions and the format and content of the drug label, container label itself and then found for this one prescription that was the case.

DR. SELIGMAN: Thank you to all our panelists. Appreciate your input. We will reconvene at 1:00 o'clock this afternoon.

(Whereupon at 12:03 p.m. a luncheon recess was taken. until 1:04 p.m.)

DR. SELIGMAN: On the record. If members of the audience would find their seats, we'd like to begin this afternoon's session. I'd like to welcome you all back to the FDA's Part 15 hearing on Medication Guides.

This afternoon's panel we have Ms. Kim Witczak, Mrs. Vera Hassner Sharav, Mrs. Ellen Liversidge, Mrs. Diane Dorlester and Dr. Anthony Ng. And we will start with Ms. Kim Witczak.

MS. WITCZAK: Good afternoon. My name is Kim Witczak and I'm from Minneapolis, Minnesota. I'm here today on my own time and dime. I'm not affiliated with any political lobby or religious organization. In fact, this is my 30th trip out to Washington, D.C.

Unfortunately, I'm here today to tell you my husband's story and the consequences of what can happen when side effects are not communicated at the patient level. I have testified several times in front of the FDA for the need of antidepressant warnings direct to consumer advertising and per due for authorization. I have also personally met with FDA and HHS senior leadership. I am here once again today because the issue of communication to patients is paramount for the safe use of prescription drugs. But there is still much work to be done.

First, I would like to tell you my husband's story and the lessons it holds. My husband of nearly ten years, Tim, known to most as Woody, died of Zoloft-induced suicide in August of 2003. Woody had just started this dream job as Vice President of Sales with a start-up company a couple months prior and was having difficulty sleeping. So he went to his general physician and was given sample packs of Zoloft

with no med guide or any other suicide related risk information. Five weeks later, Woody hung himself in the rafters of our garage, dead at age 37. Woody wasn't depressed nor did he have a history of depression or any other mental illness.

Before continuing, I would like to make a comment about Woody getting samples of Zoloft from his general physician. After just a five minute conversation about his insomnia, Woody left with Zoloft samples, three weeks worth, in a brown paper bag that he told would help take the edge off so he could get some sleep.

Right, wrong or otherwise, Woody's story represents what's happening in the real world. The situation has become all too typical of prescribing habits of prescription drugs by general physicians. In fact, with approximately 70 percent of all antidepressants products being prescribed by general physicians, this is a worrisome situation. But it's also an opportunity for us to improve overall communication from the FDA to doctors and patients. Med guides, when done right, can help fill the void of unfortunately what's not happening in a five minute conversation in your doctor's office.

Isn't the main purpose of med guides to

communicate to the public the potential serious risks of certain drugs? Well, then it shouldn't be a promotional piece about disease education or the benefits. The drug companies have more than handled that. Since most of the drugs carry a black box warning, it should be front and centered and not watered down. Don't complicate this important piece of communication by adding politics, benefits or disease related info. Keep in mind, this is a guide that is to help the public after those decisions, that this is the right drug for you, has been made with your doctor and the drug has now been prescribed and is at home with you on your counter.

The language should be simple. The more you put in it, the less apt people are to read it. Make it easy to understand and written in consumer friendly language. For example, the side effect that is associated with the suicidality of antidepressant products is called acathisia. But what does acathisia mean to the average person? I think you need to define to the public what a side effect might look like in plain English language, for example, in Woody's case, couldn't sit still, having the feeling of being outside his body looking in, wanting to jump out of his skin.

Maybe the FDA could consider running med guides by a focus group represented by a cross section of consumers. I know in the ad business which I'm in, we run key messages by focus groups all the time to see what the net take-away from the consumer was and then compare it to what the goal of the piece was. It needs to be clear and concise.

Med guides shouldn't be biasd, but if they are, they should only bias toward public safety, patient safety. After all, there are already serious warnings on these drugs to necessitate the need for the med guide in the first place. In the case of the antidepressants, the current warnings are already confusing enough with the FDA first adding the black box warning to 18 and under and now recommending updating the label to 24 years old. And even the various associations like the APA are putting out their own patient med guides and it seems to further water down the seriousness of the FDA warnings.

Med guides should not look like drug company promotional pieces. If you read the med guides for antidepressants and compare them to Paxil's marketing materials, there's not that much difference. Safety should be the single most important priority before the benefit of the disease because these are

once again when you go home with the drug. The FDA's job is to protect the public once the drug is on the market.

I am sure over the next couple days as I've heard at other FDA hearings that I've attended you'll hear from various groups that say that these warnings and communications actually scare patients from seeking treatment. They claim that the data affect the suicide risks and have actually gone up since communicating the link of antidepressants and suicide. Just be cautious when you hear that.

I don't think the warnings scare people from getting treatment. I think it should make people think twice before ingesting as many of these drugs are over-prescribed in the first place. In Woody's case, through drug company and its advocacy organization promotion and marketing, he was actually brought into the system where they claim it would discourage people to be in. Well, I can guarantee we would liked to have had this information to be just closely monitored for the suicidality risk when Woody sat on our kitchen floor one week before he died with a vice around his head saying "Help me, Kim. Help me. I don't know what's happening. It's like my head's outside my body looking in."

Never once, did we question. We should have had the opportunity to know that this might have been drug induced. Instead, we sat there with no information and was told that it would take four to six weeks from the doctor for the medicine to kick in and to give it time.

We live in the day where information is instantaneous. Look at the internet. Information is available for everything at our fingertips. Access to this sort of safety information should be no different. In the advertising business, we are immediately able to get information out about our clients' products and services as soon as news hits. The drug companies can. The FDA should be no different.

The FDA needs to be able to get information out to the public immediately even if there's just cause for concern but nothing has been officially determined. This may take several years or in the case of antidepressants could take several months, but in antidepressants, it was several years before the first black box warning was ever issued despite sufficient evidence from the first FDA public hearing in 1991. How many people would have liked to have had this information. I know we would have.

Ideally, samples, because samples are handed out by the doctor first before the patient fills the prescription, the doctor's office should be the one that provide this guide to the patient. Maybe it's made mandatory that a patient or their caregiver signs for the med guide before getting samples.

This isn't a novel concept in other businesses. People sign things every day about risk tolerance. Look at the mutual fund and investment industry. You know the risks and sign stating that you've been told the risks. Everyone involved. Most importantly, the consumer is aware of the risks and it not just benefits the drug companies, but it benefits everybody.

The second touch point of communication to the consumer is the pharmacist. The pharmacist needs to make med guides available when prescriptions are picked up. It should be a hard copy, plus maybe the prescription label itself on the bottle has a line of copy that says there is a serious, potential risk and that it's more than just the common side effects and maybe it includes a website address that links to the FDA's page on med guides. This way regardless of the argument of whether the FDA delivered the med guides to the pharmacy or the pharmacy has enough physical

space to store all the med guides, the consumer doesn't pay the price for the lack of communication. It's called out in plain English to go and look for it.

In conclusion, I'd like to just reiterate how important communication is to the drug safety process and med guides are just one of the very important tools in communicating risks, what the science in plain language that the consumer can understand. An informed consumer is your best consumer. You have the ability to give people like Woody and I the chance. It's too late for our family, but I plead for you to think outside the box and make med guides work for the patient. Thank you.

DR. SELIGMAN: Thank you for your comments. We have a couple moments. Are there any questions or comments from members of the panel for Ms. Witczak. If not, then we'll move onto the next speaker. The next speaker is Mrs. Vera Hassner Sharav from the Alliance for Human Research Protection.

MRS. SHARAV: I'd like to just tell you that the Alliance for Human Research Protection empowers consumers with information they need to protect against exploitation by the health care industry and its paid promoters. These include

providers, government agencies and so-called advocates.

FDA regulatory mission is protecting the public health by assuring safety and efficacy of approved drugs. Now systematic reviews are the building blocks underlying evidence based practice. They focus attention on the strengths and limits on evidence from research studies about the effectiveness and safety of clinical intervention.

FDA is the only authorized agency with access to unpublished clinical trial results. Indeed, FDA's mission is to help the public get the accurate science-based information they need to use medicines and food to improve their health. Yet, a common thread to all drugs scandals including Rezulin, the antidepressants, Neurontin, Ketek, Vioxx, Zyprexa, Avandia is misrepresentation of treatment efficacy and failure to disclose life-threatening risks. Companies that concealed vital safety information from physicians and the public did so under the nose of the FDA officials who failed to use the agency's considerable authority to enforce the Food, Drug and Cosmetics Act.

In 1990, FDA Safety Officer, Dr. Graham, reported the data showed higher percentages of

suicidality among Prozac patients than others and there was large scale under-reporting of suicide evens. But FDA administrators trivialized the suicide risk, calling it a public relations problem. Indeed, FDA administrators including those present here today have repeatedly overruled safety officers' recommendations, denied the evidence and the drug-related casualties. Vioxx deaths were deemed not real deaths.

In 1986 and 2003, NASA officials overruled their safety engineers and sent the Challenger and Columbia, each carrying seven astronauts to their death. After these disasters, NASA underwent structural changes in its organizational culture and NASA managers acknowledged publicly that they were responsible. "We dropped the torch through our complacency, our arrogance, self-assurance and sheer stupidity. It is time to adjust our thinking."

But FDA CDER officials continue to demonstrate a diluted sense of infallibility. In 2006, Dr. Laughren interpreted a documented doubling suicide risk, 2.30 relative risk for adults under 25 and 2.29 relative risk for ages 45 to 54, as no treatment effect on suicidality.

In 1996, Dr. Paul Leber articulated safety

and efficacy standards. An FDA determination that a drug is safe for use is not a finding of fact but an opinion. Risks have not been reliably assessed. Too few patients are exposed to capture drug-induced phenomena. In other words, increased rates of clinical adverse events are deemed potential safety signals in need of further follow-up but unlikely to ever happen.

FDA seal "Proven Effective" refers only to a statistical association of a surrogate point of uncertain clinical benefit. Now Dr. Leber acknowledged that the risks associated with the use of a drug at the time of approval are invariably fewer than its actual risks because FDA safety standards fail to detect rare but severe risks.

This is a partial list of FDA approved legal drugs. Under its truncated safety efficacy standards, the approval of toxic drugs were advertised to consumers as proven safe and effect. These drugs undermine the mental and physical health of the American people. Now of note is that the percentage of drugs that were pulled from the market after PDUFA when the Agency came under industry control in 1992 increased from 1.56 percent between `89 and `91 to 5.34 percent between `97 and 2000. Now how many

catastrophic drug disasters will it take before FDA undergoes meaningful structural changes such as those recommended by the Institute of Medicine?

Zyprexa efficacy is only based on proof in principle. FDA's approval of the atypical antipsychotic drugs is merely the latest debacle that deserves investigation. The clinical efficacy of these drugs was and remains unsupported by scientific evidence while their hazards are clinically devastating. FDA approved Zyprexa despite Eli Lilly's inappropriate trials that failed to demonstrate efficacy. When the drug was aggressively promoted with false claims and unproven off-label uses, FDA failed to take action. Even after FDA officers found an alarming number of patients on Zyprexa contracted diabetes, CDER officials waited more than 2.5 years before issuing warnings.

Zyprexa's hazards and illegitimate promotion for off-label uses are documented in secret company documents. The content was disclosed in a series of front page articles in the *New York Times*. Prominent psychiatrists now acknowledge that their perception of antipsychotics' effectiveness was false, a result of marketing hype in the absence of empirical information. Now even after the black box warnings

about deaths were added, FDA required no med guides for antipsychotics and they still don't have them.

Did you sacrifice American lives to protect the profit margins of industry? In fact, does the FDA have a policy for providing vital drug safety information to consumers? If not, AHRP urges the FDA to immediately adopt a policy requiring all drugs that carry bold and/or black box warnings to be dispensed only when accompanied by a med guide. Med guide information should include a description of all the risks in plain English. Outcomes of all clinical trials including unpublished negative trials should be disclosed in med guides.

Now two major government studies, the CATIE and AHRQ, that's Agency for Health Care Research Quality, confirmed that antipsychotics failed to demonstrate any improvement over the old neuroleptics and that the adverse effect outcomes are staggering in their magnitude and extent. Risperdal, Zyprexa, Seroquel, Abilify are being used as chemical restraints in children and the very elderly, not as medicine.

The next several slides focus on Risperdal's adverse effects on children. The data comes from two eight week studies in children with

autism. The first in the *New England Journal* in 2002 includes only adverse effects five percent and over. Notice the staggering portion of children who suffered adverse events when exposed to Risperdal for only eight weeks compared to placebo. Now dyskinesia, tremor, muscle rigidity and EPS are symptoms of neurological brain damage. Weight gain, tachycardia, respiratory infection, flu-like symptoms, these signal a potential development for life-threatening chronic disease. The other study from 2004 again confirms that the major effect of the drug is somnolence, 72.5 percent of the children. The secondary hazardous effects are neurological, respiratory, cardiovascular and hormonal.

Neither the lack of evidence for therapeutic effectiveness nor indisputable evidence of its debilitating, life-shortening effects deterred FDA CDER officials. These officials engaged in a secret science review. There was no disclosure of the data for independent evaluation, no advisory committee, no public hearing.

The latest revised Risperdal label confirms that during an eight week period, a very high incidence of the most serious adverse effects occurred in children exposed to Risperdal. A sizable

proportion of children exposed to Risperdal, but not those on placebo showed signs of neurological brain damage. Just look at the numbers yourself. I'm sorry that you can't really see it. I can show it to you.

Now since marketing, adverse events reports include cerebrovascular accident, diabetes, hyperglycermia, mania, Parkinsons, pulmonary embolism, sudden death. By granted FDA's seal of approval for Risperdal use in children despite the evidence of the drug triggering multiple life-shortening chronic diseases, you have corrupted the meaning of safe and effect.

Deceptive marketing catapulted these drugs to blockbuster status, causing irreparable harm to tens of thousands of consumers. U.S. attorneys and state attorneys general in more than 26 states are investigating the makers of antipsychotics for illegal marketing practices that undermine public health and deplete public budgets.

The AHRQ review found that data about efficacy for bipolar depression are sparse and conflicting. In fact, they found that all the off-label uses except for OCD did not match out, did not justify the use of these drugs. Yet FDA approved Seroquel for the treatment of bipolar depression.

Especially alarming is the current surge in administrative approvals for expanded use of antipsychotics for children with no clinical justification. Bristol Myers announced that FDA granted priority review for its application to market Abilify for teenagers. Eli Lilly announced that it received conditional approval to market Zyprexa for adolescents. Johnson & Johnson's application to sell Risperdal to teens is pending.

Now Abilify was granted priority review on a basis of a single six week study in 302 children. The principal author, Dr. Robert Findling, has considered financial ties to all the major drug industries including Bristol Myers. He receives research grants, consultant fees and speaker fees. His study is therefore biased.

By approving expanded use for antipsychotics without empirical basis of benefit treatment and indisputable evidence of irreversible harm, you are contributing to a false perception that these toxic drugs are safe and effective. Faulty decisions such as this have resulted in drug-induced preventable diseases and deaths affecting hundreds of thousands of consumers. Those responsible should not continue to hold the reins of power.

DR. SELIGMAN: Thank you for your comments. Do you have any questions, Members of the Panel? Thank you very much. Our next speaker is Mrs. Ellen Liversidge, again from the Alliance for Human Research Protection.

MRS. LIVERSIDGE: Good afternoon. My name is Ellen Liversidge from the Alliance for Human Research Protection.

Before I give my testimony, I would like to say just a few words about my son, Rob, who died of profound hyperglycemia from the drug, Zyprexa, in October 2002 at the age of 39. He had been on the drug for two years, having been convinced by a Medicaid psychiatrist that it would be better than lithium which he had been on successfully for 12 years.

Rob was always gentle, brilliant and funny. He was tops in his class, went to a Quaker high school and scored 1500 on his college boards. He had a beautiful girlfriend, was an excellent writer and aced advanced placement music theory being the only student to take the course. He played excellent classical and improvisational jazz piano.

He attended Cornell, but he started to waiver after getting there. Though he instantly made

friends, he was having trouble getting up in the morning. Though he searched high and low for counseling or help on and off campus, he never found any. So he ended up coming back home for a year.

Upon his second return to Cornell, he showed the same problems and leaving at midterm, he headed out West. In retrospect, I realize he was manic, becoming psychotic. He became psychotic in California and was thrown into a hospital. We brought him back east with an attendant. I put him into what I thought was the best hospital in Philadelphia which turned out to be a mistake as he was misdiagnosed and mis-medicated for three years as schizophrenic. Finally, he was moved to a good hospital, went back to college in Philadelphia, went on lithium and he had a good stretch for nine years, returning to Cornell for his masters in city and regional planning.

After getting out and working for a year at the EPA, his life started to get a bit rocky and he ran out of money. Unfortunately, he had to sign up for Medicaid. Previously, he had always had competent care except for the first three years.

We were not, however, on the alert for this new drug which the doctor encouraged Rob to take. He was not doing that well on it, but it was painted

as he needed it and he couldn't go back to lithium. Had he done, so he would be alive today. This was an FDA approved drug with no risk/benefit information at all.

His death has hurt our family in many ways, but one thing it has done. It has made me determined to improve drug safety for the hundred thousand people who are currently dying of prescription drugs every year in this country. I will honor my son's memory, the memory of a wonderful person, and will continue to fight for justice. One of the key places to fight for justice is right here at the FDA. You are our last line of defense and you failed and I see you as continuing to fail today.

I have just received a publication that Kim mentioned called *ParentMedGuide.org* which mimics the title of the FDA med guides but which carries a basic message. This document came out right after the SSRI black box and the basic message is SSRI's are good.

Of the 14 parent med guide endorsers, four are speaking today or tomorrow. All four groups take money from the pharmaceutical industry. Speaking after me is the group called Mental Health America and they are one of the organizations that are supported

by PhRMA. Tomorrow's final panel includes the American Academy of Child and Adolescent Psychiatry, The American Psychiatric Association and CHADD for Attention Deficit. All are supported by the industry. I'm sure you can guess what the party line will be. Don't scare parents with warnings. Their children need these drugs. Ladies and gentlemen, I would have given my life for a warning to have saved my son.

And now to go on to the med guide that I wrote -- I thank you for the opportunity to speak about the med guide system. However, when I sat down to read over the material, I discovered there was no Zyprexa or a typical med guide. None at all. These are drugs, all of which have two black box warnings.

So with nothing else to do, I searched through the FDA website to see what was given to consumers at that location. Lo and behold, the warning that I had fought so hard for and that the FDA had required finally of Lilly and the other makers to put on their product as a black box warning in early 2004 had been watered down. It was not noted as a black box warning and it was not the first one on the list. The first one on the list had to do with dementia. The second one had to do with neuroleptic malignant syndromes, something that does not have a

black box warning. The third down was tardive dyskinesia, again does not have a black box warning and there at the end, number four, said diabetes, high blood sugar and diabetes, whereas the initial requirement of the pharmaceuticals that made for atypical were diabetes, hyperglycemia and death.

Why was this wording changed and whose decision was that? It was mentioned that people should get frequent blood glucose monitoring and that was a plus. But that was it. Following this fourth statement, there were several other risks listed in no particular order.

Thus, the current document on the FDA website about Zyprexa for patient information and presumably about the other atypicals is basically useless to a consumer. There is no mention, for example, that the CATIE study found Zyprexa to have the most lethal side effects. Isn't that something that a patient should probably know? There was no mention that use for bipolar disorder should be brief and should be for meaning. My son was on this drug for two years. He was not on it briefly until he fell into a coma and died. This document would not have been helpful to me.

There was no warning guide at all when he

was taking this medication, no warning from the doctor and quite frankly, in terms of consumer information, I can see little progress if this document represents what the FDA is sharing with families. There was no mention of hyperglycemia. It might have helped my son. He might have lived if we had known what hyperglycemia was. But it's not even written down.

I went back to ask myself why there would be no FDA med guide in 2007, all these years later for Zyprexa and that's when I came up with the title of this testimony, "Too Little Too Late."

Back in 2001 before my son was killed, the FDA got together with its equivalent agencies around the world. I don't know if it was a teleconference or what, but I read about it and one of the things they agreed to do was cooperate on drug safety. Well, as you might guess, this didn't happen. In the spring of 2002, both Japan and the U.K. required Lilly to put a warning on Zyprexa. So it wasn't as if the FDA didn't already know about this. At the end of 2001, Dr. Doraiswamy from Duke and an FDA researcher reviewed the Med Watch data and they found over 200 cases of diabetes and 23 deaths. Yet nothing was done. Nothing.

I finally found the answers to what

happened to my son since the doctors in the ICU had no idea on the Public Citizen website, not on the FDA website. If the FDA had followed its stated intentions of working with other countries, maybe my son might have survived. I found out about Med Watch, filled it out diligently since I figured the doctor wouldn't and I never heard a word back from Med Watch, another shock. I expected a phone call, a survey, consolation. I didn't know.

In the March of 2003 "Desperate to Save Others," seeing nothing else happening, I contacted the *Baltimore Sun* and asked them to do a story about this drug. As I was helping Tim, I also worked with Geeta Anand at the *Wall Street Journal* who did another large front page article on Zyprexa. All the FDA would say in this and subsequent stories was that they were looking into things with Zyprexa and maybe the other atypicals. It was clear to me that the FDA did not want to single out Zyprexa even though its lethal effects were the most blatant.

Finally, late in the year 2003, the agency required all makers of atypicals to place the same warning on their product, no differentiation as to which one was the most dangerous. I heard at the time that Lilly was very relieved not to have been singled

out, but meanwhile, they had gone ahead with their dementia campaign that I read about in the *New York Times*, afraid that their sales of Zyprexa would go down otherwise.

Since the warning not to use the atypicals for dementia which came out in 2005, the FDA has done nothing about this class of drugs. There has been no word about the Zyprexa's twenty-eight thousand plaintiff cases for diabetes, death and other chronic problems, nothing about the documents from Lilly that were revealed and have been subpoenaed by both the House and the Senate. Nothing.

And now we come to today, the day I had hoped to comment on the Zyprexa med guide, a document which does not exist. Do you think I am surprised by this after what I have observed over all these years, after hoping that the FDA would ban off-label use of these drugs particularly for children, finding out that the atypical makers are now going to try to give these drugs to adolescents? So I can only pray that the Waxman-Markey bill will be strong and will require the FDA to do what its job is supposed to be.

Before I take my marbles and go home, let me make a few general remarks about the med guides since I didn't have a particular one to talk about. I

reviewed a few of them, found them to be mainly verbose and confusing. The real dangers are often varied and in the middle of the text. There's extraneous text. Obviously, not all drugs with black box warning have a med guide. The risks that are black box warnings should be so noted and in order from greatest risk to least risk.

Words like hyperglycemia should be explain just like acathisia. In a better word, if we had known what hyperglycemia was, my son would probably be alive. I looked at the SSRI, the antidepressant med guide, and you have on there MAO inhibitors? Tricyclics? I thought it was supposed to be about the SSRIs. What would be the reason for that? Is it to confuse or to spread the blame to other less relevant drugs?

The med guide should be written by professional writers who will deliberate reading levels, second language learners, similar format and length. A five or six page document with some of these are maybe inappropriately long given the purpose of the med guides. The most serious and dangerous effects should be listed first.

I don't know the breakdown of death by dementia versus death from profound hyperglycemia for

Zyprexa, but there's no explanation or reason that the diabetes, hyperglycemia and death warnings should be diluted and placed lower on the list. If there is a reason, the overused word "transparency" should come into play. It should be explained that the dangers are listed in order, most dangerous down to least dangerous.

If the med guides are to be effective, no matter whether they are delivered by computer, paper or both, perhaps the bottle should have a small but prominently colored and shaped symbol to alert the customer that the drug has a particularly serious risk. As it stands now, this is not the case. The use of graphics to break up the text which was mentioned earlier as well as to inform a lower level reader should be considered. I thought, ironically, that maybe a skull and cross bones or a snake as in snake oil might be one of the symbols, but knowingly that this would not meet with approval, the use of effective graphics might be carefully thought through. Even a series of symbols denoting a level of risk might be helpful.

Although this is off topic to some degree, I urge the FDA once again to please review carefully the material that is on its website. I have to tell

you that it took me five minutes to find a Zyprexa patient information sheet. Hopefully, the FDA and its new advisory committee should engage a firm or an individual to organize the material in a better way.

Finally, I suggest that the med guides appear to be tainted by politics. What is the point of drug safety if it is not to save lives but rather to save sales? I would like to recommend that an outside agency be the entity to develop politics-free med guides and I hope to see a med guide for Zyprexa in the very near future. You have known of the risks of Zyprexa since 1991 at least. I submit that six years is long enough.

I would ask the FDA what could possibly be preventing this drug and the other atypicals from being on a med guide. I would ask why the FDA would not single out Zyprexa as the most dangerous in its class. If the purpose of med guides is truly to warn and to protect the public health, then we should do it. Because if the purpose is to look like something is being done but it really is not, the FDA should spend its money on a more worthy cause.

Both the CATIE study and the American Diabetes Association clearly stated that the risk is the highest with Zyprexa. How could the FDA not state

this clearly and how could the FDA not have acted on this drug knowing its dangers for at least six years? How many other drugs are hiding in the bushes known to be dangerous but due to politics not recognized as such by the FDA due to political situations and considerations? As I see it, in the FDA, the watch word unfortunately is too little too late. Thank you.

DR. SELIGMAN: Thank you for your comments. Are there any questions, members of the panel? Seeing no questions, let's move onto the next speaker please, Ms. Diane Dorlester from Mental Health America.

MS. DORLESTER: Hi. Good afternoon. My name is Diane Dorlester and I do work for Mental Health America. I'm here today, however, to share my personal story with you because I think it may be a surprise to the panelists that have gone before me that I overwhelming agree with the majority of the recommendations they have given you today. I and Mental Health America are equally concerned about the life-threatening risks of not giving complete and appropriate information to consumers.

I want to tell you about my story and how antidepressant medications saved my life and the outcome may have been different had I been given

information out of context. About ten years ago for no apparent reason, I spiraled into a depression. My life was going very well at the time. I'd achieved great personal success, socially, family. Everything in my life was going just great.

And for no reason, began over a course of months to feel increasingly depressed and also suffer a number of other symptoms like sleeplessness, like loss of appetite. I went to see a psychiatrist. I was also seeing a counselor and they had urged me to consider taking antidepressant medications to help alleviate some of these symptoms as one part of my course of treatment, and I resisted that. I resisted that for about a year and a part of why I resisted that was because of the stigma associated with taking antidepressant medications. I felt that it was almost weakness or a personal failing on my own part if I had to resort to taking medications.

Eventually and fortunately, my doctor was able to persuade me to, while it was my choice, begin taking a course of SSRIs and for about a year, it helped. I was feeling a little better. But then at about a year, my depression spiraled and became much, much worse. I was not able to function. I had to take an extended leave of absence from my job. I

spent days on end not able to get out of bed. I couldn't eat. I dropped down to 92 pounds. I woke up most days with just a gut-wrenching pain that the only other time in my life I have felt that level of pain was when I had personally lost a loved one and many, many days that pain never went away. It was with me all day long.

My doctor was trying to persuade me, give me options, to switch to a different SSRI. He explained that it's hard to tell ahead of time what drugs might be most effective with what people and that we did have other treatment options with different medications and despite how devastated I felt and how unfunctional I was in just about every aspect of my life at that time, I was terrified that switching medications might, in fact, make me worse.

And, in fact, during that time, I spent many days if I got out of bed in the car in the garage with the car running, turning the engine off and on. I did not want to die, but I knew I could not continue living the way I was living and I was terrified of what might happen despite the fact that I didn't think I could get any lower, but what might happen if I changed medications.

Well, eventually, I did agree to try a new

SSRI and about three weeks later, I literally woke up one day and felt that a light switch had been switched on and I was alive again. It wasn't that my symptoms were completely gone. I continue to take medications today and at times I do have some symptoms or setbacks. But I've learned how to look for early warning signs and how to with my doctor in a consultative role decide what at any given time an appropriate level of medication might be for me.

And as well, my medications do have side effects and at times when for a prolonged period of time I'm feeling well and doing well, I talk to my doctor and let him know with his blessing that I want to lower my dosage because I do want to minimize some of these side effects. So we do that and I monitor for awhile and I'm in frequent consultation with him to see how things are going and sometimes they stay at very low doses for periods of time and sometimes they don't.

I think you have a real opportunity today to craft the medication guide program in way that provides balanced information so that those who need to be aware as well as everybody should be aware of potential side effects. That the other side of these medications can be lifesaving is equally important. I

think when you communicate the risks and especially the life-threatening risks that there's a way to do it, that also makes suggestions about ways to mitigate those risks, early warning signs to detect those risks.

You know, there are 19 million people in this country with depression and at any one time, half of them do not seek treatment at all of any kind. We know that there are 30,000 suicides a year, which exceeds the homicide rate in this country by well over 50 percent. You have a responsibility to do everything you can to save every life through the communication that you put out, through the resources that you have. But I would be very concerned, if in an effort to address the very understandable concerns that the other panelists have about warning signs and risks, that it was done in a way that dissuaded other people from taking these medications.

It is something that is very difficult to make a choice to do. Again, in my case, I was even irrationally so, but terrified of what would happen if I changed medications and, had I had one additional piece of information or something that in my mind was another reason not to make that lifesaving switch, there's no doubt in my mind that within weeks I would

have left the car running.

Now, I want to acknowledge that I support a lot of what you've heard today. I think the ideas that Ms. Witczak had put forward about doing focus groups with consumers to find out effective ways to balance is excellent. I think there have been a lot of other good suggestions that you should really take to heart. But again, I urge you to do that in a way that gives all people who may benefit as well as those who may not the accurate information, the science-based information, that they need.

I do also, in closing, want to thank you for letting me speak to you today. I do feel it's necessary to offer a point of clarification that my role at Mental Health America, my being here today and, in fact, all of the work I do on a daily basis working with consumers of mental health services is in no way funded by pharmaceutical money. My entire department, my entire program, is not at all funded by that money. So I am here speaking again on my behalf, on the behalf of the 19 million others who may benefit from antidepressants and I urge you to consider that in making any decisions. Thank you very much.

DR. SELIGMAN: Thank you for your comments. Any questions from members of the panel? Seeing no

questions, we'll move onto the final panelists in this session, Dr. Anthony Ng, also from the Mental Health America.

DR. NG: Good afternoon. My name is Anthony Ng. I'm a psychiatrist practicing in Washington, D.C. and a board member of Mental Health America, the national mental health consumer organization for which I am speaking on behalf of today. I first want to express my appreciation for being given the opportunity to present here today and also to hear the important testimonies of the other speakers.

Mental Health America, formerly known as the National Mental Health Association, is the country's leading nonprofit dedicated to helping all people live mentally healthier lives. With more than 320 affiliates nationwide, we represent a growing movement of Americans who promote mental wellness for the health and well-being of the entire nation. The century old organization is committed to supporting the development of a healthcare system that is based on being responsive to consumer values, the latest research and clinician expertise.

Mental Health America commends the Food and Drug Administration for its efforts to ensure the

safety of medications and we feel the FDA Medication Guide Program offers the agency considerable opportunities to educate consumers on potential risks of medications. We also believe that the medication guides should be used as a tool to support the decision making partnership between the consumer and the provider.

In the field of mental health, scientific research demonstrate that treatment are highly individualized. Therefore, medication guides should encourage consumers to review the health history and treatment goals with the physician to weigh the risk and benefits of any medication choices. Consumer preferences on potential side effects and physician expertise are critical components of the decision making equation. While one individual may weigh the side effects and benefits of the medication with his or her provider and decide that it's an appropriate treatment option, another may find the side effects too risky given all the factors such as other health problems or the medications impact on day-to-day functioning.

We recognize the right of consumers to learn about side effects. We strongly encourage consumers and families to take an active role with the

provider to inquire and discuss such issues. We encourage the development of tools for promoting the dialogue between patients and the physicians.

Consumers and physicians have a unique and essential perspective on treatment. The FDA must involve these key stakeholders in a meaningful way in the development of the medication guides. Indeed, all health care decision makers must be given a more meaningful inclusion of consumers. Such consumer engagement might include participation of focus groups as mentioned by the other speakers at the development stage of the medication guide. Ensuring consumer health literacy and numeracy is an important challenge to making guides more accessible and relevant to individuals. In addition, medication information must be put into the perspective to relative risk for the individual. Blanket warnings taken out of context could likely dissuade people from seeking or receiving treatment from which they could benefit.

It's important for the FDA to communicate both the risks and benefits of the medication. Warnings that fail to provide balanced information by focusing exclusively on risk could lead to consumer's discontinuation of treatment and to misinterpretation by the consumer which could subsequently lead to

incomplete dialogues between consumers and providers. It's important for the medication guides to include key questions or points that lead to dialogue and decision-making between consumer and family members and the physician. Actions related to risks and side effects, crafting treatment goals and developing prompts to help a consumer articulate what they experience and the mental and physical health may and can inform decisions about which treatment might work best.

When communicating information about drugs' risks, the FDA and/or other federal agencies must also offer suggestions on mitigating that risk. For example, just as the FDA shares information about treatments' potential risks, it must promote treatment of wellness through educating Americans about the health problems, the benefits available from treatments and the risks associated with no treatment at all or it must work seamlessly with another federal agency to do so.

And finally, Mental Health America believes that the FDA has an obligation to monitor the impact of its actions on public health and access to care and to revisit specific decisions when, and if, warranted by subsequent data and research findings.

For example, the data that was released by the Centers for Disease Control and Prevention concluded that there was an increase in the suicide by 18 percent from 2003 to 2004 for individuals under age 20. We believe this increase coincides with regulatory action by the FDA that led to a black box warning on prescription packages cautioning the antidepressants could cause suicidal behavior in children. Other research links certain antidepressants with decreasing suicide rates. We must, therefore, wonder if the FDA's actions and the subsequent decrease in access to these antidepressants, in fact, have caused an increase in suicide.

It's for these reasons that we believe the FDA has an obligation to monitor the impact of the actions. We believe that if implemented these recommendations represent a significant step towards improving health outcomes, especially for the millions of Americans living with mental illness in our country.

Thank you again for this opportunity to present the views of Mental Health America.

DR. SELIGMAN: Thank you for your comments. Do we have any questions from the members of the panel? Yes, Dr. Temple.

DR. TEMPLE: Obviously, we've been somewhat concerned about the effect of the antidepressant warning. But I'm curious about what you think an appropriate remedy would be. The black box never says don't use the drugs. It says, "Watch out. Make sure you talk to the patient. Be aware that suicidality can occur early in treatment." It would be hard to say you don't want to tell people that and yet it's probably true that some physicians and patients are scared off by that. Do you have a remedy?

DR. NG: I'm glad you actually brought that as an example because actually I had a patient come to me the other day for the same concern. Because again, I explained to them the risk of using a certain medication and because of even -- It was just a warning. It wasn't a contraindication. It was just a warning which another physician picked up and told the patient "Stop taking this medicine" and the patient got all scared and called me about it and said, "What should I do?"

First, I praised him for calling me first of all to discuss this because that's what's important because I wouldn't want to see him go four weeks and then come back. I think the important thing is really

to educate providers what is meant to have warnings. I think certainly FDA and other agencies have done education on that, but I think it's still not hitting a lot of the providers in terms of what those different labels mean whether a black box or contraindications or just moderate warnings or whatever it is. So certainly, that's an important piece.

Again, I think putting in a relative risk for individuals may help them in terms of identifying how risky the particular side effects could be. Often times, I may try to use analogies with my patients and families. If there's a risk that may be very low but it's still just given as a risk, I kind of give them the equation like as if you were riding a car which people could relate to there's a risk that you could get into car accidents so often. But then taking this medication does not have the same risk based on what we know. So that kind of stuff may help the patient understand what that risk is and they say, "Okay. So it's not as bad." Or they could say, "Hey I don't want to take that risk" and that's fine.

DR. SELIGMAN: Dr. Woo.

DR. WOO: Again, I'd like to thank all the panelists for the presentations and I think that the

breadth of the concerns that are expressed represent some of the things that we have to deal with every day.

I do want to go to a point that Ms. Witczak had made about the role that medication guides play and perhaps either Dr. Ng or Ms. Dorlester could respond. The medication guides themselves are attached to the prescription that's given to the patient, so to the extent that it's information after a decision has been made to, at least, start or consider starting the medication. To what extent does that seem to represent a barrier to patients getting good information or good dialogue with their providers on the risks and benefits of taking the medications?

MS. DORLESTER: I'm sorry. Could you just clarify the risk? You're saying if -- Clarify your question please.

DR. WOO: Sure. What I heard was the concern expressed that information put out by the FDA or with FDA approval can be an hindrance to patients getting good care and having a good dialogue with their physicians on what treatment options are available. Ms. Witczak pointed out that the medication guides come after a decision has been made.

MS. DORLESTER: Right.

DR. WOO: And to that extent, do they represent a barrier?

MS. DORLESTER: Yes. I think it's interesting and with all respect, the decision has been made at that point by the treating physician and by the consumer to go fill the prescription. The consumer still has a choice to make when they are at home reading risks and benefits.

I do think it could be a potential barrier for an individual that was similar to being in my situation or someone else who's maybe just still on the fence and when they left the doctor's office they felt that's what the doctor wants me to do. That's what I should just do and I'm going to go home and take this and then again, they may, in fact, read the pamphlet before taking the pill and if the information is only about risks, it is not put in context similar to what Dr. Ng was saying, a relative level of risk. I do think that could be a barrier.

Now I think some of the suggestions again you've heard today about putting risks in a relative order of the most severe or the most devastating outcome, those may well be good things to consider. But again, I think at any point it could, in fact, represent a hindrance. But it's an opportunity just

for the patient to get more information to talk about with their family, with their doctor, to decide to begin taking or continue taking any medication.

DR. SELIGMAN: Do any of the other panelists wish to comment? Dr. Jenkins.

DR. JENKINS: This is in some ways a follow-up to what Dr. Woo was asking. We heard some recommendations earlier today that the medication guide should really be handed out to the physician, excuse me, handed out to the patient by the physician. As Dr. Woo suggested, maybe handing it out by the pharmacy is not the right point. So I'm interested in any perspectives from those on the panel about whether that's the more appropriate local for communicating the information that's in the medication guide.

We do have some risk management programs in place for certain drugs, for example Accutane, where there's a lot of information that has to be conveyed by the physician at the time of writing the prescription or making the treatment decision. That's not the model that the medication guide was envisioned when it was created. But I'm interested in any feedback on is that a more appropriate point in the cycle where the information should be conveyed.

DR. SELIGMAN: Anyone?

MRS. SHARAV: Can I take a crack at it?

DR. SELIGMAN: Yes. Mrs. Sharav and then Ms. Witczak.

MRS. SHARAV: There is an issue. Now in an ideal world where the physician, in fact, sought the patient's best interest rather than as we read in today's *New York Times* that even oncologists are prescribing drugs not for the patient's interest but for their cash profits, we have to really take all of that into consideration as to what, in fact. How many patients really have the ideal relationship with a physician that they can trust?

What happens, that some of our people tell us, is that they need a distance sometimes from a doctor who is pushing something too hard. They need to think on their own and what the pharmacist is giving them, they're not going to ask all that many questions of pharmacists. They will then go back to the doctor and ask them once they are more educated. I think they're not in the greatest spot if the doctor is really aggressively pushing for something.

DR. SELIGMAN: Ms. Witczak, did you care to comment?

MS. WITCZAK: Sure. In my husband's case, he was given a sample pack, three-week sample pack, at

the doctor level in a brown paper bag with no information. So I actually believe that that's how a majority of these drugs especially coming from the GPs are being handed out. I think it should come from the doctors. I'm not even opposed to having somebody sign it. I'd rather. I don't mind signing something. I don't know what all the issues around that is.

Then I think as follow-up, it would be at the pharmacy whether it's something on there that says that there's a med guide or I know you'll probably hear from the other side saying we don't have physical room. But I think that's a second point. I think that would have been an opportunity from when Woody got his prescription that there would have been some information there. But I think the real point is people go home with these as samples and we can't forget about the GPs are a majority of how these people are getting the drugs.

DR. SELIGMAN: Dr. Ng.

DR. NG: I would agree also with the speaker that I think the doctors should have the access to medication guides partly because I think that one, if you shift that to the pharmacists there's a tendency over time that people may neglect to do that. I think this is a way to safeguard some of

that. Now certainly, I think pharmacists should reinforce that and then bring it back to the attention of the doctor to say "Hey, you didn't mention this. What happened" kind of thing like that.

I think the important question is also just before you even get to medication guide, I think doctors need to know is there medication involvement. Is medication needed? I mean often times I think patients in the dialogue that happens where patients could have big expectations or visa versa with the doctor that the medication is a panacea to solve all your symptoms and it isn't and what I often tell patients is the fact that it's part of everything else that we're going to be doing for you including the psychosocial interventions and whatsoever. So the medication piece, it's up to you.

Now there are risks and go from there and then if the patient says, "You know what? It's bothering me so much. I need to have medicine," then you work with them about the next level, the different types available and get the guides.

DR. SELIGMAN: Yes. Ms. Liversidge.

MRS. LIVERSIDGE: I think Kim and I both mentioned just an idea knowing that the pharmacists are concerned about the clutter that they have of med

guides sitting around, that the actual bottle have a symbol of some sort and a phone number, an 800 number, where the customer could make a contact. That would be another way that the information could be obtained by the consumer off the internet. Not everybody has an internet, but you could get some people that way.

DR. SELIGMAN: Yes. Dr. Jenkins.

DR. JENKINS: I'd like to follow up with one other question for Dr. Ng, if you could describe your experience. Are your patients actually receiving the medication guide when you prescribe antidepressants and they go to the pharmacy. Do you have any knowledge of how often your patients are actually getting the medication guide? And then also can you provide any experience of how they communicate back with you if they do get the medication guide?

DR. NG: Well, I work in two settings. I work in the psychiatric emergency room as well as a clinic. So it's like different settings and the relationship is a little bit different. With the clinic per se, those are patients often that I would encounter who are basically connected to the clinic somehow. So there's a relationship and therefore after I see them, I have time and I would actually present them with the information about the medication

and sometimes a medication guide is used and sometimes it isn't probably just because we may not have access to it at the clinic. But we try and give them supplemental information from sources that we can identify that may provide that for them.

And then what I do is also recommend that they come back and have this periodic discussion with me, not just a one time thing. "You know, I'm going to see you next visit, be it a week, two weeks or whatever it is. Let's go over this." And every six months, I try to go over this again and then also when you have a dosing change and a medication change and also advise the therapist that this is happening and if that's the case, if there's a concern, because sometimes they may not tell me everything because of trust or comfortability issue and then they may go to the therapist and say, "Hey, Doc gave me this medicine. It seems to work but it's causing me to do this." Then I encourage them to let me know so I can quickly fix that or address it with a patient and that's usually how I try to resolve some of those issues and sometimes they just say, "I don't like it and it's not doing anything for me." We have to respect that and change it.

The other situation where I work is the

emergency room where it's a lot tougher because my patients are often sicker. I mean, sometimes like if it's family members included, I can provide some sort of medication education. It may not be the medication guide per se, but medication education to family members or some patients who can appreciate and understand the risks and benefits of the medication. While others, it's because they are so acutely ill at the time, it may very hard to relate that information and all you can just encourage is that once they move onto different level care, they encourage that the doctors re-examen and ask them again, discuss these issues about risks and benefits.

So it's different for every patient. But I try to do my best at least if I can to educate them about the medication risks and benefits.

DR. SELIGMAN: Yes. Toni Piazza-Hepp.

DR. PIAZZA-HEPP: Yes. Some of the panelists expressed that our current medication guides may not be the most understandable or the most useful to them. Have you seen other sources of medication information that you actually find more useful that you would like us to look at?

MRS. LIVERSIDGE: Well, I've used material from *Public Citizen*, Best Pills/Worst Pills which is

clear. It may not be totally thorough as I might like, but it's also succinct and it's all in one place, alphabetical order.

DR. SELIGMAN: Others who wish to comment? Yes.

MRS. SHARAV: I wanted to just a little bit underscore and maybe get your views. What's the purpose of the black box? How is the black box a warning? How is a drug that has a black box warning different from a drug that doesn't? I mean you must have criteria for deciding on a black box warning and I think that that criteria having seen some of the process, having gone through with you some of the process for quite a few years with the SSRIs at least, there's a great deal of resistance to having that kind of a warning. So then finally after all the evidence supports having black box warnings, why would you want to diffuse, cut down, the sharpness of the warning? These drugs are different from other medicines and particularly, particularly with those drugs such as the SSRIs and the antipsychotics where you really do not have evidence, scientific evidence of efficacy.

DR. SELIGMAN: I'm not sure I can tell you everything about why something does or doesn't get a black box, but it has to do with the nature of the

thing that you're warning people about, its seriousness. Usually it has to be something serious and we are particularly inclined to do it when there's something you can do about it. So that for the antidepressants -- By the way, it's not the SSRIs. The black box is about antidepressants more generally than that and we have data on a number of antidepressants that are not SSRIs and I think our bias is that it has to do with being an antidepressant.

But in any event, in that case, the particular focus of the black box was to remind people that the period after starting an antidepressant is a treacherous time. It's treacherous in the first place because those are people who have come to get an antidepressant for a reason and it's treacherous because the rate of suicidal thinking and behavior is approximately doubled, at least in children and adolescents and it turns out young adults. So that was what people needed to be told and the med guide has the same emphasis.

In no sense was this an intent. This isn't one of those ones where we particularly wanted to say, "Maybe you don't want to use it." That is something obviously that the physician and patient

need to decided also. But this was about taking steps to keep something bad from happening and so that you could know about it.

DR. TEMPLE: I'm not sure what you mean by weakening the black box. We've recently altered the box to say that the risk applies to people who are older. But, in fact, the data show that people over 24 don't have that increase in suicidality. A pretty good analysis. The same one, the same kind of analysis that we did for the younger people and we also added the thought that suicide happens in people who are depressed and you should know that.

And that's at least partly, it's not secret, because we're a little worried that people are being scared off more than they should. We didn't try to tell people that seriously depressed people shouldn't be treated. We tried to tell them that people should be watched. So there's a constant balance and I'm sure people will disagree or agree on the particular balance that we choose.

I should mention that the antipsychotics don't have a med guide. Maybe they could for certain purposes. But the first warning was that we wanted to tell people that when they're used in people who are demented for whom they're not indicated, there's a lot

of evidence that there's an increased mortality first with the atypicals and you probably know there's a recent report out of some Canadian databases that suggest the older ones do the same thing. So that's advice primarily to physicians. Whether a demented person could make use of a med guide could be debated, but that's directed at physicians which is why you have a warning but not a med guide. Short course. Sorry.

Yes. Ms. Dorlester.

MS. DORLESTER: Yes. I would like to respond to the question that was asked of the panel. I think it is something to gather all the resources you can to make sure that these materials are culturally and linguistically competent for all different populations who may need them that I don't have a specific recommendation for that, but I imagine some of your fellow government entities such as SAMHSA, they do that all the time with their publications. They may well be able to refer to some good sources for that.

DR. SELIGMAN: Yes. Dr. Ng.

DR. NG: I just want to comment on what Dr. Temple had mentioned. I think the other issue is not scaring patients and consumer families, but

scaring off the doctors, too. I think that's what -- And I guess that's the level of education which I think probably we need to do, you know, have a better understanding of the different warning criteria from FDA. But I think most of the doctors when you hear them say "Black box. I can't even discuss that with the patient because God knows what happens if something bad happens. That means I'm going to be sued." No. I mean medically, legally, that's another issue. But again, that's how they interpret the black box label and I think that's -- Like I said, we need a lot more education on the provider piece as well as the consumer piece what these labels actually mean.

MS. WITCZAK: I'd like to make a comment on the black box --

DR. SELIGMAN: Ms. Witczak.

MS. WITCZAK: -- when you're saying putting in that suicide is an inherent risk of depression. That seems to water down what the black box warning is supposed to be about which is something to be cautiously aware of. If that's part of it -- I mean, the black box warning, Woody, he got it for insomnia. He had no history of it. So to put that -- It almost seems to like go -- It kind of conflicts and confuses the consumer and then putting that it might

for the older people have a beneficial effect to deal with helping depression.

There are so many mixed messages in there and I think the whole idea of a black box warning is it's a serious enough risk that you have deemed serious enough that the public should be aware of it. And in terms of doctors right now, my opinion is doctors are being educated by the drug companies who are definitely downplaying that risk. I mean, even looking at some of the med guides that they use your word "med guides" that these other associations put out, they even conflict with what you guys are saying.

So it's like no wonder why the consumer is out here going "What's real?" And I don't feel like -- You know, I found a lot of our information on the internet and that's the reality and that doesn't seem that should be and coming from other countries. We should be the ones leading it.

DR. SELIGMAN: Yes. Dr. Woo.

DR. WOO: I have another question just for this panel as a whole in sort of contrast to what was said earlier, actually from the other panels. I actually heard an interest in having more information in the medication guides including clinical trials, a broader understanding of the risks and benefits and to

the extent, do you think that would actually make the message more difficult? Because what we heard earlier today was the concern that the messages are already not well understood.

MRS. SHARAV: No. I think that we ought to really have more respect for consumers. Consumers are a very large population. They include educated and less educated and people do generally want to know what does the science say and this is getting lost in a sense. This is one of my major criticisms of FDA's procedure is that a lot of the real science is really not there and it's not being conducted in a scientific way and the science evidence somehow gets buried.

Now, for example, when we take a study like the CATIE study, that's a thunderbolt. It completely shatters current practice in schizophrenia because these drugs were touted to be far safer, more effective. They were the end-all and be-all and they are the blockbusters. How is it that drugs that get approved for only schizophrenia and short-term bipolar? That's each one percent of the population. That's a small percent. How did they get to be blockbusters? $10 billion sellers. It's because people are being prescribed those drugs who don't have schizophrenia and who don't have bipolar. There's

such a push because of the profit margin.

So the med guide needs to inform consumers who the drugs are really approved for. Remember the consumer never saw the label. The label is addressed to doctors and what we're saying really is that the med guide now that we're finally talking about consumers should contain straightforward information that is science-based, that is relevant. Some of it is going to be better than what you now have in the label.

I don't think that we need to be afraid of providing accurate information to consumers. What we need to be afraid of is the advertising, the misleading, false advertising that is selling some of your most lethal drugs that I don't really know that you're so happy about having them become blockbusters. But advertising works and we're looking to those med guides to be the countervailing, accurate information that consumers can rely on finally.

DR. SELIGMAN: Yes. Dr. Ng.

DR. NG: I think certainly information about risk and all the different things that talk about those risk should be somewhat identified. Whether putting it on a medication guide, all of it together, one packet, I don't know whether it's

feasible in the sense of whether it would hold the attention span of anyone who reads that.

Again, just being a lay consumer watching TV is my attention span in watching commercials is like whatever that 30 seconds is. If you have a longer commercial, I start losing it and drifting off and most people find the same thing about guides or information sheets. They need to know the pertinent things about what they're looking at, risk/benefits.

Now certainly, I think it is important for FDA to provide them with a roadmap. If you want to know more about these risks, this is where you should go. Give them that information, phone number or whatever it is to call so they can get more information that can be more tailored to their specific request. But I think just blanket putting everything in, you are basically at the end of the road but you don't give any directions where to go at the end of the road. So I think that's a point.

MS. WITCZAK: Can I?

DR. SELIGMAN: Yes. Ms. Witczak.

MS. WITCZAK: I was going to say. I like to think of it like this. I mean, what *Consumer Reports* does is a great way, the Good, the Bad, the Ugly and it just lays it out really simple for

consumers and whether it's bad tests that maybe it wasn't effective, put it in there, the Good, the Bad, the Ugly. I think *Consumer Report* is a really good idea.

MS. DORLESTER: I'd just like to add to that. I think two things. I want to add to what Dr. Ng was saying that I think however it's done, the most important thing is that it facilitates and encourages a communication between the patient, their family if it's relevant and the doctor and any other science-based objective resources that they might be able to go to get more information. I'll leave it at that. Thank you.

DR. SELIGMAN: Yes. Dr. Temple.

DR. TEMPLE: Yes. I must say my aspiration in this is a lot like Mrs. Sharav. I would like everybody to be very well informed about the things they're putting into their mouths so that they know all about them and all that stuff. But we hear from other people who have testified that the aspiration to do that gets in the way of communicating anything and I guess I'd be interested in a little more discussion about how one is supposed to manage that.

I mean, you can't put -- We've never put

all the results of the clinical trials into a med guide and I think that most people would tell us that if we did, everybody would doze off. We do say when something isn't known to be effective so the box and the med guides all say that the antidepressants haven't been mostly shown to work in children. So they all say that. I'm not sure how much effect that has, but they all say that.

But do you have, do any of you have more views about that? How much can we put in and still continue to be useful or does it really have to be telegraphic and how do you feel about that?

MRS. LIVERSIDGE: I think it partly depends on are we talking about a couple of pieces of paper or are you talking about a couple of pieces of paper and another thing that you can access. If it's a couple of pieces of paper, though I agree with Vera to see a real live clinical trial would make me very happy since I've never seen a Zyprexa clinical trial, only heard about it.

I don't know if you can fit that on a couple of pieces of paper and accomplish everything else that you want to accomplish taking into account reading levels, taking into account the Good, the Bad and the Ugly. This one gets the gold star and you

might have to get into an issue of ranking.

DR. TEMPLE: Yes.

MRS. LIVERSIDGE: I don't know if you can do that.

DR. TEMPLE: Well, it's a longer discussion, but it turns out that rankings are very subjective so that expert societies can do that. But when we, who would have to have actual data with comparisons and stuff like that have to do it, we often find that it's very hard to confirm your impressions. So it's a very hard area for us.

MRS. LIVERSIDGE: I was thinking of ranking like MedWatch death as a factor.

DR. TEMPLE: Oh, which adverse effect is more important you mean?

MRS. LIVERSIDGE: Yes.

DR. TEMPLE: Well, right. You could try to do -- We do try to do that.

MRS. LIVERSIDGE: I mean, which one of these is safer than the other one. I have no idea in the SSRIs.

DR. TEMPLE: If there's really good data, we --

MRS. LIVERSIDGE: I do have a good idea in the atypicals. I know which one is the least safe,

the one that killed my son. It would be nice to see that right there on the paper, "look out for this one," the most.

MS. DORLESTER: I think --

DR. SELIGMAN: Ms. Dorlester, go ahead.

MS. DORLESTER: I think this gets to you have a tough challenge in this because I think part of what needs to be effectively communicated is how individualized treatment is and I would be very concerned about kind of a -- You know, there should be as much information for these and other resources that we can possibly get out there to consumers and their families. I'd be very concerned about something that said this is better. This is definitely going to have a harmful effect. This is definitely going to have a negative effect because it does kind of -- It doesn't acknowledge how individualized treatment is.

I again think it just does need to be that balance and that encouragement to the extent it can be to have the discussions with the treating physician to have suggestions about what factors might increase if the science is available on this to certain negative side effects. You know, are there lifestyle issues? Are there issues of heredity issues that might make certain individuals more prone to a certain benefit or

side effect? But again, I'd be a little concerned about making blanket statements about one treatment being specifically better for everybody than another.

MRS. LIVERSIDGE: That's not the issue.

DR. SELIGMAN: One last comment, Dr. Ng. And then we'll --

DR. NG: I just want to comment that before I guess any changes are made, I think one thing needs to -- Again, this may be outside the purview of this panel, but one thing that needs to be understood is I don't think doctors or providers are using FDA like they're supposed to use. I mean, it's just my feeling because again, honestly, we don't go through medical education talking about FDA. You go through residency. They don't talk to you, "Hey, this is what FDA means" and "this is what they do." So we come out just doing whatever our residents told us to do or attendings told us to do and, "Yes, there is a black box warning which means that you get sued. You do this." And that's how we practice. That's a lot of people unfortunately fall into that category.

I think maybe an important thing could be like -- I'm just throwing this out as an example. Maybe during relicensing or recertification for DEA numbers or licensing that people are required to take

a short course in how to address these warning labels, what it means to discuss warning labels, what black box actually means and I think then you at least get the awareness that people say, "Hey, this is supposed to help you talk to your patients and discussion what is the best option," not as a deterrent for care or any other thing. I think that would be helpful to many doctors who basically need some guidance sometimes in terms of relating some of these risks to the patients so that a good decision and partnership can be made.

DR. SELIGMAN: Thank you very much and thank you for this excellent panel, both for your presentations and willingness to answer questions. We'll now take a 15 minute break and reconvene shortly after 2:45 p.m. Off the record.

(Whereupon, the foregoing matter went off the record at 2:36 p.m. and went back on the record at 2:52 p.m.)

DR. SELIGMAN: On the record. If everyone will have a seat, I'd like to begin the next panel please. On the final panel of today, we have Mr. Tom Lawlor from the Walgreen Company, Mr. Thomas Flottman from the Pharmaceutical Printed Literature Association, Dr. John Coster from the National

Association of Chain Drug Stores, Mr. Steve Heidenthal from CVS/CareMark and Ms. Cathy Russos and Mr. Ben Stone from Pharmex. Our first speaker is Mr. Tom Lawlor from the Walgreen Company. Mr. Lawlor.

MR. LAWLOR: Good afternoon, members of CDER and FDA. My name is Tom Lawlor. I am a registered pharmacist and my current position is Director of Quality Assurance for the Walgreen Company. Thank you for the opportunity to express the Walgreen perspective on the issues, the requirements and the challenges that medication guides present to us in daily pharmacy practice and to suggest some practical solutions that will help retail pharmacy overcome these challenges and improve the entire med guide program.

As background, today at Walgreen's we operate over 5700 retail pharmacies in 48 states and in Puerto Rico, making us one of the nation's largest retail pharmacy chains serving over four million customers and filling almost 1.6 million prescriptions every day.

The purpose of a medication guide is to ensure that patients get all the information they need in order to make information decisions about the drugs they take. Med guides focus solely on providing

patients with information on the specific risks of taking a particular medication since a prescription drug only becomes a candidate for a med guide, if the FDA determines that the drug in question poses a serious public health concern, which can best be addressed by providing additional information about its safe and effective use. More specifically, a med guide will be required if it is determined that this additional information will help prevent serious adverse effects. Or, if use of the drug has serious risks relative to benefits that patients should be made aware of because such information could affect the patient's decision to use or not to use the product. A medication guide will also be required if the drug product is one that is important to health and patient adherence to critical directions is crucial to the drug's effectiveness.

Admittedly, this is all part of the effort to respond to public pressures for additional information on certain medications that have been associated with high profile risk incidence and which is supposed to benefit patients in their health care management. Please know that no pharmacist is opposed to providing information to patients and every pharmacist takes patient safety very seriously.

Everyone's goal in the practice of pharmacy is to help the patient and improve his or her quality of life. As pharmacists, we believe that the information patients receive about their medication should be balanced in terms of presenting the risks as well as the benefits of prescription drugs.

Patients should not be unnecessarily frightened about their prescriptions lest they fail to comply with their medication regimen. Alternatively, patients need to understand the risks associated with taking medications in such a way that they can make the best informed decisions for themselves about starting or continuing therapy.

Currently, FDA mandates a medication guide for almost 60 different drugs including three major drug classes covering hundreds of prescription drug entities. The largest classes of drugs requiring med guides are the non-steroidal anti-inflammatory drugs or NSAIDs, the antidepressants and now the drugs used to treat attention deficit hyperactivity disorder or ADHD. In raw numbers, medication guides are currently required for over 1600 individual NDC numbers. Many of these drugs are very popular and highly utilized.

Literally, millions and millions of prescriptions that are dispensed every day require the

additional dispensing of a med guide. It is estimated that eight to nine percent of all the prescriptions dispensed in the United States require the addition of a med guide and currently there are over four billion retail prescriptions filled each year. Medication guides are not short documents. They typically average 3.5 pages and can range anywhere from two pages to 30 pages in length.

To compound this problem by law, med guides are not the only written drug information that retail pharmacists have to provide to patients. To meet the current action plan for the provision of useful prescription medication information, a community pharmacist often has to print two to three additional sheets of consumer medication information or CMI to hand to the patient. If the patient is also receiving a mandatory medication guide with their prescription which as stated averages three pages in length, that would mean at least five sheets of patient risk/benefit information dispensed with one prescription.

Very important to pharmacists as we concern ourselves with educating our patients especially the new patients that come to our stores because of Medicare Part D, for example, is that each

manufacturer who ships a drug product for which a med guide is required is responsible for providing these med guides in sufficient numbers so pharmacies have enough of them to dispense to patients. If a drug requires a medication guide, we are currently required to dispense one with every filling whether it is a new prescription or one that the patient has refilled many, many times. Is this really necessary?

The proposed regulation for med guides back in 1995 stated that they would be provided to patients with all new prescriptions and that one be made available upon request for subsequent refills. However, the final ruling stated that a medication guide must be dispensed with every filling, new and refill, of that particular prescription. We believe that this is not necessary because it provides no new or additional benefit to patients.

Manufacturers are using different methods for distributing med guides including, but not limited to, providing tear-off pads shipped directly to pharmacies, attaching the guide to the product container, including it as part of the prescribing information or package insert, providing a toll-free number for stores to call to order hard copy medication guides or the manufacturer may choose to

simply provide us the means to produce the medication guide in sufficient numbers. The means to produce may be in the form of a PDF file on a website which has to be downloaded and then printed in our stores. Our challenge here is not only having access to the internet in a retail setting and knowing where and how to locate the PDF, but also the cost of printing, the cost of paper and toner and hardware plus the time involved.

The point is there is no adequate and consistent directive that manufacturers must follow in order to ensure that they provide med guides to pharmacies. And, in fact, there is no enforcement to ensure that they even do provide them. The phrase "provision in sufficient quantities" is a very subjective one that has unfortunately equated to mean "in short supply" for pharmacies, thus making our compliance very difficult. In addition, all of these supply options have a cost associated with them and either the manufacturer incurs the cost or the pharmacy incurs the cost, but eventually, the consumer incurs the cost which subsequently will increase the overall cost of health care.

Even though there are very specific legal requirements outlined in the Code of Federal

Regulations that govern both the content and format of medication guides, manufacturers are not adhering to these requirements. In fact, there are as many formats, styles and font sizes being used as there are the drug makers' methods of distribution.

A logical solution to the provision and distribution problems as well as the format variations is to allow stores to electronically print these guides in their stores based on the NDC number of the drug being filled. This accomplishes two things. It guarantees compliance and availability and it guarantees a consistent format for the patient.

At Walgreen's and in retail pharmacy overall, we are concerned that this preponderance of paper which patients currently receive with their prescriptions is being driven by FDA guidance for CMI and by FDA mandates for medication guides and it is not serving its intended purpose of risk/benefit communication, mainly because it is excessive. Retail pharmacy is very concerned that the current medication guide program is providing patients with too much written information about their prescriptions causing many patients to not read any of it.

We believe one viable, long-term consideration is to combine both the CMI and the med

guide content to create a single manufacturer developed document no more than two pages long that could be distributed by the pharmacy data vendors. And we really feel that emailing a medication guide to a patient if we had their email address is another very viable, practical and cost conscious solution.

No evidence exists that demonstrates that medication guides enhance a patient's understanding of drug risks and very little information exists in the literature anyway regarding the effectiveness of this type of a risk communication tool. We all may feel better that we are covering our bases by giving patients all this paper. However, if it does little to reduce adverse events or if the volume of paper reduces compliance because patients don't read it and therefore don't know how to take their medication or if they do read it and don't take the drug because they become frightened, we are defeating our intended purpose and sadly doing no good for the patient at all.

Let's look at what patients are telling us. This time last year Epsell's Public Affairs conducted two focus groups among daily prescription drug users to elicit public reaction to two of the types of the current written drug information, namely,

the CMI and the medication guides, in order to determine patient acceptance. Specific respondents' comments on med guides felt that the information imparted through the medication guide because of its predominant risk content would be more useful if presented to them and discussed with them by their doctor in his or her office before the prescription was written. Patients felt that this would be the best time and place to decide if they do or do not want to accept that potential risk and fill that particular prescription.

In fact, the general response to the information presented in the med guides was one of alarm. Comments included, "A doctor can't just hand this type of a prescription to you and assume their job is done." Patients wanted counseling from their doctor as well as their pharmacist. Providing the med guide after the prescription is filled is not in the patient's best interest. Finally, most of the consumers did not even realize that the med guide content was not comprehensive and only included risk rather than risk and benefit information.

In summary then, to aid retail pharmacy and to improve on the intent of the original medication guide program, several recommendations

become obvious. Namely, we have to reduce the volume of paper we are currently required to give patients. The CMI and the med guide has to become one shorter document at a sixth to eighth grade reading level comprised of both benefit and risk information that can be given to patients. Medication guides should only be dispensed when a prescription is filled as a new script, not with all subsequent fillings. Where entire classes of drugs are involved, a single med guide for all drugs in the class should be made available to pharmacies and a single method of distribution must be decided on, mandated and enforced by FDA, the cost of which should not be born entirely by retail pharmacy.

Pharmacies must be allowed to electronically print these medication guides in their store based on the NDC number of the drug to ensure compliance as well as consistency and there must be cost sharing with manufacturers here as well. In this era of phenomenal technology, emailing a medication guide to a patient if we had their email address is certainly a viable as well as a cost effective means to provide useful drug information to patients.

Lastly, the medication guide program as a long-term goal should seriously consider how to make

prescribers responsible for providing this information to their patients before they actually write the prescription. Patients and their doctors have a relationship and patients choose to go to their doctor for a reason. Pharmacy and pharmacist need to further that relationship through counseling, education, providing answers and guidance, including educational material like the medication guides in order to help and inform that patient.

Thank you very much to the members of FDA and CDER for the opportunity to address the med guide program.

DR. SELIGMAN: Thank you. Are there any questions from the panel? Yes. Go ahead. Toni Piazza-Hepp.

DR. PIAZZA-HEPP: Thank you. Regarding your comment of combining the CMI document and the med guide document, has Walgreen's come up with any kind of prototypes of that possible format?

MR. LAWLOR: We worked with NACDS to come up with possible formats.

DR. SELIGMAN: Please speak into the microphone. Sorry.

MR. LAWLOR: Sorry.

DR. SELIGMAN: That's okay.

MR. LAWLOR: We've worked through NACDS through the pharmacy organization to come up with a sample document.

DR. PIAZZA-HEPP: Have you shared that with the FDA to date? I'm just not aware if you have.

MR. LAWLOR: I believe John has it with him.

DR. PIAZZA-HEPP: Okay.

MR. LAWLOR: We have in the past, actually a couple years ago, when we presented and we've also had good interaction with our data vendor who has helped along the same lines.

DR. PIAZZA-HEPP: Okay. Thanks.

DR. SELIGMAN: Ilisa Bernstein.

DR. BERNSTEIN: Thank you. Thank you very much for sharing those thoughts from Walgreen's. I have two questions, kind of separate. One is one of the things that I've been hearing lately is there are some pharmacists out there that don't even know what a medication guide is let alone what their responsibility is and obligation to dispense it. I'm just wondering what kind of educational programs that Walgreen's may have to educate pharmacists about not only medication guides, but also CMI and that whole host of information, whatever they hand out.

MR. LAWLOR: The training that -- in our specific case, the training that we put our pharmacists through when they're hired addresses all of that. Plus on our intranet we have retraining materials as well as the policy, what a medication guide is, what the -- we call it patient education monograph is and we post all the med guides on our intranet.

DR. SELIGMAN: John -- did you have another question?

DR. BERNSTEIN: Yes, one more question.

DR. SELIGMAN: Please.

DR. BERNSTEIN: Thank you. You had mentioned that Walgreen has gotten a PDF and when we wrote those medication guide rules many years ago we envisioned that the means would be a PDF. But back then, people weren't connected as much as they were in networking with the networks and I'm just wondering. How often do you get PDFs and do you actually incorporate them somehow into the workflow so that you can use that PDF or is it not useful?

MR. LAWLOR: No. We do get from the manufacturers periodically especially if we find out after the fact that a med guide has been required. Through our purchasing department, we'll contact the

manufacturer and demand that they send us a PDF, and yes, we do post all of your from your website site FDA medication guides. We post them all on our intranet. So it is incorporated in our workflow. The pharmacist can just -- as they're filling a prescription based on the NDC number, we will print the med guide.

DR. SELIGMAN: Dr. Jenkins.

DR. JENKINS: Yes. Following up on the question about the combined CMI and medication guide, I think I heard you suggest that that would be provided by the sponsor which I think would mean that you're advocating for FDA approved patient labeling for all drugs. Is that a fair summary of what you're recommending?

MR. LAWLOR: Yes, Doctor.

DR. JENKINS: Because that's kind of taking us back to the future. FDA suggested that many years ago and we ended up with the CMI approach that we're under right now. So you're now suggesting that there should be FDA approved patient labeling for all drugs.

MR. LAWLOR: I think in a perfect world if the data vendors that currently write the CMI worked with sponsors, manufacturers and FDA to come up with a

combined document that was acceptable of the proper length and readability that that would be the best of both worlds.

DR. SELIGMAN: Yes. One last question. Ms. Golson.

MS. GOLSON: Yes. I was wondering. How do you alert your pharmacists that a new medication guide is available? How do you let them all know?

MR. LAWLOR: Quite honestly, we pop up a red box warning that says "medication guide required" right when they're verifying a prescription before bagging it. So we try to make sure that we keep on top of that corporately and push that data down to the stores.

DR. SELIGMAN: Our next speaker is Mr. Thomas Flottman from the Pharmaceutical Printed Literature Association and while you're taking the podium, is there someone from the FDA who can check to see whether Dr. Temple is still in-house or whether he's been kidnaped.

(Laughter.)

DR. SELIGMAN: Thank you. Shirley Murphy is checking. Thanks, Shirley. Was that Diane? I'm sorry. I couldn't tell. It is Diane. Thank you. Please. Go ahead.

MR. FLOTTMAN: Thank you. My name is Tom Flottman and I am with the Pharmaceutical Printed Literature Association. The PPLA is a nonprofit trade association that promotes the role of printed literature and the proper dispensing and consumption of medicine.

DR. WOO: Excuse me. Could I ask you to raise your mike?

MR. FLOTTMAN: Sure.

DR. WOO: I'm having a hard time hearing. Thank you.

DR. SELIGMAN: Everyone's been too short and now you're too tall.

MR. FLOTTMAN: Is that better?

DR. WOO: That's better.

MR. FLOTTMAN: In addition to my responsibilities with the PPLA, I am the CEO of Flottman Company. Flottman Company is an 86 year old, third generation, family run company and we provide printed literature to the pharmaceutical industry.

Thirty-five years ago, our company was one of the first to provide this product to the pharmaceutical industry. Over the 35 years, I've seen many changes, both operational and in advances in technology in both the pharmaceutical manufacturing

industry and at the pharmacy.

What has remained unchanged, however, is the benefits of ready access to reliable, consistent information about the drug products that printed literature provides. We provide this to all parties in the health care chain, the professional, the manufacturer, and most importantly to our conversation today, the consumer.

Medication guides are an important component of this effort and the PPLA has supported this from the beginning. We have repeatedly commended the FDA for requiring med guides for products of special concerns. Examples discussed today were the antidepressants and the NSAID classification of drugs. I and the PPLA feel that the consumer has the right to know and the FDA has properly exercised its authority to require that this information be dispensed with the prescription package.

A few years ago at the behest of the FDA, the Wisconsin College of Pharmacy did a study where it evaluated the medical information disseminated at the pharmacy and gave it a very poor grade. This is especially disconcerting when special concerns and warnings make it so critical.

Last year, in 2006, the Institute of

Medicine wrote a report entitled "Preventing Medication Errors." This report specifically directs consumers, and I quote, "to ask for written information about the medication and ensure that providers give or direct the consumer to written information about the drug appropriate to their level of literacy when filling the prescription." My point here is in light of the importance of written information coupled with the record of the information developed at the pharmacy level, we and others urge that consumers receive pharmaceutical manufacturer produced, FDA approved written information with prescription drugs.

We understand pharmacy concerns regarding their ability and their efforts involved to dispense this information and the potential liability in sanctions coupled with that. However, in light of information discussed earlier today and I'm referring to a comparison between the Northwestern study and the Duke study, where the Duke study referred to printed information that was with the package that came from the manufacturer compared to the Northwestern study where it didn't and the record of the consumer getting the information was almost universally received in the Duke example, but almost never received in the

Northwestern example.

In addition, these concerns we feel are mitigated by recent innovations indicating an ease to dispense this information with the package from the manufacturer. I brought some examples of some literature printed by my company which combines the professional prescribing information with the med guide. On one side of the literature is the professional information. On the other side is the med guide. This is contained in the package and it's ready for dispensing.

In addition to this example, my company is currently producing piggyback literature where numerous patient information, med guides, either one, are combined in a deck of a certain number appropriate to the package that comes from the pharmaceutical industry. I could go on with other examples. So the FDA has also encouraged unit of use packaging with the NSAID class of drugs as well as the antidepressants. However, this has not been universally produced in this manner to date.

In summation, we feel that med guides are important risk minimization tools that provide critical information to the consumer and that the FDA is to be commended for requiring their use and is to

be encouraged to require it at their discretion in the future. Because of their benefit to the consumer, they should not be swayed by pharmacy concerns about dispensing the information because for the most part, they are no longer valid.

Thank you for your time allotted to me today to discuss this matter and for your attention to this important issue.

DR. SELIGMAN: Thank you for your comments. Questions or comments, members of the panel? Dr. Woo.

DR. WOO: Thank you again, Mr. Flottman. One question about when pharmacies aren't receiving or don't have adequate med guides, as a third party company, do you get many complaints about that or do those complaints get directed to the manufacturer and how do you address them when you do receive them?

MR. FLOTTMAN: You're talking about non receipt of information from the pharmacy?

DR. WOO: As Mr. Lawlor was saying, one of the concerns being that some of the pharmacies don't receive adequate med guides or that there's -- at any rate, if they don't receive an adequate number to dispense with the prescriptions that they're giving, do they return complaints about that to you? Do you

receive those and how do you address them?

MR. FLOTTMAN: Those complaints, I'm not aware of those complaints, but they would not be directed to my company or to someone in my position. In situations where we have printed med guides, it is done in a manner that an appropriate amount of med guides are available with the package. This is a package design, package engineering issue and it's something that can be resolved. It should be resolved and discussed at that stage of development.

DR. SELIGMAN: Ilisa Bernstein.

DR. BERNSTEIN: So the information that you held up, is that something that a manufacturer would put in as a unit of use or do you then sell that to somewhere in the supply chain to dispense?

MR. FLOTTMAN: This was produced at the behest of a pharmaceutical manufacturer and this literature is inserted into the package that they ship to the supply chain through the supply chain.

DR. BERNSTEIN: So would it be that they would put in the case and then it goes to the wholesaler, if it goes to a wholesaler, or wherever it goes afterwards or is it unit of use, actually individually packaged?

MR. FLOTTMAN: In this particular example,

the one I held up, there is a folding carton that the product is inserted into along with the literature. There are other examples where there would be a carton of 36 units, that would be dispensing units, and there would be a pad of 36 med guides included at the top of the package on top of the case and there are other situations where the med guides would be produced in like a deck where there would be several attached to one another that would be available either to be put into the carton that the product is shipped in or most often that method would put it actually the drug product. It would be attached to the drug product.

DR. BERNSTEIN: And would that be -- I'm sorry. Is how that is that's strictly the decision of the manufacturer of what works best for that particular product or what?

MR. FLOTTMAN: That's a product of the design of the package and the manufacturer's packaging lines and their ability to package those, what method they have and there are several examples of that and it varies by manufacturer.

DR. SELIGMAN: Yes. Lillie Golson.

MS. GOLSON: So do you do the bulk packages like bottles of 5,000? How would you determine how many to include in a package of that

size?

MR. FLOTTMAN: It is determined -- if you have a bulk pack of 5,000, you would have to determine what the dispensing amount would be and divide that by -- and you would have to include that many med guides per however many the bulk pack would have.

DR. SELIGMAN: Any further questions for Mr. Flottman? Thank you very much.

MR. FLOTTMAN: You're welcome.

DR. SELIGMAN: Our next speaker is Dr. John Coster from the National Association of Chain Drug Stores.

DR. COSTER: Thank you very much. I'm John Coster, Vice President of Policy and Programs with NACDS and I'm pleased to be able to present here today at this important hearing on medication guides.

I want to introduce someone who was not originally listed on the panel, Ronna Hauser, who is a pharmacist also with NACDS. She is Director of Pharmacy Practice and Operations at NACDS and she has a couple of examples with her today of what pharmacists are actually seeing behind the counter. She's one of the few pharmacists at NACDS that actually practice pharmacy on a part-time basis.

And also, Dr. Seligman, I want to thank

you for the many times that you have answered phone calls from us in terms of issues and concerns we've had with this program. We know we've chewed your ear off probably more times than you care to admit about this.

But the recommendations that we're going to present today should not be new to the agency. We submitted a comprehensive list of recommendations to you about the medication guide program last June, as you know, and over the last couple of years, we've had the opportunity to meet with you several times as well as talk with you, as I said, many times on the phone.

NACDS represents the chain operated retail pharmacies, but while you have two on the panel today, CVS and Walgreen's, two of the nation's largest, our members include some of the smallest chains in the country as well, many of whom are not as technologically sophisticated as the two companies that are on the program today, and tomorrow you'll hear from the independents and other professional pharmacy organizations. But we represent about 35,000 of the 55,000 community retail pharmacies in the United States. We're the largest provider of pharmacy services and as you've heard from other speakers, most pharmacies provide some sort of consumer medicine

information, CMI, to patients already, some better than others admittedly. But consumers are already getting information from pharmacies and the medication guides that they also get that are required are in addition to what pharmacies may already be providing.

Now as you heard also from Tom from Walgreen's and as you'll also hear from CVS, pharmacies want to do the right thing. We want to provide information to consumers. But again, as you've heard from us before, we have several concerns with the medication guide program. We're concerned that it's not being implemented consistent with the agency's own regulation. The program is in need of major reform to be effective for patients who we're all here to serve.

We believe little evidence suggests that distribution of the guides actually increases patient understandings of risks. We're concerned with overwhelming patients with too much written information. Information not read is not useful and we do think that a long-term solution because we do have two regulatory structures now, one that's regulating CMI and one that's regulating med guides, is at least for the products containing medication guides, merge that into one single document. We

strongly support the efforts that the private sector has made and continues to make in providing useful information to consumers, but we don't believe the current system using two regulatory tracks is sustainable.

You also know that over the last couple of years we've met with you several times and asked for certain things in terms of relief so that pharmacists were more efficient in providing medication guides to consumers. This is a list of some of the meetings we remembered dating all the way back to January of `05. About two years ago, we asked the agency to allow pharmacies that were capable to print medication guides as part of the single pass document that comes out with the prescription. We provided mock-ups to the agency to show how it could be done. These are things that Tom referred to before. We worked with the database companies to produce these mock-ups. We think the mock-ups look pretty good in terms of a single pass document and as you might imagine we were disappointed when what we got back from the agency was a letter basically telling us to go work with the sponsors, and these were for antidepressants, to go work with the sponsors to try to effectuate the simple printing by pharmacies of medication guides. There

were 19 of the same letters sent to 19 different companies. We were very disappointed in this response and we thought that the agency two years ago would at least give pharmacies relief to print the medication guides electronically if they had the capabilities of doing so as part of the single pass document and we would hope the agency would grant this soon because we don't know how long it will take for the agency to make or consider any changes to the program.

Now just in sum, some of the concerns we have with the program. I'm not going to elaborate too long because I'd rather have Ronna spent some time talking about what we're seeing in practice today, is the program was never intended to be used for classes of drugs. In fact, in 1998, the agency said that they estimated that no more than five to ten products would be required to have med guides each year and if you go back and read the economic impact analysis of the rule, you estimated about 100,000 prescriptions for each product. So even assuming that there were ten products a year, that's a million prescriptions, our current estimate is close to eight to ten percent of all prescriptions require medication guides which means about 300 million prescriptions are to be dispensed with medication guides. That's

unsustainable.

In 2007 when you released the medication guide announcement for ADHD drugs and sedative hypnotic drugs, that's 28 drugs alone not counting dosage forms and genetics. Again, the original intent of the medication guide program was a few drugs a year. It's now become a few classes a year. It's too much paper. It's inconsistent with your intent on electronic filings. I know no pharmacist that wants to store pads of paper or paper documents in their pharmacies. That's not the world we're living in anymore. The Coumadin medication guide is five pages long. Some are up to 20 pages long. Consumers also get, as I said, CMI. How much paper is too much?

We also agree that the decision should be made at the point of prescribing not dispensing.

In terms of the operation of the program, it needs to be substantially improved. There is no central place for the pharmacy even if he wanted to get every medication guide necessary. He would have to call as many 1-800 numbers as there are medication guides unless there was some central place to get them. But that's not the case right now.

There is no consistent rationale for when class med guides are used. A class med guide was used

with antidepressants and NSAIDs. That was positive. But it was not used with ADHD drugs and sedative hypnotics. Obviously, class med guides are easier to maintain and distribute. We need a program that allows for one medication guide for all drugs in a class and for all brands and generics. Even if there is one for one brand if there are ten generics, each generic company has to produce their own medication guide and we have to obtain each one of them to distribute them unless there's a class guide.

We need a single place to get all the medication guides and we think FDA should operate this process. If the burden is going to be placed on pharmacies to find all these pads if they're not printed electronically, that is incredibly burdensome for pharmacies and we also think manufacturers need to bear the cost of distribution and printing.

Here's the five page medication guide for Coumadin, one single drug, which is provided in additional to whatever CMI the pharmacist provides. But here it was the medication guide for NSAIDs which was for all the drugs listed on the right-hand side. Yet here are the medication guides for all the ADHD drugs. Not only is there one for each drug, but there is one for extended acting forms and long acting

forms. What is the rationale in terms of how you decide whether to use a class medication guide or not?

Our recommendations are very consistent with what Tom Lawlor mentioned, allow for electronic printing with other pharmacy documents even if the waiver of the formatting requirements are needed and we're not asking for pharmacies to just dump out a bunch of words on a page. The documents we gave the agency two years ago are very neatly formatted. They may not be totally consistent with the formatting, but the content is the same. Would it be better to give patients a medication guide that's slightly different than the 10-point type formatting requirements or give them nothing? Return the program to its original intent. A few drugs a year. Class med guides should be used if that is necessary. Dispense on first fill and then upon request. And the program needs to be organized differently.

Over the long term again, we believe that if the agency is going to continue to require medication guides, the two documents should be merged into one document. Either have the private sector produce the document that includes the medication guide information with some oversight by the agency or have the manufacturers produce one document that

includes the medication guide information and all the other CMI information that's necessary. The current dual track approach is unsustainable and we think it needs to be reformed.

If I can for a few moments, I would like Ronna Hauser to just show you some examples of what pharmacists are seeing in actual practice today.

MS. HAUSER: Sure. Thank you, John. I'm here on behalf of a practicing pharmacist, registered pharmacist, who works on the weekends just to show you the reality of med guides in community pharmacy today and how the program is overwhelming and very confusing.

There is confusion with the antidepressant class med guides. I brought a sample of the sheet, one page front to back. It is part of the tear-off pads that pharmacies receive. However, when we need to replenish these, we don't have any more left in stock to dispense with antidepressant medications, oftentimes we need to use the fax as a copy machine to make extra copies until we can replenish our store.

There are also different formats of the antidepressant medication guide. I found this on the shelf in the pharmacy I work in. That was the exact same thing as the antidepressant med guides, but it's

on one big sheet where the pharmacist would have to take scissors and cut the individual antidepressant med guide to dispense.

In addition, some antidepressant products have their own med guides attached. For example, I have an empty bottle here of a generic antidepressant medication. The pharmacist normally, this is a unit of use bottle, would grab the bottle of the shelf, make sure it's the right NDC number, put the pharmacy label on the product, etc. However, in this case, hidden, kind of difficult to know until you look really close you have to pull the label off. I was going to do this for effect here. You need to pull the label off. Behind the label of the bottle you find a PI. Embedded in the PI is a medication guide, all part of the same document that again is hidden behind the prescription label.

Another example would be an oral liquid antidepressant medication. Again, real big red print "Attention dispenser, accompanying medication guide must be dispensed with this product." There would normally be a bottle, 240 milliliters of a liquid in here. There is one med guide. However, based on filling of this prescription, often times you're not going to dispense the entire bottle in one filling.

You're going to need more than just one med guide to go out with this prescription the number of times you fill it and again, a PI. A med guide is embedded into the PI. So you would need to dispense the entire prescribing information plus med guide to the patient and as we all know, the prescribing information is meant for prescribers and health care professionals.

Next up off of a generic, again a generic antidepressant medication, there was a PI attached to the bottle with a tear-off sheet up top. It says, "Pharmacist, detach here and give leaflet to patient. Also provide an approved medication guide about using antidepressants in children and teenagers." So here we have patient information that we're being told to tear off, scissor off, and hand to the patient in addition to a med guide. So that in this case, I would have to go pull a med guide hopefully off of a pad that I have laying in the pharmacy. So there's a lot of confusion too in pharmacists' minds about the difference between patient information leaflets and med guides. Again, that was a class for antidepressants. There is some similar confusion with the NSAIDs.

Two more examples. This is a warfarin product just to show you how it comes to the pharmacy.

It shows up with the PI glued to the med guide. This is a bottle of 100 tablets. Again, four med guides are included. Again, the pharmacist or the technician, has to take time out of their day and take scissors to cut the four individual med guides and again probably for a bottle of 100 it may or may not be enough depending on the dosage and the quantities that you are dispensing to your patients.

Lastly, the confusion with the patient information sheets and the med guides. It's my understanding that both Protopic and Ketek require med guides, but the only patient information I could find with these medications in the pharmacy was again a PI with an attached patient information about Protopic. So I never saw the words "medication guide" on here which leads me to question is this the med guide? Should I dispense this to the patient?

Again, the same situation with the Ketek leaflet that came with the product with the bottle. It's the PI and then embedded in the PI is patient information about Ketek. So I'm still confused as to if this is the med guide that I'm supposed to dispense with the product or not because there was no other information that came with the bottle.

Those are just some of the realities.

There are many more, but those are just a few of the examples of the realities of the confusion of med guides in community pharmacies today. Thank you.

DR. SELIGMAN: Thank you both. Before we lose you behind that growing stack of medication guides, are there any questions from the members of the panel? Bob Temple.

DR. TEMPLE: I guess several people suggested that it might be best to not necessarily package everything under the sun in the same place, but package the CMI and the med guide together. When the med guide rule was first written the idea for it was a sort of thorough patient package insert. It had all the things you would include if you were writing a patient-directed version of the regular insert.

I think as time has gone by, we've come to believe that those are so long and difficult that med guides are better, at least, in many cases, if they're targeted toward the one or two things you want to emphasize. So I just wondered, first of all, maybe you don't agree with that. But if you tried to put it all in one document, wouldn't you lose that laterability to focus on the particular thing that's most important and do that in dark print because you would then have attached all the other stuff that is

of some interest, but not quite as much? Is my question clear?

DR. COSTER: Yes. I'll attempt to answer and I don't know if, Tom, that's okay. I think the concern is that there is so much paper being distributed now that nothing's being read by patients and I'm not an expert to know whether this is the best way to do it or this way is the best way to lay it out or not. But it would seem to me that it's better to give a patient a two page max document that perhaps highlights with a box or some sort of distinctive markings the warnings you want to communicate to them within the context of the two pages rather than giving them a separate document that focuses solely on the risk of the particular drug.

I don't know. I'm not an expert on determining what the best way to communicate risks to patients are. I think from a practical perspective patients are not reading all the information they're getting. The current system is unsustainable. So we have to find a way to combine the two so that the patient gets the full risk and benefit of the drug in one document and maybe if there is a certain risk with the drug that needs to be more fully or more distinctively communicated, find a way to do that

within the context of those two pages.

DR. SELIGMAN: One of the more important FDA initiatives in the last couple of years has been the creation and the development of the electronic professional label that's now available through the DailyMed and the National Library of Medicine. I was curious given that the medication guide is indeed part of the labeling whether you or any of your members have had experience in accessing electronically a medication guide and whether that may serve as a ready and easily accessible way for pharmacies to get at that electronic version of the guide that's supposed to go out with the prescription.

DR. COSTER: Again, I can answer, but if others want to. First, not all pharmacies have internet connections. So not every pharmacy can go out into the internet. I mean, some have internet connections but only for certain websites. Others just don't have internet connections.

Second, I don't think DailyMed is fully populated yet with all the documents that are necessary or all the labeling that's there. So I don't know what percent of all DailyMed labeling includes drugs that have medication guides.

But third, I think as you'll hear again if

you ask the gentlemen sitting at this table, the most important thing you can do with the medication guide short of integrating the information into a single document is integrating into the workflow of the pharmacy. So to the extent that you need to go a separate website, print the medication guide out, it disrupts the workflow of the pharmacist which is the most important thing for patient safety. So I would say that while it's useful to have that information available through DailyMed or some internet or through the FDA website, if the pharmacy can't integrate that into the documents they're printing out when the prescription is printing out, it disrupts the workflow of the pharmacy and compromises patient safety.

DR. SELIGMAN: So the message then I presume is if you're going to print something, print it once. Right?

DR. COSTER: Integrate it into the --

DR. SELIGMAN: Right.

DR. COSTER: And as you know, we provided to you information that shows at least two years ago, now there may have been more advances made and I'm sure there have been, how that could be done and integrated into the workflow. So short of, again, combining the two documents together which is I think

our preferred long-term solution, that is to us an intermediary intermediate solution to solving part of the problem.

But I guess you also have to recognize that not all pharmacies as I said before are as sophisticated as the two sitting up here. So integrating, providing for electronic printing, is part of the solution, but it won't be the solution for all pharmacies.

DR. SELIGMAN: You mentioned a request to waive aspects of the formatting that's in the current rule and particularly you talked about the 10-point font. I'd be interested in your reaction or justification for, I presume, allowing for, I guess, smaller fonts and also interested in what other aspects of formatting that are currently contained in the rule would you feel need to be waived in order to effectively print those documents in the pharmacy.

DR. COSTER: This is over my head. So the way I'll respond to that is saying the documents we gave you a couple of years ago were the state of technology in terms of printing at that time. I don't even remember whether these, the ones that we provided you, were 10-point font.

MR. LAWLOR: I don't remember what they

were, but it's not so much a variance in the font, Dr. Seligman. It's however we're going to print it. If that isn't totally compliant with the current regs, we're looking for a pass there. However we would print out the CMI and the med guide, if it's not 10-point font or 12-point font and if it's not the way the regs specify, as long as we've got it and it looks good to the patient, that's where we're asking for some leeway.

DR. BERNSTEIN: Can I follow up on that?

DR. SELIGMAN: Please.

DR. BERNSTEIN: One of the things that we have said is we were going to try and attempt to do a guidance for electronic printing of medication guides and when we started working on that, we did run into this very issue of what are the formatting of elements that are necessary which could you have some -- we would have some flexibility with and which can't we. So I think that -- although here, not to put you on the spot, at least for the record, I think it would be very helpful if you could help us in trying to identify some of those so that it does help make the workflow more efficient, but recognizing that those formatting requirements were put in for a reason and which ones even based on whatever other literature is

out here or even what the capabilities are of the printers, which we don't have that expertise either.

DR. COSTER: We're happy to work with you. As you know, we've been in many times to see the agency about how we could do this. There are not a lot of database companies that produce this information. So I don't think you can -- and we met with you with the database companies to demonstrate that they had the capabilities of printing information in an integrated fashion.

Again, I don't know what the current state of technology is in terms of printing. Two years is a long time in terms of improvements in technology. So I would suggest that tomorrow which I think some of the database companies are also on these panels that you ask them and we can certainly dialogue with them about whether or not there's even a need at this point to waive those requirements. I don't think we're asking for content requirement waivers. It's more along the lines of formatting. But those could be minimal at this point.

DR. SELIGMAN: Yes. Lillie Golson.

MS. GOLSON: When you're printing for a product like Zyban, where it may have two different indications you have Zyban which is for smoking

cessation, however it's also a antidepressant, so you need the med guide. Plus you need the information specific to smoking cessation, how do you print that out because I think right now you're mentioning you have two things on the insert that you have to give out? How would you incorporate that information in what you would print out?

MR. LAWLOR: The CMI is specific to the Wellbutrin or the Zyban whichever one you're filling based on the NDC number of the drug.

MS. GOLSON: Okay.

MR. LAWLOR: The med guide that would go along with it would go along the same way. We would just associate the same med guide with each product, but the CMI would be different.

MS. GOLSON: Would be different.

MR. LAWLOR: Right.

DR. SELIGMAN: Dr. Woo.

DR. WOO: Again, thank you for the understanding of the complexities and challenges in trying to meet the regulatory requirements. I think what it also speaks to is some of the confusion that comes because where our regulatory authority ends and where the State's authority start. There was, I guess, both Mr. Lawlor and Dr. Coster addressed issues

about enforcement or at least implementing programs and with our regulatory authority fairly focused on the manufacturers. From your perspective, is there any leverage that you can bring to try and help manufacturers comply with or develop more consistent methods of producing and supplying med guides to you?

DR. COSTER: I'll answer and then -- as Tom said, there's no shortage of different ways that manufacturers provide these. We thought a good model was when, I believe, it was the antidepressant manufacturers were required to develop and distribute medication guides that they formed a consortium that was responsible for assuring pharmacies got sufficient quantities. There was one single 800 number. There was one medication guide required for all brands and generics. That was a good model and then I think after a year that fell apart and then the NSAID manufacturers were trying to do the same thing.

But as we said to the agency, you know, the manufacturers do that voluntarily. They're under no obligation to form those types of consortium. It's going to take the agency's leadership. You have the leverage over the manufacturers. We don't. So if you're going to require medication guides for classes of drugs or a class of drugs, only you can leverage

them to form these types of entities to make it easier for us to distribute these products for patients. I mean we just have little, if any, and Tom or Steve Heidenthal hasn't spoken yet can talk about that, but I don't think they would argue that they can go to manufacturers and say, "Hey, you guys get together and form a consortium and form an 800 number." That's -- the agency that has to provide that leadership.

DR. SELIGMAN: Thank you very much. Our next speaker is Mr. Steve Heidenthal from CVS/CareMark. Mr. Heidenthal.

MR. HEIDENTHAL: Good afternoon. Can you hear me okay?

DR. SELIGMAN: Yes, we can.

MR. HEIDENTHAL: My name is Steve Heidenthal. I'm a pharmacist and I'm here today representing CVS/CareMark Corporation. In advance, I'd like to thank you for allowing me the time to come before you to discuss medication guides, our current challenges and more importantly some recommendations that we believe will enhance overall desired outcomes.

DR. SELIGMAN: Actually, if you wouldn't mind putting the mike just a little closer. That would help. Thank you.

MR. HEIDENTHAL: As it's getting late in

the day, I'll be brief in an effort to not repeat the fine panelists' comments that have come before me today. Permit me to briefly provide context on the day-to-day experience CVS/CareMark brings to the discussion today surrounding medication guides.

When you hear CVS Pharmacy, I'm sure many of you think of our retail stores. However, with the recent merger of the CVS and CareMark organizations, we now provide integrated pharmacy services to the payors, medical community and the patients of this country. This integrated pharmacy services organization includes in excess of 6200 retail locations, CareMark Pharmacy Services which includes pharmacy benefit management, mail order and specialty pharmacy divisions, Minute Clinic which provides a retail-based in-store health care clinics and CVS Online which delivers internet-based pharmacy services. And in the course of our daily business operation, we provide consumer medication information to our patients with prescriptions.

As I talk you through the current situation we face today, our general observations and a few recommendations, a few overarching themes that hopefully resonate to you are that pharmacists want to help patients improve their quality of life. This

objective is the foundation of the profession of pharmacy and I am sure is a keen interest of many here today.

Additionally, I think we all agree that patients need to understand their medication therapy and while it is certainly important to comprehend the risk associated with medications, let us not lose sight of the need to provide balanced information on the benefits of prescribed therapy as well. Also medication information needs to be provided to patients in a simple, direct and understandable manner that enables informed decisions regarding the initiation or continuation of prescription medication therapy. And finally, that successful, large scale programs require standardization and a commitment to focus on the finer details necessary to support execution and deliver the desired outcome.

So where are we today? Information that is designed to advise patients of serious and significant risks associated with prescription medication is being delivered at the relative end of the therapy process whether the patient is initiating or continuing treatment. In addition, patients on the whole are receiving duplicative information across variant sources and format designs which include, but

are not limited to, med guides, CMIs and PPIs where required.

Pharmacists today are dependent upon a myriad of distribution methodologies that Ronna showed to obtain the rapidly expanding volume of med guides. These methodologies are inconsistent and are not universally viable. As a whole, the medication guide program lacks the current end-end program standardization necessary to support execution and as such, the end distributor is forced to continually intervene manually to employ information and even with the very best intentions, our consistent execution is prohibitively difficult.

General observations at our stores and with patients include, but are not limited to, the reality that the current point of delivery of med guides at dispensing with the predominant focus on providing risk information often complicates rather than facilitates the health care system. The pharmacist's focus on the risk of medication fails to recognize the full patient history, subsequent diagnosis and overall thought process employed by the prescriber when weighing risks versus benefits for the individual course of treatment prescribed.

Furthermore, today, the sheer volume of

consumer information is simply put, overwhelming and may not be useful. And I would be remiss in my comments today if I did not convey the thought that even with the very best intentions, the lack of detailed and consistent program standards designed to support the distribution of med guides to the end user will continue to negatively impact program execution.

And finally, in an era where large amounts of critical patient, financial and claims information are communicated in seconds, it is evident that successful execution must entail a solution that integrates better in today's workflow and does not rely on an approach that demands constant manual intervention.

So faced with the program challenges today, the reality of our daily observations and ever mindful of the need to provide medication information in a manner that supports improving the overall quality of life for patients, the following recommendations are offered. First, as we've heard from many before me today, assess the point of delivery to maximize the ultimate patient outcome so that it is not only at the pharmacy. Second is to consolidate information delivered to patients in a consistent, concise and easy-to-read format. Third is

to develop program standards to support total execution and success. And fourth is to provide reasonable flexibility within the program to achieve overall desired outcomes.

And permit me just for a minute to expand upon these. The first concerning the point of delivery, it's our goal to engage patients early on in their therapy and in doing so, to improve overall compliance and outcomes. Medication guides by design are associated with drugs that present serious and significant risk and embarking on a course of therapy for these medications warrants an informed decision. These decisions include not only understanding the risk associated with the medication, but also comprehending the underlying condition that requires treatment, the inherent risks that accompany the condition, any alternatives and the anticipated benefits, all discussions that occur at the point of prescribing.

Please let me be clear, however, that no pharmacist is opposed to providing medication information and in fact, it is at the very core of our job. However, absent the more comprehensive understanding of the patient's overall diagnosis, the associated lab values, etc. in the current design

today, pharmacists are delivering a risk-centric message that if unbalanced with benefit may potentially contribute to greater risk for the very patient we are all seeking to help in that it may contribute to reduce compliance with the prescribed therapy. In focus groups previously conducted to review med guides, consumers echo the concept that the preferred location to receive and discuss this detailed information is at the point of prescribing it.

Our second recommendation surrounds the volume and different types of information that are involved when a medication guide is required. As you know, pharmacies are providing information from multiple sources, containing different writing styles with variant objectives. When med guides are combined with the keystone monograph, our experience is that the patient is faced with upwards of five or more pages of information. This difference in style and content structure not to mention the sheer volume make for a very difficult read that based on observation of consumers I would quantify is almost nearly impenetrable.

Now while I personally prefer the conversational tone of the med guides, I urge you to

not evaluate med guides in a vacuum independent of other material because it is with these multiple combinations that we are further contributing to losing the very patients we are trying to help. Pharmacies and patients alike are overwhelmed with the sheer volume of information that is required to be distributed on new and refilled prescriptions and we would prefer as Tom articulated earlier that when med guides are required for the FDA to consolidate all information into one concise, approved document that is easy for consumers to read and understand.

The final two recommendations involve actions needed to better support the large scale program execution required with med guides. With our experience gained across thousands of retail mail and specialty pharmacies, one constant theme that echoes through successful programs we have launched and maintained is that defined standards designed with a desired outcome in mind coupled with consistency will reduce confusion and support successful execution.

We have moved from an environment where the antidepressant med guide was available by a single clearinghouse to a situation that now involved individual med guides, thousands of NDCs, no single consistent process that governs the distribution

methodology for all the products that require this added information. Situations vary from three med guides being distributed on a hundred count stock bottle to guides incorporated with a bottle that is perceived to be a unit of use size to guides that require a contact to the manufacturer by a supplied number to guides that require the submission of an order form for guides or guides that require the reprinting from a CD or accessible from an internet location. Simply put, mandating the means to produce or that sufficient numbers of med guides be provided is not enough. Lastly, if this is to be truly successful across the multitude of operators, the reality is that organizations delivering the information cannot be expected to bear the financial burden solely necessary to support the distribution.

Our final recommendation involves the critical issue of the process involved to support med guide distribution. In today's pharmacies, we are heavily dependent on technology systems to communicate large volumes of information in mere seconds. Whether it is an electronic prescription, an insurance adjudication or a formulary rejection, we rely on integrated information transmission to survive.

To ensure success, we need an integrated

distribution solution complete with the necessary flexibility to support such implementation. While the reliance on a manual process may need to be remain temporarily depending on the level of flexibility permitted for the options developed, any manually maintained solution in today's world of pharmacy significantly increases a level of difficulty and contributes to inconsistent execution.

If the desired outcome is consistent execution of the communication of med guide information to patients, a guiding principle of reform must be to reduce the current dependence on a manually maintained program. Doing so will necessitate greater flexibility while not losing sight of the desired outcome.

So in summary, there is little debate that pharmacists strive daily to improve their patients' quality of life or that providing balanced, clear and concise medication information is critical to the engagement of patients concerning their own medication regimen.

With that in mind, it is our true desire to foster changes in today's program in such a manner that permits this higher level of patient engagement. Successful outcomes entail not only taking into

account the distribution and location of varying degrees of information but also will involve a standardized, integrated distribution methodology that is flexible enough to permit widespread and consistent program execution without undue financial burden.

Again, I'd like to thank you for the opportunity to share our observations and recommendations on improving the dissemination of med guide information to our patients in this nation.

DR. SELIGMAN: Questions? Bob Temple.

DR. TEMPLE: This is the same question I had before. My understanding is that it's within the electronic capability of most pharmacies anyway to not only print out the CMI which they're already doing with every prescription, but to print out an additional document that looks like a med guide. Several people have now said they ought to be consolidated and maybe indeed that will turn out to be good, but they are fundamentally very different documents.

The CMI has to be more or less an extract of the complete prescribing information. I don't think anyone would think that's targeted, emphasized, has a lot of big words and all that stuff. It's not the same thing as what a med guide is mostly nowadays

intended to do. So I'm not sure how well it's going to work out to try to make a single document, but I don't understand why you want to so much have a single document, if it's very easy to print out the two documents separately. It's not such a big deal or am I misunderstanding something?

MR. HEIDENTHAL: If I may answer that. Dr. Temple, from our observations at the pharmacy, again it goes back to your previous consumer focus groups that were completed but also standing at the pharmacy. The consumers are overwhelmed with the volume of information they're receiving. So we're going from five to twenty pages varying with the information that you're providing to consumers and the question that has yet to be really demonstrated to us has been is this a viable method for a consumer to walk away and understand what they need to understand about medications being in two formats. You know, I look at it as almost a tax guide booklet when I receive 20 pages and I step away and say, "I'm not going to read anything," as opposed to understanding the few salient points that I really need to be articulated to me to take away what I need to know about that medication.

DR. TEMPLE: But then it wouldn't be the

CMI anymore which is intended to be a sort of extract of the whole package insert. Maybe that's not a great idea, but that's what they currently are. They list all the adverse reactions. It's a very lengthy piece. It's not at all like what we aspire to for a med guide. So how do you combine them or maybe you throw away the idea of having a CMI and get rid of the idea of having a patient package insert that resembles the physician insert. Is that what you're saying and you just have the stripped down version with a couple of things emphasized for the ones that get a med guide and they wouldn't have the complete one anymore. Or what's -- I'm not sure I understand the proposal. They seem like very different documents.

MR. HEIDENTHAL: I think you have a lot of duplicative information in the two documents. I think you have a very well-received conversational tone in the med guide document and I think the challenge to the FDA is to say, "Can you meld the two into a document that provides the med guide conversational tone, adds on the additional pieces that are prevalent today in the other documents and get to a concise document that reduces the volume count that we have today that we're very concerned that we're losing our patients with." As we watch the reactions at the

pharmacy counter and we watch them strip off that information, I can tell you that the reactions from the consumers today are for many consumers is this is too much.

MR. LAWLOR: I'd just like to echo what Steve said. There is duplication and there is both risk and benefit information in the CMI and we're asking to if we said it once we don't need to say it twice. So whatever is duplicated in the med guide and the CMI, we just need to say it once and we've seen historically that patients don't usually read something if it's more than a page long. So when you have these big documents that come out, we've seen patients throw them out on the way out of the store. It's just not serving its purpose.

DR. TEMPLE: So you're really saying there's no point to the CMI and that whole program is just really silly.

MR. LAWLOR: No, I'm saying that there is good information in there and patients we do know read it. But when it gets to be excessive or that CMI document is saying some of the same things that's in the med guide, if a med guide is required that for that particular product, patients become confused because why does it say it twice. Why do I have two

different pieces of paper saying the same thing?

DR. TEMPLE: So if the goal is to write a short med guide with a few paragraphs that talked about the most important things, suicidal thinking and stuff like that, but the rest of the CMI had all the other side effects that antidepressants do, how exactly do you combine those in a single document which as I understand is what you're proposing?

MR. LAWLOR: I don't see why that's difficult.

DR. TEMPLE: Well, you wouldn't have the short document anymore. You would just have the long document. You would have the CMI. So the idea of having a short punchy document that people might read, that would go out the window.

MR. LAWLOR: We're advocating a one to two page document that's easy to understand, sixth to eighth grade level that has both the risk and the benefit information there for the patient.

DR. TEMPLE: Okay. But that's not what current CMIs are. They're longer. They're not so easy to understand. They have very small print. I mean, I get them and I throw them away.

DR. SELIGMAN: Bob, in some respects, I think I've heard two things. One is this notion of

combining. The other, what I thought I heard earlier, was the potential for what was called sort of first pass printing where you could print both the CMI as well as the medication guide at the same time and with the caveat that -- with a couple caveats. One was that as currently practiced some of these medication guides are viewed to be just way too long and that printing out 20 pages or 30 pages may be more than either what the pharmacy can bear either in terms of time or what even would be valuable to the patient. That, in and of itself, is a distinct issue about the length of the medication guide.

But at least, that's one of the things that I heard was this notion of maintaining the integrity of both documents, shortening the medication guide so it's more cognitively or readily accessible and then having the opportunity to sort of do first pass printing for both documents simultaneously at the pharmacy.

DR. TEMPLE: But that's different from a single document though.

DR. SELIGMAN: That would be different from a single document.

DR. TEMPLE: I agree that makes the most obvious sense since it's apparently now easy to do.

DR. SELIGMAN: Jeanine first. Jeanine Best.

MS. BEST: Yes. We have been actually working on more of our recent med guides. We have been working on shortening the length, but most of our med guides do contain comprehensive information with regard to, of course, the serious side effects which triggered the med guide. But also they contain the indication, side effects, serious and common side effects, etc., etc. So possibly with some of those, most of our med guides are comprehensive. They aren't targeted like the antidepressant class med guide. So perhaps we need to look to see where we can make our med guides CMI compliant and just have one document.

And as for three documents, a patient should never -- we always tell sponsors that if they have an existing patient package insert when the med guide is approved, the med guide supersedes the patient package insert and that should go away. And what you may be seeing is product that was produced -- you may have product on the shelf that was produced before that approval is why you are seeing the patient package insert along with a med guide. But that's the reason for that.

So perhaps we can work on making some of

our comprehensive med guides more CMI compliant.

DR. SELIGMAN: But your point then essentially reinforces what we heard both from Mr. Lawlor and Mr. Heidenthal about the fact that there is some duplication and an overlap between the content of the CMI and the medication guide.

MS. BEST: Yes.

DR. SELIGMAN: And that basically having information that's repeated twice in two separate documents may not be in the best service of the patients.

MS. BEST: Now also -- but in our medication guides because of the regulation, our medication guides only contain approved indications. We do not talk about off-label uses in the medication guides which I know some of the CMI does discuss. We do not talk about that.

DR. SELIGMAN: Yes. Toni Piazza-Hepp.

DR. PIAZZA-HEPP: Yes. Basically, I was just going to make a few comments to give an introduction and to turn it over to Jeanine. But yes, I thought the concept that you've suggested earlier about an effort to possibly make a combined document that could be used as the one piece of information for patients was something that we should really look at

and I was going to turn it over to Jeanine to talk about the feasibility of doing that based on her experience as a patient-product information specialist. So thank you, Jeanine.

DR. SELIGMAN: Okay.

DR. BERNSTEIN: I have one more question.

DR. SELIGMAN: One more question. Please.

DR. BERNSTEIN: Thank you. We're here trying to look for some solutions on how to address this problem and as we've just heard, we need to reduce the dependence on a manual system. But we've also heard from several of you that pharmacists don't want the burden of paying for all this paper. If we're going to move towards more of an electronic system, that there's paper and toner and all these other printer costs associated. Well, that's a challenge. That's something that would be difficult for us to try and keep in mind. We would need your help in that aspect and I'm not sure if you guys have, any of you have already given any thought to that because there's that balance that if the manufacturer isn't going to be providing, they are going to be providing the electronic means, then how do they end up paying for the paper that's printing out at your pharmacy? There may not be an answer to that right

now, but it's something that if that's what you're saying we need to keep in mind we would need some help there.

DR. COSTER: I'll just try. I don't know that there is an answer. It's the same issue with the paperless labeling issue, if the patient wants a copy of the professional labeling which tends to be anywhere from 20 to 30 times longer than the medication guide when printed out on 8.5" X 11" paper, that's another issue right there. But this whole question of what's two more pages or three more pages or four more pages of paper. Multiply that by 300 million prescriptions and that's a lot of trees and I think that's something that the agency has to be conscious of.

And the other thing I would raise again is that there are two distinct regulatory schemes here still working. One is the 1997 appropriations scheme with the CMI and you have specific goals and you'll be in the field looking at that and then you have the medication guide regulation. Our view is that those two eventually should be merged and that one single document that combines information for the patient on how to store the medication, those that meet the goals of the CMI as well as meet whatever risk information

you want to communicate be incorporated into a single, two page document. That would be our recommendation.

The single pass issue is a short-term solution in our view. It's not a long-term solution in terms of having the pharmacy print something that's going through at the same time the CMI is printing out. It's in our view a short-term solution. A longer-term solution is incorporating the two documents together.

DR. SELIGMAN: Incorporating the two documents together and having the manufacturer ship that document or --

DR. COSTER: Or having the manufacturer produce the document that's provided to the database companies that we use in our systems.

DR. SELIGMAN: And then Ilisa's point is the pertinent one then which is ultimately then we would negate the need for distribution of paper by manufacturers which would essentially then put the entire burden on you all in terms of expense of paper, printer, toner, etc., in printing that information. The primary place, in other words, where this information gets printed and handed to the consumer then would be at the pharmacy. Right?

DR. COSTER: Well, we said there wasn't

any good answer to that question when it was originally asked.

DR. SELIGMAN: Right. I understand that.

DR. COSTER: And the answer is the one that you just gave essentially, but I know the agency always has concerns when we talk about some of the economics of these issues. But millions of dollars in paper is being spent by pharmacies right now and other related supplies. So I think there are tradeoffs here between having the work flow easier -- would pharmacies being willing to absorb some of these costs have the work flow easier? I think the answer is probably yes, but I don't think they're willing to absorb the whole cost.

DR. SELIGMAN: Right. It would certainly in my mind clearly shift the burden. I mean, instead of having manufacturers absorb as they do now presently, pay for the printing and shipping of this paper, essentially that cost burden essentially shifts to pharmacies.

Okay. Let's take our last speaker for today. I don't know who is going first, Ms. Cathy Russos and Mr. Ben Stone from Pharmex.

MR. STONE: Actually, I drew the short straw. So I'll be presenting by myself.

DR. SELIGMAN: Okay. That's Mr. Stone.

MR. STONE: Yes. My name is Ben Stone. I'm with Pharmex. Let me start by thanking you guys for letting me present today.

A little background. Pharmex is a division of TimeMed Labeling Systems. We are a total pharmacy supply provider. Pharmex has been in the pharmacy supply industry for 58 years supplying the pharmacy with products including prescription vial labels, warning labels, promotional items, etc. Pharmex serves over 20,000 pharmacies throughout the United States, Puerto Rico, Canada, Europe and the Middle East. Our parent company, TimeMed Labeling Systems, serves over 5,000 hospitals worldwide.

We supply a variety of pharmacies including independents, chains, grocery, mail order, central fill, outpatient, acute care and specialty. So med guides are a concern for all of our customers, most of whom are unable to attend these hearings. That's why we're here today to present their responses.

We sent out the eight questions posed by the FDA being discussed today to some of our key customers understanding that different types of pharmacies operate uniquely. We feel that it's

important that you hear and consider the responses of all types of these pharmacies. The collective responses we are presenting represent all pharmacy types that we serve.

We've provided the answers to your questions that we received. Following those, we have the collective recommendations based on the information we gathered from the industry.

The first question, "Currently how are you informed that a med guide is required to be distributed with the specific medication?" If and when pharmacists are informed a med guide is required to be distributed, they receive the notification in a variety of different ways ranging from sent as a tear-away tablet from the manufacturer, attached to the manufacturer's pill bottle, word of mouth from other pharmacists or from the FDA website, an email from the FDA or a third party vendor email.

Our recommendations for this are that the pharmacists who responded do not care whether the information is distributed by the FDA, the drug manufacturer, a third party or even if they need to look it up themselves on a website. Their biggest concern is that there is no set standard or guidelines for the distribution. The pharmacist's main concern

is that there is a standard in place so that they are not dispensing prescriptions for months at a time before they realize they were supposed to be handing out a med guide with that prescription.

Question No. 2, "How do you receive med guides from the manufacturers?" Attached to the drug bottle again, in a tablet form, either emailed or given by the drug manufacturer representative, from the manufacturer's website either in PDF or Word format or emailed from a database provider like First Data Bank or MediSpan.

"Should the way you receive these be changed? If so, how?" Our recommendations, again it's not important how the pharmacists receive these med guides, but that they receive them for every drug that requires it. It's important that either or both PDF and Word formats be supported. It's also requested and recommended that the format be reduced to one single page with bullet style formatting so it's easier to read for better patient compliance.

Question No. 3, "What are the challenges in complying with the med guide regulations, maintaining adequate supply of med guides or distributing med guides to consumers?" Some of the challenges that we got back: making sure that a med

guide is given out with each necessary prescription; a lot of times you must rely on the staff member to remember each drug that requires a med guide; shelf space can be a challenge because some of these med guides are up to 20 pages in length; many pharmacies would like but cannot find electronic copies of the med guides or cannot find them in the right format; poor compliance; people do not want to read the lengthy documents, meaning this tool is not as useful as it could be; the supply issues, sometimes both the pharmacy and the manufacturer run out of the med guides; and again it's difficult to provide adequate shelf space for the med guides.

"What changes should be made to the med guide program to address these challenges?" Information could be incorporated with the information updated by MediSpan and First Data Bank; computer software that flags when a med guide is needed; or you could provide the information in electronic format that is 8.5" x 11" page, reader-friendly guide that is combined with, we call it a patient advisory leaflet, the CMIs; this could be on either or both the FDA or manufacturers' websites.

Our recommendations are, the first one is to supply the med guides electronically whether

they're sent via email when they are initially implemented or having them on the FDA or manufacturers' websites. Since the pharmacists use numerous different software vendors, it's important to make these files available in multiple formats.

The second recommendation is to shorten the med guide to one 8.5" X 11" sheet of paper. This will do two things. It will reduce the cost of printing and more importantly, customers will be more likely to read one page instead of upwards of 20. It's also recommended that the med guide and patient advisory leaflet be combined into one single document which again will increase the likelihood of the patient actually reading the instructions.

Question No. 4, "What steps would you need to take to facilitate electronic distribution of the medication guides?" Have the med guides available in electronic formats. Add med guides to the current pharmacy information system so that it is done automatically when a prescription is filled. And some systems do not offer email capabilities. So that would not be possible to -- or that would be needed to be added to the system. And sometimes it's not possible because so many patients do not have email capabilities or refuse to give out their email

addresses.

Our recommendations are that if a consumer would like it electronically, it would require a lot of work and a lot of money at the store level to change and update their current software systems. The customer would like to view the med guide electronically. The easiest way to do this is to put them on a website and direct the customer to that website when the pharmacist is going over their prescription with them.

Question No. 5, "Do you consider the med guide to be a valuable tool in counseling patients about drugs with serious risks?" Fifty percent of the pharmacists that we talked to said, "No, it is not a valuable tool." Seventeen percent said yes. The other 33 percent said that it is too redundant with the CMI information.

Our recommendations again are to reduce this to one page, include it with the CMI and this way if the information that is pertinent is on page ten of the med guide and somebody only decides to read the first five pages because it's just information overflow, they're going to miss out on the information that's pertinent to them. If you reduce it to one page and put the main keys on that page, you're going

to be able to get that information to the patient.

Question No. 6, "Do med guides have a unique role compared to other communication vehicles that patients receive at the pharmacy?" Every pharmacist that we surveyed said that med guides do not have a unique role compared to other communication vehicles.

"Should the information be combined or simplified into fewer communication vehicles?" Again, every pharmacist that we surveyed said that med guides should be simplified into one page either by itself or with the CMI which contains most of the, a lot of the same information.

Recommendations. Since the pharmacists we surveyed do not believe that med guides serve a unique role compared to other communication vehicles, it's recommended that the med guide either be eliminated or more realistically be combined with another communication vehicle such as the CMI. Along with combining these tools together, it's recommended that it's condensed into one page with bullet formatting so it's reader friendly.

Question No. 7, "What process improvements could be made to ensure the patients receive the appropriate drug risk information at the pharmacy?"

The med guide could be combined with the CMI into a one page leaflet that would be printed when the prescription label bar code is scanned; provide key points that need to be covered but allow the vendors the latitude to format and incorporate into already existing material; a pharmacy software update with automatic flags alerting pharmacists when a med guide needs to be distributed.

Recommendations. It's recommended that with the current distribution of a separate med guide when a prescription is filled and a bar code is scanned that a flag is sent up on the screen to alert the pharmacist that a med guide is needed to be distributed with that prescription. However, combining the med guide and the patient advisory leaflet into one page would alleviate the problem of remembering to distribute a med guide with specific prescriptions because the information from the med guide would already be included in the single informational sheet.

Question No. 8, "What are the advantages and disadvantages of having med guides to cover a class of drugs versus med guides for each individual product in a class?" The advantages are that it would reduce paperwork, they are easier to distribute and it

will save space by reducing the number of med guides. Disadvantages. There may be a drug specific warning that may not be included in general information and specific side effects or interactions per product in class may not be mentioned.

The recommendations. By implementing the previous recommendations, the FDA will not have to decide if a med guide should cover a class of drugs or each individual drug within a class. Printing out one sheet of information with the information from the med guide included would mean that each individual drug's information would be distributed in a patient-friendly fashion and improve patient safety.

I thank you for your time.

DR. SELIGMAN: Thank you, Mr. Stone, and you're commended for answering all of our questions.

MR. STONE: I didn't answer them. The pharmacists did.

DR. SELIGMAN: Or at least directing your responses to our specific questions. Comments? Yes. Janet Norden.

MS. NORDEN: I'm sorry. I may have missed this. How many pharmacies did you survey?

MR. STONE: I think we got about 25 responses back.

DR. SELIGMAN: Yes. Jason Woo.

DR. WOO: Yes. This is a follow up to some of the comments earlier or questions from Ilisa and John. I guess what I'm hearing from across the panel is the burden of having to deal with the multiple types of information that you're getting and the multiple different formats. That really to reduce that burden, the solution I'm hearing is that we, the agency, should have more regulatory authority or approval of the information that is being provided by the manufacturers. Be it either to standardize the process or to make more consistent the information that they are providing. But to that extent, that burden would then, at least, within terms of assimilating that process into the practice of pharmacy would put a greater burden on you, that you would be willing to accept in terms of having to produce the documents from either electronic standard or to store the information that's being provided.

DR. COSTER: I don't know if I want the headline to read, "NACDS supports shifting burden." I don't want that to be the message here because pharmacies are printing information now. So they're already bearing the burden of the cost, but that's part of what they do. That's part of the professional

services they offer.

Where I think it's becoming increasingly burdensome is when the agency approves these multi-page medication guides and then doesn't have a real organized plan for getting them to the pharmacies, leaves it really basically up to manufacturers, expects the pharmacies to scramble around to find them. Or we're willing to incorporate that into the workflow but then expects us to bear the cost of printing five, six, seven, eight, nine pages. We're not living in a paper environment anymore, but having said that, I think we recognize that we do this because this is what pharmacies do. But you have to help us make it more efficient to distribute the information and provide a sufficient quantity of information that's useful to the patient, but not so burdensome for the pharmacies to print.

I don't know if that's a good answer. I'm not saying that we're shifting our views that we should bear the burden for this. There's always going to be pharmacies, I think, that don't have the capabilities of printing all this stuff. I mean that's just the reality. I mean there is a lot more pharmacies that are technologically capable of doing this, but it may not be that all of them are at a

point where they can print all this information. But clearly, the ones on the panel today are.

DR. WOO: Yes. Actually, what I think I was trying to assess is that to do what you're proposing requires us to have more authority over the information that goes into the CMI and the med guides and the format. And then to impose upon the multiple manufacturers of the different generics or whatever to work together to make that consistent which requires us to have more regulatory authority.

DR. TEMPLE: I keep asking this, but I'm going to try one more time. When we have tried in the past to make a med guide that had the characteristics of a CMI, the ones Jeanine was talking about, they ran four or five pages because that's how long given the format requirements they had to be to get all that stuff in it. And if we were to try to keep doing that again, they would run four or five pages and then indeed they might replace the CMI. I think that was what the regulatory requirement had in mind. It's a relatively complete document that has all the information in it.

Our most recent med guides, however, have not followed that format. The ones that are numerically most important for antidepressants and for

the anti-inflammatory drugs have been shorter and punchier and have focused on a couple of things.

What I'm hearing is that you don't want that possibility to exist anymore. You want a single document that does both. A lot of the earlier discussion this morning suggests that you make it too long and don't focus on the things that are important, you lose people's attention. So, I really don't think you've begun addressing that yet.

At least in some cases, the most recent examples, we've thought that the large classic med guide, if you like, the one in the regulations which could replace the CMI wasn't what we wanted to do because it wasn't the best way to communicate it. So I think you have to keep in mind the possibility that there would be one document that would be relatively complete but a shorter, punchier one that was designed to get people's attention. And I don't seem to be able to get anybody to address that.

DR. COSTER: I guess let me see if I -- I'm trying to look for the CMI guidance. There is a CMI guidance which the agency published, I think -- you know, the years run together. Maybe it was `05 or `06 which lays out what the agency's view is of the elements of a document that communicates useful

information and I'm almost certain that part of that document requires the communication of information about adverse effects and side effects and contraindications.

I mean, maybe this is an over-simplistic way to say this, but part of what the medication guide is supposed to communicate is serious potential adverse effects or other risk information. That information, in my view, and I think in the view of at least the operators up here can be incorporated into the format of the CMI. It could be made more prominent in such a way that the patient would visually, however it's best done, focus on that. That would communicate the same risk that you have in the medication guide and you'd have the complete information that the patient would need, obviating the need for a separate five page document.

DR. TEMPLE: Well, just to give an example. With the non-steroidal anti-inflammatory drugs, the med guide is focused on the cardiovascular risk. Okay. That's prominent in any -- that would be prominent in any labeling. But if you wanted to tell people about all the side effects with anti-inflammatory drugs it will be a much longer document and by the time you're done it will be much larger

than the med guide we focused on. They are two somewhat different documents and the reason was the new information, the most important thing people wanted to get, was the cardiovascular risk. They had a different purpose.

I'm not saying you couldn't choose not to do that. We could and the original concept of the med guide in the regulations was for a complete document. But I think as we've thought about it, we've worried about whether we were getting so diffuse that people were missing the main points and at least, in the most recent two, they've been focused on specific aspects of the whole thing.

I mean antidepressants do a million things. The whole list of adverse reactions is going to be very long. But the focus of the document was on some of the most important things. So they had somewhat different purposes and I think that's a problem you're not really coming to grips with. They might be different documents.

DR. SELIGMAN: Yes. Toni Piazza-Hepp.

DR. PIAZZA-HEPP: Yes. Just to provide some additional information. Our CMI guidance, that is the guidance on useful written consumer medication information did publish in final in July of 2006. We

made an attempt to help interpret the criterion laid out by the Keystone Group called the Keystone Criterion to assist stakeholders in meeting the 2006 goal that 95 percent of patients will receive useful written information with new prescriptions.

And as we wrote that, we did strive to make it focused on the criterion laid out in the action plan for usefulness, but also to give advice so that it really didn't contain every single piece of information that might be expressed in what we considered the main source document. That is, the professional information. So for example, we specifically state not to list every side effect, but that you should -- at minimum we would expect the information from the warnings and precautions to be listed and maybe the most frequent side effects and also not to include every single drug interaction but maybe the ones that are actually contraindicated. So we tried to give advice to make it a more useful, concise document and not horribly lengthy that hopefully would be useful. But yes, that was in July 2006 is our guidance date.

MR. HEIDENTHAL: If I can respond from just a practical perspective. I think to just speak in very practical terms you can look at it from two

different ways and I guess what we're trying to offer here today is the idea that I understand the regulations were drafted for different reasons to communicate different things. I think the assumption is that all of those pieces individually are working fine and as opposed to a top-down approach, I would say from what we are seeing realistically at the store level when we are communicating with patients. What we are proposing is to step back and say look at this from the bottom up and say the reality of this with regard to consumers. We're trying to share information. It's too much information. The system is too manual for us to sustain it and we really want to execute it. We want to do it well. It's a viable responsibility that we have in our jobs everyday, but we're struggling to do that.

One of the recommendations that we put on the table is to say, "Do you consider when you need to have a med guide?" to throw everything out and say, "What is the information I need to give to the patient and a concise amount of information?" and there may not be regulations that exist today that say it's acceptable in the current mindset that you have today. And that's what we're saying is that there has to be a solution out there that's an alternative.

Now you asked a previous question about the shifting of the burden of the cost and how do we end up doing that and not all pharmacies will be enabled to electronically print. I think we're all very smart individuals, FDA, PhRMA industry, the retailers that are out there, and at the end of the day, we can't lose sight of what it is that we're trying to do which is provide information to consumers and really help with our health care and we can figure this piece out around how does the cost shift and how does it shift for the manufacturers with the burden today on printing the paper cost to putting funds in a pool that for those who print electronically would be able to demonstrate the X cost on that.

I mean, things can be done to develop that. I wouldn't want us to be get bogged down in it and I would just encourage you to look at it from the perspective of the bottom up and say at the end of the day we need to get the information to the consumer and we want them to understand that information and how do we do that.

DR. SELIGMAN: Thank you very much. I think that was a superb comment and I think probably -- is there an additional comment from the panel?

MR. FLOTTMAN: Yes. If I may.

DR. SELIGMAN: Go ahead.

MR. FLOTTMAN: My comment is that in 35 years I've been involved with disseminating a product information through the supply chain, the amount of information is increasing. It's not decreasing and I'm the only non-pharmacist on this panel and from an outside perspective, I'm thinking about what is the core competency of the pharmacy. Obviously, it's not the store literature and go to try to find it to meet the requirements to dispense med guides, etc., with the product.

It also seems to me that they don't want to be in the practice of having the burden of printing out all this information, 20 pages, etc., for the consumer. The cost of doing that with laser printers and toners and the amount of paper that you're going to need to print out the information on a dot matrix printer is much higher than if you're doing it professionally. The resolution is not as good.

I hear a real willingness on the part of this industry to try to provide this information, to try to print out this information, but the continuing theme is how do we do it. It's a very difficult process for us. We're not good at it and I think that the pharmacy industry should focus on what they're

good at and maybe what we should look at is to have professionally printed and packaged information with the drug package from the manufacturer provided to the pharmacy in a manner that they can distribute it with ease. I think that's the common theme and I think that's the answer here.

DR. SELIGMAN: Any additional questions from the panel? FDA folks or from our panelists? Thank you very much. You've given us an awful lot to think about, some creative ideas and certainly some incentives to think freshly and creatively about ways to deal with the current situation which is as amply demonstrated, clearly a situation, which at the end of the day is probably not serving the most important client, which is the patient, very well in terms of getting them important information.

With that, I would like to adjourn this afternoon session and we will reconvene tomorrow morning at 8:30 a.m. We'll see you then and thank you again for the members of the panel. Off the record.

(Whereupon, at 4:40 p.m., the above-entitled matter adjourned for the day.)