

UNITED STATES OF AMERICA
 DEPARTMENT OF HEALTH AND HUMAN SERVICES
 FOOD AND DRUG ADMINISTRATION
 CENTER FOR DRUG EVALUATION AND RESEARCH
 FDA'S COMMUNICATION OF DRUG SAFETY INFORMATION
 WEDNESDAY, DECEMBER 7, 2005

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

PRESENT:

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

PANELISTS:

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

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

8:14 a.m.

CHAIRMAN SELIGMAN: Good morning and welcome to the FDA's Part 13 hearing on Communication of Drug Safety Information. My name is Paul Seligman.

I'm the Director of the Office of Pharmacoepidemiology and Statistical Science at the Center for Drug Evaluation and Research at the FDA. I would like to welcome you all and thank you for being here at what is an unseemingly early hour for most people here in Washington, D.C. Thank you for being here on time and I do apologize for starting a few minutes late.

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

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1 address the panel.

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

10 Let me take then a quick moment and have
11 the Members of the FDA Panel who are here in front
12 introduce themselves, I guess, starting with my right.

13 Nancy, you want to introduce yourself?

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

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

17 DR. SMITH: I'm Nancy Smith. I'm the
18 Director of the Office of Training and Communications
19 in the Center for Drug Evaluation and Research. My
20 office handles most of CDER's communication with the
21 general public. We have the communications with the
22 Trade Press, the toll free phone number and email
23 system that people can write in to the CDER web page
24 and the public service announcements that we develop.

25 Many of our materials are on display out in the lobby

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1 if you would like to look at them.

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

25 Stepping back a few steps, in May 1999,

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

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

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

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

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

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

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

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

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

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

25 CHAIRMAN SELIGMAN: Thank you, Dr. Galson.

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

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

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

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

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

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

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

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

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

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

13 The amount of linguistically isolated
14 households 11.9 million, this is census data, these
15 are people in which no one in the household speaks
16 English, you know, to any significant degree. You can
17 see how LEP is going up, and I'm assuming that you are
18 getting this on your screens. Good, good, all right.

19 The companies are responding, especially in the area
20 of Spanish. Then this is what Nexium puts up on their
21 site in terms of contraindications for Nexium. They
22 do have something in Spanish.

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

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

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

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

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

20 CHAIRMAN SELIGMAN: Okay. Okay.

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

25 LEP and health, and I'll do this very

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

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

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

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

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

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

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

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

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

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1 I'm not a fan of unrestricted importation,
2 but that's an interesting issue that these people are
3 actually looking for linguistically appropriate,
4 culturally appropriate labeling and drug information.

5 They are not getting it in the United States. They
6 are resorting to a potentially very unsafe means to go
7 get it. So there are some cross issues here.

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

16 Here are the top 10 LEP languages:
17 Spanish, obviously, is the big one. And the companies
18 and the FDA, I noticed a couple of the brochures out
19 today on the table are in Spanish. People are doing
20 good efforts there. But there are a lot of other
21 languages and these are the people who don't speak
22 English at home and either speak English not at all or
23 very poorly. And these are the numbers based on the
24 2000 census.

25 Okay. And these languages that we might

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

8 But the Office of Civil Rights, the Title
9 6 regulations which control what hospitals have to do,
10 for example, in terms of translation, their safe
11 harbor if there is 3,000 patients or more, they have
12 to translate all their documents into the appropriate
13 language, if that hospital faces 3,000 people or more
14 in a given year to satisfy the Safe Harbor. This is
15 the Health and Human Services Office of Civil Rights
16 Safe Harbor on limited English proficiency.

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

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

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

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

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

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

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

5 So efforts are being made and they are
6 being made in the largest category. My suggestion is
7 that the Civil Rights Act of 1964 actually requires
8 federal contractors and Health and Human Services to
9 evaluate these issues for limited English proficiency.

10 The OCR's Safe Harbor is 3,000. We would see that
11 with at least 20 languages, and as far as I can tell
12 not much is being done.

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

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

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

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

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

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

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

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

8 DR. OUTTERSON: All right. Thank you.

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

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

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

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

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

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

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1 today.

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

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

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

25 Our basic approach extracts severity terms

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

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

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

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

8 So now we can ask how serious is serious?

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

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

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

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

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

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

3 And then people would see an individual
4 side effect, one at a time, and judge in the severity.

5 This time it was a numeric scale from 1 to 5. And we
6 used both the descriptive terms and the action terms.

7 Does it matter? Well, here we are plodding perceived
8 severity from least to most for each category of side
9 effects and, as you can see, the results are
10 identical. And that's great because this says that we
11 have multiple options for how we communicate the
12 severity of side effects that might be used with
13 different populations.

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

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

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

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

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

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

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

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

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

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

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

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

13 And where it says Adderall may decrease growth and
14 cause weight loss.

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

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

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1 The metric doesn't go higher than 12th grade. And the
2 bullets tend to be much lower. This is between 8th and
3 9th grade reading level. So something to think about.

4 Also, the use of passive, when people lapse into
5 text, they tend to write impassive. There is huge
6 research literature in psycholinguistics showing that
7 people have trouble processing passives quickly and
8 efficiently and accurately. So there are implications
9 now for comprehension, memory and behavior from all of
10 this. And that will then drive how we provide risk
11 communication tools.

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

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

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

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

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

25 And seeing the picture of how these

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

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

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

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

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

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

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

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

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

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

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

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

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1 showed the potential for 100 percent comprehension.

2 DR. DAY: Yes.

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

5 DR. DAY: This is not hypothetical.

6 CHAIRMAN SELIGMAN: It's not hypothetical?

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

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

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

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

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

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

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

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

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

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

15 So I've done research sponsored by the
16 USP. I used to put out a lot of patient information.

17 I recently attended an American College of Physicians
18 Foundation conference where some of this came up. I
19 think all the stakeholders need to provide risk
20 information in a cognitively enhanced way so people
21 can get it and know what to do about it.

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

25 DR. GOTTLIEB: Some examples of -- not

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

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

8 DR. GOTTLIEB: Fair enough.

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

17 Within companies, I think there are
18 different issues. A lot of times documents are
19 serving multiple needs. There is a legal need. There
20 is a regulatory need. There is a communication to
21 whoever the users are need. And very often, I think
22 that the legal need then drives putting in more risks,
23 just so the company is covered should anything happen.

24 But then how do you handle that increased load? It's
25 not necessarily the case you should leave most of them

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

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

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

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

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

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

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

25 This we view to be both a patient safety

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

5 The broader question we are looking at is
6 do patients understand how to safely take their
7 prescription medications and how do they get that
8 information? Our team has long studied health
9 literacy, which over the past year has become an issue
10 of national concern with reports from the Institute of
11 Medicine, Agency for Healthcare Research and Quality.

12 It has been something that has been included in
13 Healthy People 2010. And the body of literature over
14 the past decade has grown to about nearly 200
15 publications in professional journals.

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

25 So when patients gravitate towards the

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

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

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

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

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

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

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

25 There are no standards or regulations to

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

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

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

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

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

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

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

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

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

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

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

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

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

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1 be published in early 2006. Thank you.

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

25 The lessons we take away from this

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

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

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

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

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

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

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

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

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1 symptoms.

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

10 And then in this particular case, risk of
11 heart attack within 10 years is described as a 30
12 percent increase over their baseline risk. Most of
13 these women said they felt that their baseline risk
14 was the population baseline risk. In the case of the
15 other questionnaire that described absolute risk, that
16 information was presented as a 10 year risk of 65 per
17 1,000 or 6.5 percent.

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

25 And what we show here on the data on

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1 myocardial infarction risk is you see on the Y axis is
2 the maximum acceptable risk and on the X axis the
3 level of benefit. Women who were presented with risk
4 as an absolute risk were willing to accept a higher
5 level of risk to achieve therapeutic benefit than
6 those who were presented information as relative risk.

7 And, interestingly, the dashed yellow line shows the
8 estimated risk, absolute risk level determined from
9 the Women's Health Initiative Study.

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

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

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

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

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

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

25 We also conclude that the patient

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

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

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

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

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

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

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

12 DR. DAY: I think my microphone is off.

13 CHAIRMAN SELIGMAN: The button should be
14 up.

15 DR. DAY: Yes.

16 CHAIRMAN SELIGMAN: There you go.

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

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

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

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

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

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

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

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

4 DR. WOLF: May I make a comment?

5 CHAIRMAN SELIGMAN: Yes, please.

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

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

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

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

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

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

15 CHAIRMAN SELIGMAN: Dr. Kweder?

16 DR. KWEDER: I have a comment and a
17 question to clarify, that you might clarify, Dr. Wolf.

18 One is thank you for bringing up the point about the
19 warning labels are not always necessarily based on
20 very much. My own experience is that I have taken
21 medication regularly, and every time I pick up my
22 prescription it has a sticker on it that says "Do not
23 drink alcohol while taking this medication."

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

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

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

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

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

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

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

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1 sweet.

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

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

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

25 "For external use only," which is at a

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

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

17 DR. KWEDER: You did.

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

25 Does that change? Should that change any

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1 of our thinking here?

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

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

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

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

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

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

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

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

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

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

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

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

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

17 DR. ANDREWS: I would like to add --

18 CHAIRMAN SELIGMAN: Please.

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

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

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

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

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

15 CHAIRMAN SELIGMAN: Yes, Dr. Smith?

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

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

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

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

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

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

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

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

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

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

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

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1 find out.

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

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

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

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

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

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

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

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

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

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

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

6 DR. KWEDER: That panel.

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

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

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

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

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

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

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

25 So over and beyond my particular computing

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

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

7 DR. DAY: Oh, many times.

8 DR. KWEDER: And how did you do?

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

11 DR. KWEDER: Okay.

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

18 DR. KWEDER: Okay.

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

25 I like the array, but it's a dizzying

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1 array, what are these and what is a press release and
2 what is a talking point and what is a da, da, da, da?

3 And, yes, there's always buttons for them. Well,
4 now, the good thing is is that when you're in a given
5 tool, there will be appropriate links and then, you
6 know, they say something. You can click on them and
7 try them, so that's good.

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

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

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

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

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

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

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

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

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

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

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

5 DR. SMITH: That's different.

6 DR. ANDREWS: Yes.

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

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

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

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

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

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

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

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

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

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

10 MS. TOIGO: Yes.

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

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

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1 such.

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

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

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

23 MS. TOIGO: Thank you.

24 CHAIRMAN SELIGMAN: Last question, Dr.
25 Trontell.

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

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

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

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

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

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

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

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

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

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

17 What is lost in all of this "be
18 representative" testing is that all people are people.

19 They have basic cognitive processes. Barring any
20 disease processes, such as Alzheimer's Disease,
21 etcetera, we all process information in similar kinds
22 of ways.

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

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

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

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

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

25 So, for example, if it is an injectable

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

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

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

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

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

25 So I am suggesting an overlay within, not

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

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

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

24 (Whereupon, at 10:18 a.m. a recess until
25 10:33 a.m.)

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1 CHAIRMAN SELIGMAN: Before we begin, just
2 a reminder again that the National Transportation
3 Safety Board does not permit food or drink here in the
4 auditorium. With that, let's begin the second panel.

5 Our first speaker is Dr. Sidney Wolfe from the Public
6 Citizen's Health Research Group. Dr. Wolfe? You can
7 use the podium if you like.

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

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

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

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

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

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

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

7 And the first example is approving drugs
8 whose preapproval risk clearly outweigh the benefits.

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

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

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

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1 evidence of liver damage caused by Trovan in animals
2 and humans before the drug was approved in December
3 1997. In one preapproval study in which the drug was
4 used to treat prostatitis, 10 percent of the men given
5 the drug developed evidence of liver toxicity, 14 out
6 of 140.

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

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

25 At the time of our 1999 petition to ban

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1 the drug, there were eight cases of liver failure,
2 including five deaths and three liver transplants.
3 There were as of December 31st of last year a total of
4 58 cases of liver failure, including 29 deaths and
5 nine transplants. This is especially alarming since
6 for the past several years there were a total of only
7 350,000 prescriptions filled in the whole country.
8 This is over a three year period.

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

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

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

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

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

19 Another example is Baycol or cervistatin.

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

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

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

17 The third category in this Question 3 is
18 the information on risk benefits adequate? Is failing
19 to promptly warn the public with black box warnings
20 when there is new risk information of sufficient
21 concern to merit black box warnings? And the case
22 example here is Vioxx Rofecoxib. A randomized control
23 study published more than five years ago, November of
24 2000, found a 4 to 5-fold increase in heart attacks in
25 people using Vioxx compared to those using Naproxen.

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

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

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

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

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

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

25 Dr. Howard Pomerance, the neuro-

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

7 The fourth category is failing to require
8 FDA approved medication guides for all drugs, even
9 failing to provide them for all drugs with black box.

10 24 years ago, in 1981, and in terms of guaranteeing
11 information going out, it's hard to beat this, I mean,
12 yes, a lot of people don't have Internet access and so
13 won't have to think about ways in which everyone
14 affected is going to get warned.

15 24 years ago in 1981, a carefully
16 researched field tested in a diverse group of people a
17 regulation requiring patient information leaflets
18 approved by the FDA to be dispensed was canceled by
19 the Reagan Administration just before it was to have
20 gone into effect at the behest of drug companies,
21 pharmacy organizations and some physician groups.

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

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

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

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

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

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1 information that they were getting was pretty
2 pitifully deficient. As measured by eight objective
3 criteria, the overall usefulness was about 50 percent.

4 According to the author, "the majority of leaflets
5 did not include adequate information about
6 contraindications precautions and how to avoid harm."

7 The notion that consumer drug information would be 50
8 percent useful is unfathomable.

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

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

25 Because of previous evidence from the

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

8 The preliminary results of the survey of
9 13 pharmacies are summarized very simply in a table,
10 which I have given out here. Of 13 pharmacies, only
11 one of them was giving out a medication guide. None
12 of them explained, as they are supposed to, what the
13 medication guide is for. All of them handed out the
14 non-FDA approved patient information leaflet.

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

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

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

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

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

19 DR. WOLFE: I'll answer afterwards later.

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

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

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

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

16 Okay. Okay. Here we go. Here is CDER's
17 home page. It has an incredible amount of
18 information. And, of course, a lot of people do use
19 the web and could use the web to get that information.

20 So the question is how easy is it to understand it,
21 to find what they need? Let's think of some parents
22 who have a depressed 16 year-old and they are trying
23 to decide whether that child should take
24 antidepressants. And they have heard all this
25 controversy in the news and they are not sure what to

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1 do.

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

10 They would really have to go to
11 information about specific products, specific drugs.
12 So they are looking on here and they are trying to
13 decide where to go. Maybe they would go to the Drug
14 Information Pathfinder. Maybe they would think that.

15 Well, it's drug information, that sounds like what we
16 want. What happens if they go there?

17 Well, they get all of this writing. You
18 get an idea of how difficult it would be to maneuver
19 and how to get this information. It would just be
20 overwhelming. It's not clearly organized and it's not
21 really clear who is this for. Is this for consumers?

22 Is this for doctors? Is this for policy folks? Is
23 this for nonprofit organizations? And I think the
24 truth is it's supposed to be for everybody and because
25 of that, it might not be too clear for anybody.

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

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

17 Now, here is the next one, the patient
18 information sheets. Of the, approximately, 250 drugs
19 on this website, we have calculated only 41 percent
20 have patient information sheets. And we think these
21 patient information sheets are important. We think
22 the design is pretty good. The content is quite good.

23 We do think it's a problem that the date is often
24 missing, so the patient is left or the person looking
25 at it is left not knowing exactly how up to date this

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

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

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

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

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1 This is an example of a drug information
2 page that a person might access through the index of
3 drug-specific information website. And the available
4 documents in this include the FDA drug label, which is
5 62 pages long, a Q&A information about the FDA's
6 announced revision to the drug's label, an FDA press
7 release about its plans and reasons for changing the
8 label and a consumer information sheet that has not
9 been updated since August 2003.

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

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

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1 detailed information.

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

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

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

21 Oops, I don't know why this keeps doing
22 that. Sorry. Okay. So again, this one has no date
23 listed and, actually, the incorrect year is listed on
24 the website. Here it's listed as an advisory from
25 2005, but actually the actual date is June 9, 2004.

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

5 A consortia of nearly three dozen
6 multidisciplinary stakeholder groups, consumer and
7 patient organizations developed this action plan
8 criteria in 1996. The action plan was subsequently
9 reviewed and accepted by the Secretary of HHS in 1997.

10 FDA is, therefore, encouraged to draw on the action
11 plan for guidance and producing consumer-friendly,
12 balanced with respect to risk and benefit and quality
13 of life information and useful patient information
14 sheets.

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

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

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

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

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

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

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

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

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

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

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

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

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

25 In a 2002 presentation entitled

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

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

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

25 Do patients understand the information,

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

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

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

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1 prescriptions.

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

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

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

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1 of Useful Prescription Drug Information.

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

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

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

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

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

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

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

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

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

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

15 If the patient information sheets are
16 going to be produced for all approved drugs, even
17 those that do not have an emerging safety issue, it is
18 important that their purpose and utility is clarified.

19 As NCPIE just stated in it's comments, and I quote,
20 "We would ask FDA to clarify the development and
21 utility of the patient sheet, including its
22 relationship to other written information consumers
23 routinely receive with prescription medicines at
24 community pharmacies."

25 If, however, the patient sheets are

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

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

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

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

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

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

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

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

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

10 The patient information sheets provide an
11 excellent opportunity to promote the MedWatch system.

12 These sheets could direct patients to report adverse
13 events to their health care professional, but would
14 also provide consumers with the MedWatch web address
15 and toll-free number to encourage direct reporting.

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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1 Finally, FDA asked for comment on the
2 specific mechanisms it should consider using to convey
3 risk information, particularly to special populations.

4 First, it is unclear how the Agency plans to get this
5 information out to the general public, let alone
6 special populations. Will the sheets be printed off
7 at the pharmacy, given out by physicians or only
8 accessed through the Internet?

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

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

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

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

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

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

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

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

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1 documents.

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

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

18 I also wondered what CDER was. The term
19 was all over the website and I found this neat program
20 that lets me highlight things. And I had no clue what
21 CDER was since I wasn't a health professional, but I
22 decided I didn't really care. It didn't matter to me.

23 It was just sort of "background noise" in the
24 information I was looking for and I suspect that most
25 consumers would have the same feeling.

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

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

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

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

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

4 So I picked the first one and I went to
5 drugs at FDA. That seemed like a good thing to go to.

6 I came to an alphabetical list. That's good. I like
7 alphabetical lists. Picked one, went to it and then I
8 got overwhelmed. If I were looking for this drug, you
9 know, which of these, I wouldn't know. I picked one.

10 I went to it and decided this isn't the information
11 I'm looking for. This looks more like it's for your
12 health professional or, you know, not your customer.

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

25 The site is supposed to be -- you know,

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1 who is the site for? Think about who the site is for.

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

7 You have the ASCI survey on your website.

8 I know, because it popped up on me several times as I
9 was clicking through, focus groups, useability tests.

10 One thing I didn't list was what are the 100 top
11 terms that people search for on your website. You
12 take those, you make sure that when they search for
13 those 100 top terms they go to a page that gives them
14 the right kind of information for those terms. It's
15 sort of your hot list.

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

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

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

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

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

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

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

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

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1 65 who probably use more prescription drugs than
2 anybody else but, still, you can reach an enormous
3 amount of people for not much money and, yet, you do
4 have a website that is not useable by consumers,
5 basically.

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

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

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

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

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

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

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

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

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

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

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

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

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

25 And, you know, I recognize that you are a

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

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

11 MR. BULLMAN: Yes.

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

15 CHAIRMAN SELIGMAN: Could you activate
16 your microphone, please?

17 MS. BURKHOLDER: Now is it on? Now?

18 CHAIRMAN SELIGMAN: Yes.

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

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

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

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

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

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

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

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1 was just in passing.

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

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

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

25 DR. ZUCKERMAN: Could I add one thing?

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

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

16 PARTICIPANT: It's off the market.

17 DR. GOTTLIEB: Just to follow-up.

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

21 DR. CHEEK: Right.

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

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1 of reliable information.

2 Do you have examples of some of the
3 websites you think are doing a particularly good job?

4 I think we found out the one website you think is
5 challenged, but what is working well out there?

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

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

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

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

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

9 CHAIRMAN SELIGMAN: Ray?

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

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

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1 That is just one small point.

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

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

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

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1 So you can put in sexual dysfunction and
2 130 drugs will pop up and all the information. And
3 the fourth is just by general categories like drug
4 advertising or whatever. So, I mean, I'm sure it's
5 not perfect but assume as one goes to search, it
6 bifurcates into these four ways.

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

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

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

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

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

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

13 CHAIRMAN SELIGMAN: Thank you. Yes, Anne?

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

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

25 Can you elaborate a little more if FDA was

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1 to seek expertise in this area where we might start?

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

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

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

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

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

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

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

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

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

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

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

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

25 And it would be great if somehow the

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

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

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

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

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

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

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

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

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

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

3 DR. CHEEK: And there is always AARP.

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

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

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

25 DR. WOLFE: Right.

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

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

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

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

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1 being shipped to the pharmacist.

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

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

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

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

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

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

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

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

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

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

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

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

25 DR. ZUCKERMAN: Well --

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1 DR. WOLFE: It's a start.

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

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

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

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

12 CHAIRMAN SELIGMAN: Any other questions
13 from Members of the Panel? Well, thank all of you
14 very much for excellent presentations and for
15 responding to our questions. We will reconvene at
16 1:30 this afternoon, in an hour and 15 minutes. Thank
17 you.

18 (Whereupon, the meeting was recessed at
19 12:13 p.m. to reconvene at 1:33 p.m. this same day.)
20
21
22

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

2 1:33 p.m.

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

8 Let me start by first of all apologizing.

9 We originally had two full panels scheduled for this
10 afternoon but, unfortunately, due to various
11 cancellations beyond our control, we now only have one
12 panel which consists of two individuals.

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

20 Tomorrow morning we will again begin at
21 8:00 in the morning and then, as it turns out,
22 tomorrow we, indeed, do have a full day of sessions
23 and panelists that will take us through the end of the
24 day. Again, I apologize. Ordinarily, we like to have
25 the first day a little heavier than the second but,

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

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

5 MS. LIVERSIDGE: Okay. Good afternoon,
6 ladies and gentlemen and Members of the Panel. My
7 name is Ellen Liversidge and I am the mother of a son,
8 Rob Liversidge, who died after taking Eli Lilly's top
9 seller, Zyprexa, an atypical antipsychotic in October
10 2002 and of a daughter who is thankfully alive.

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

8 17 years of life my son had on lithium
9 followed by two years of sliding into death with no
10 warning at all. His death came quickly. On September
11 30, 2002 he said he didn't feel well and thought he
12 should go to the hospital. He was not exhibiting any
13 psychiatric symptoms and to my eternal regret, I did
14 not take him.

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

25 I hope I never have to meet a Lilly

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

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

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

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

25 This presents an opportunity to make my

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

8 It is obvious that several other countries
9 are much more apt to require warnings from
10 pharmaceutical companies than this country, much more
11 apt to act on the side of public safety quickly. If
12 the U.S. had followed the lead of Japan and one or two
13 other countries in 2002, my son would be alive today.

14 Why was this step not taken?

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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1 person taking the drug is the doctor.

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

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

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

25 Eighth point, trust. I know that a lot of

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

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

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

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

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1 families is poor as well.

2 Tenth point, communication responsiveness.

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

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

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

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

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

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

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

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

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1 times?

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

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

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

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

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

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

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

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

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

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

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

14 Let's look at prescription drug compliance
15 in the United States. Of the 63 percent of adults who
16 were prescribed prescription drugs in the last year,
17 33 percent did not take their medications as
18 prescribed, according to Harris Interactive. I have
19 seen other research out there with a much higher
20 number. Some research that about half of all patients
21 are not taking their drugs as prescribed and there are
22 many reasons for this.

23 64 percent of the respondents in this
24 survey said they simply forgot to take their
25 medications. 35 percent wanted to save money. But

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

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

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

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

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1 understanding and acting on health information.

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

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

11 So first, let's look at attitudes and
12 opinions about health care and pharmaceuticals. And
13 if you look at the top row, I have segmented the data
14 by age group. Age 18 plus, 18 to 34, 35 to 49, 50 to
15 64 and 65 plus. Respondents were asked a series of
16 questions and whether they agreed a lot or a little on
17 the following statements.

18 The first one, "I research treatment
19 options on my own and then ask my doctor about them."

20 Almost a third of the population said they agreed
21 with that statement. And the numbers on this slide
22 don't vary very much by age group. But on subsequent
23 slides that I'm going to show you, you will see that
24 they do vary quite a bit.

25 The second statement, "I always read the

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

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

12 Okay. More on attitudes and opinions
13 about health care and pharmaceuticals. The first
14 statement here, "Finding information on health
15 treatments on the Internet is very helpful to me." 32
16 percent of the population agreed with that statement.

17 But if you look at the last column, the age 65 plus
18 group, only 15 percent of the population agrees with
19 that statement. And, of course, that is mainly just
20 to the fact that they don't have very much Internet
21 access.

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

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

4 And the last statement, "Health
5 information put out by drug companies and available at
6 pharmacies is credible and useful." 38 percent of
7 respondents agreed with that statement. And you can
8 see that an even higher number in the older age
9 segments agreed with it. For example, 65 plus group,
10 42 percent of the people agree with that statement.
11 So that may be a good place to reach this segment of
12 the population.

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

23 52 percent of the population values
24 friends and relatives as an information source, but
25 only 31 percent of the 65 plus age group. And I would

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

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

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

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

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

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

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

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

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

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

5 49 percent of these respondents said that
6 prescription advertising provides clear information on
7 the drug's benefits and a slightly smaller number 42
8 percent said prescription advertising provides enough
9 information about the drug's side effects or risks.

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

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

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

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

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

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

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

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

12 CHAIRMAN SELIGMAN: The button should be
13 up.

14 MS. LIVERSIDGE: Should be up. Okay.

15 CHAIRMAN SELIGMAN: There you go. You got
16 it.

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

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

6 CHAIRMAN SELIGMAN: Thank you.

7 DR. KWEDER: I have a question.

8 CHAIRMAN SELIGMAN: Sure.

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

12 MS. LIVERSIDGE: Thank you very much.

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

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

23 MS. LIVERSIDGE: Yes.

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

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

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

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

14 MS. LIVERSIDGE: No.

15 DR. KWEDER: Okay. Thank you.

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

25 DR. KWEDER: Right.

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

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

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

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

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

10 CHAIRMAN SELIGMAN: Maybe that answers the
11 question.

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

16 CHAIRMAN SELIGMAN: Would it be fair to
17 interpret a lot of what you said, is it we really need
18 in this society an approach which provides multiple
19 sources of information?

20 MS. ROTHKOPF: Oh, absolutely, absolutely.
21 And I also think it's a learning process. You don't
22 get everything from just going to one doctor visit.
23 You learn a little from your doctor and then you go to
24 various sources and it could be friends and relatives
25 and it may be the Internet or media, but you do need

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1 multiple sources. And I think new information also
2 comes out at different periods of time and you have to
3 keep up with whatever your ailment is.

4 I also think it would be a good idea if
5 people suffering from various conditions were directed
6 to some of the association websites. I can't imagine
7 why if you have something like diabetes or a heart
8 condition that you wouldn't be on the American Heart
9 Association website or American Diabetes Association.

10 And so many illnesses do have a website that has a
11 wealth of information.

12 CHAIRMAN SELIGMAN: One of the findings in
13 your study that I found a little striking was that a
14 third of the respondents regarding attitudes and
15 opinions indicated that they always read the small
16 print in magazine and newspapers --

17 MS. ROTHKOPF: Yes.

18 CHAIRMAN SELIGMAN: -- and pharmaceutical
19 ads.

20 MS. ROTHKOPF: Yes, I also found that --

21 CHAIRMAN SELIGMAN: I have a hard time
22 actually focusing on it myself.

23 MS. ROTHKOPF: Yes.

24 CHAIRMAN SELIGMAN: Let alone reading it.

25 MS. ROTHKOPF: I found that a little bit

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1 hard to believe and I also think, too, that there are
2 better ways to ask that question. I know the FDA's
3 earlier research said to people if you were very
4 interested in a drug for yourself or someone that you
5 knew or loved, did you read the information? Because
6 most of the time if that's not the case, you really
7 don't have any interest in reading it.

8 And then I think you also have to ask
9 people well, did you read a little bit of it, all of
10 it, just a tiny little piece of it? So I think that,
11 you know, Time Inc. does research periodically on this
12 category and I would like to ask that question, but a
13 little bit more differently. And also ask about the
14 package insert and reading that.

15 CHAIRMAN SELIGMAN: Good. Any other
16 questions, comments from Members of the Panel? Then
17 let me ask if there is anyone in the audience, at this
18 time, who wishes to make a statement or add anything
19 to the record in today's meeting? Again, for those of
20 you who may have missed my opening remarks at the
21 beginning of this afternoon's session, we had a number
22 of cancellations unexpectedly over the last two days,
23 and as a result, we're going to shorten this
24 afternoon's session, because many of tomorrow's
25 speakers couldn't be moved to today.

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1 So we have a full day of panel and
2 panelists and speakers tomorrow. But if there is no
3 one then who wishes to make a statement, I want to
4 thank both of our speakers this afternoon for their
5 input and then call us adjourned until tomorrow
6 morning at 8:00 a.m. Thank you.

7 (Whereupon, the meeting was adjourned to
8 reconvene tomorrow at 8:00 a.m.)
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