

UNITED STATES OF AMERICA
DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION
CENTER FOR DRUG EVALUATION AND RESEARCH

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FDA'S COMMUNICATION OF DRUG SAFETY INFORMATION

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THURSDAY,
DECEMBER 8, 2005

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

MEMBERS PRESENT:

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

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

NANCY OSTROVE, Ph.D.

TERRY TOIGO, Rph, MBA

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

SCOTT GOTTLIEB, M.D.

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PANELISTS PRESENT:

DOUGLAS McNAIR, Cerner Corporation

CHERIF BENNATTIA, AphaRC

ALAN GOLDHAMMER, PhRMA

JOHN WOLLEBEN, Pfizer

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

JANICE DUNSAVAGE, ISMP

JOE CRANSTON, American Medical Association

SUSAN WINCKLER, American Pharmacists Association

TOM LAWLOR, National Association of Chain Drug Stores

NICHOLAS RATTO, First DataBank

WENDY JEZARIANT, Time, Inc.

JOHN KAMP, Coalition for Healthcare Communication

SUSAN KLEIMANN, Center for Plain Language

PETER MAYBERRY, Pharmaceutical Printed Literature
Association

HARRY SWEENY, Dorland Global Health

VANESSA CULLINS, Planned Parenthood Federation of
America

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P R O C E E D I N G S

(8:02 a.m.)

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

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

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

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

FDA's role at this meeting is to listen

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

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

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

15 Before I begin, I would like to just take
16 a moment and have the other FDA members of the panel
17 who are joining me up here today introduce themselves.

18 Nancy, let me start with you.

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

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

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

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

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

7 CHAIRMAN SELIGMAN: Thank you.

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

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

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

24 Dr. Gottlieb.

25 DR. GOTTLIEB: Thanks.

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

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

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

25 Let me take a step back first and give you

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

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

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

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

25 That knowledge is what you read on our

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

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

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

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

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1 consumers.

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

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

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

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

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

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

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

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

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

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

24 Thank you.

25 CHAIRMAN SELIGMAN: Thank you, Dr.

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

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

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

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

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

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

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

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

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

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

4 Mr. McNair.

5 MR. McNAIR: Thank you.

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

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

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

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

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

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

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

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

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

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

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

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

25 Much of what is available both in print

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

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

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

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

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

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

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

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

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

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

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

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

25 There are a variety of issues,

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

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

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

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

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1 rows are prescription, plus-minus, exposed, unexposed.

2 The columns are whether in connection with these 18,
3 19 million odd cases there were or were not new
4 instances of ischemic heart disease, MI or ACS or TIA
5 or stroke, plus or minus in the columns.

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

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

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

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

6 And there are ways familiar to
7 statisticians for seeing whether those two curves are
8 different. SAS and other traditional methods familiar
9 to the FDA are ones that Cerner uses as well, and it
10 turns out that those two curves are different at the P
11 .003 level, a significant difference ascertained by
12 comparing those two.

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

19 Thank you very much.

20 CHAIRMAN SELIGMAN: Thank you, Dr. McNair.

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

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

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

4 I'm going to skip this one.

5 So this slide summarizes somehow all my
6 presentation. I think we all agree now that
7 communicating about risks from any sources to any
8 audience is a challenge, and there is an urgent need
9 to change the way safety information is communicated.

10 That's why we're here for these two days.

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

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

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

25 So why risk communication? I think we all

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

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

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

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

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

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

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

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

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

25 But I think that transparency is

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

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

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

25 The European directives and guidelines

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

25 I've seen some opportunities and I would

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

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

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

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

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

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

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

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

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

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

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1 the Web site, too.

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

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

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

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

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

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

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

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

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

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

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

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

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

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

13 Thank you.

14 CHAIRMAN SELIGMAN: Thank you, Dr.
15 Bennattia.

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

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

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

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

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

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

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

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

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

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

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

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

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

16 However, no clinical program can be large
17 enough or lengthy enough to understand all the risks.

18 Rare adverse events are seldom detected during the
19 clinical development process. It's well recognized
20 that new information on both benefit and risk will be
21 acquired during the post market period.

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

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1 the drug moves into widespread use.

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

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

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

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

25 In addition, consideration must be given

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

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

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

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

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

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

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

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

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

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

25 The first question that FDA posed: one

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

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

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

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

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

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

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

21 This was Question No. 3 that the FDA
22 posed.

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

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

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

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

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

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

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

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

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

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

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1 needs to click down several screens to get this
2 information.

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

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

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

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

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1 This was Question 5 posed by the FDA.

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

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

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

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

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

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

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

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

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

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

25 Collectively, we all have a stake in

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

7 FDA should consider how disparate patient
8 and health care provider information should be
9 presented on the Internet. The current Web site is in
10 bad need of overhaul so that the information is in one
11 place and easy to access. Patients and health care
12 providers should not have to go back and forth between
13 multiple Web pages in search of information. We
14 suggest a single Web portal that's searchable by drug,
15 though it might also be useful to create a separate
16 section on classes of drugs that raise certain issues.

17 There should be a hierarchy of information that
18 begins with the FDA approved drug label and clear
19 notice being given to new safety information if that
20 information has not yet been validated, and as we note
21 here, perhaps the portal could be daily met.

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

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

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

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

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

19 CHAIRMAN SELIGMAN: Thank you, Dr.
20 Goldhammer.

21 Our next presenter is Dr. John Wolleben
22 from Pfizer.

23 Dr. Wolleben.

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

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1 Safety and Risk Management at Pfizer.

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

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

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

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

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

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

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

18 So we commend FDA for its efforts in
19 general to improve medicine safety and specifically
20 for holding this public hearing on communicating risk.

21 It demonstrates the agency's responsiveness to public
22 input and commitment to improving its public
23 interfaces.

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

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1 communicate medicine risks, as well as benefits in a
2 way that advances patient well-being. Today's focus
3 is on FDA tools for communicating pharmaceutical risk.

4 Since Pfizer does not have direct involvement in the
5 production of these FDA vehicles, we will avoid
6 commenting on the specific aspects of them, and as
7 others have done so, we actually support most of the
8 comments that have already been made.

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

15 The first fundamental principle has to do
16 with the maintenance of the benefit-risk perspective.

17 As FDA evaluates risk communication tools, we urge
18 you to consider that any communication it provides on
19 risk be in the context of benefits. The agency cannot
20 effectively inform, educate or guide on safety issues
21 without providing this broader perspective.

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

25 We note that all examination vehicles are

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

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

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

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

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

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

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

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

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1 substitute for it.

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

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

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

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

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

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

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1 and how persons understanding risk concepts and
2 communications.

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

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

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

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1 and writing content at a sixth grade reading level.

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

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

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

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

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

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

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

15 Thank you very much.

16 CHAIRMAN SELIGMAN: Thank you, Dr.
17 Wolleben.

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

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

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

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

19 It's the best possible information to be
20 utilized in treating patients, individual

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

25 I'm going to be addressing four questions,

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

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

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

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

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

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

4 So that's clearly an information extender.

5 Now, the FDA also has, I believe, up to 20 free
6 listserves, and many of us are subscribers to that.
7 Sometimes you get the same notice from more than one.

8 There are all terrific if you know they're available,
9 and if they don't vanish into the white noise of all
10 the things you're receiving every day because we plow
11 through hundreds of E-mails, and that's one of the
12 problems you run into with even terrific information
13 sources, is they get lost in the morass of information
14 that we do get.

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

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

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1 over the last couple of days.

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

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

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

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

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

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

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

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

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

23 So you might look at that and say, "Gee,
24 97 percent were not co-prescribed. Maybe it was an
25 effective notification program."

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

25 A multi-faceted approach, another terrific

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

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

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

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

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

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

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

25 Other things, and this came from a

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

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

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1 they heard as opposed to what they actually did hear.

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

17 Thank you.

18 CHAIRMAN SELIGMAN: Thank you, Dr.
19 Goldman.

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

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

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

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

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

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

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

10 It does not cross that line.

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

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

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

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

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

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

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

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

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

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

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

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1 communication.

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

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

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

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

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

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

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

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

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

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

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

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

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

17 CHAIRMAN SELIGMAN: Thank you.

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

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

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

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

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

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

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

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

25 But I think that in the development of the

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

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

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

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

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

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

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

25 It is a hard balance to strike as to what

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

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

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

18 CHAIRMAN SELIGMAN: Yes, she did.

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

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1 the contact goes out?"

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

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

16 CHAIRMAN SELIGMAN: Dr. Ostrove.

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

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

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

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

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

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

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

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

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

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

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

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

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

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

25 MR. McNAIR: And likewise, Cerner would

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

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

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

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

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1 stays on the market or it doesn't.

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

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

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

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

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

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

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

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

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1 deal of trepidation and with the caveat this is not a
2 PhRMA position; may be, but it's not right now --
3 we're going to be sitting down to talk about what the
4 PDUFA program should look like as we reauthorize it.

5 We heard at the public hearing about four weeks ago a
6 lot of people talking about drug safety. Drug safety
7 needs to be part of PDUFA.

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

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

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

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

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

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

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

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

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

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

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

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

12 CHAIRMAN SELIGMAN: Thank you.

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

20 CHAIRMAN SELIGMAN: We can start with
21 first actually.

22 MR. GOLDHAMMER: I think the first thing
23 to do is you really need to revamp the Internet site.

24 I mean, there's a wealth of information up there, but
25 when I was preparing my talk and I was going back and

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

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

16 CHAIRMAN SELIGMAN: Others that wish to
17 comment?

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

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

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

9 MR. BENNATTIA: I favor with what John
10 said. I think the Web site is important, especially
11 what you do on the Web site, but I think you guys
12 really need to step back a little bit and define what
13 do you want to achieve in terms of risk communication.

14 What are your goals and objectives? What does risk
15 communication mean really for FDA? What's your role?

16 And starting from that, really work with
17 professional agencies, with other partners, maybe
18 PhRMA companies to define, to have your own risk
19 communication strategies and risk communication plan.

20 There you will have the priorities that will come in
21 that plan.

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

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

3 CHAIRMAN SELIGMAN: Dr. Trontell had one
4 more question.

5 DR. GOLDMAN: Did you want responses from
6 us?

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

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

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

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

23 CHAIRMAN SELIGMAN: thank you.

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

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

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

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

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

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

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

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

18 CHAIRMAN SELIGMAN: Go ahead.

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

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

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

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

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

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

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

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

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

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

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

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

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

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

8 Thank you.

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

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

20 I know that some of you sat here patiently
21 now for two days, and I do want to afford the
22 opportunity for individuals who may not be able to
23 stay for this afternoon to say something this morning.

24 If it turns out you are going to stay this afternoon,
25 we will also have some time as well in the afternoon

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

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

8 MS. DUNSAVAGE: Thank you.

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

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

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

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

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

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

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

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

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

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1 formats.

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

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

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

25 The institute already collaborates with

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

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

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

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

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

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1 including physicians, nurses, pharmacists, et cetera.

2 And interestingly, from the pharmacy staff, I can
3 tell you that on an ongoing basis, as front line
4 practitioners are practicing, they almost always have
5 the FDA Web site up and the ISMP Web site up, looking
6 at information as their day goes on.

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

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

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

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

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

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

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

23 CHAIRMAN SELIGMAN: Thank you for your
24 comments.

25 Our next speaker is Dr. Joe Cranston from

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1 the American Medical Association.

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

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

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

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

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

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

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

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

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

25 However, I will also comment on some of

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

22 One, the FDA alert describing the emerging
23 safety concern;

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

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1 on Drug Watch;

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

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

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

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

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

21 CHAIRMAN SELIGMAN: Thank you, Dr.
22 Cranston.

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

25 MS. WINCKLER: Good morning. Thank you

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

17 While all of this information is
18 important, using one type of communication vehicle to
19 communicate a wide variety of information may have the
20 unintended effect of diluting the safety information.

21 Simply put, the number of communication vehicles and
22 the lack of a uniform system to communicate risk
23 information is confusing to providers. There are too
24 many communication tools for pharmacists, other health
25 care providers and consumers to track. Many are also

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

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

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

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

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

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

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

25 While some of the patient information

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

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

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

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

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

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

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

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

25 We've identified some challenges to the

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

7 But these barriers are not insurmountable.

8 They may be overcome. A few simple changes could
9 improve the quality of risk communications and
10 increase providers' and consumers' use of this
11 information.

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

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

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

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

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

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

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1 and what information they need to know.

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

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

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

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

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

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

6 Thank you.

7 CHAIRMAN SELIGMAN: Thank you for your
8 comments.

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

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

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

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

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

3 I am here today to discuss the views of
4 the chain pharmacy industry regarding the
5 effectiveness of the FDA's current risk communications
6 strategies for patients and health care professionals.

7 Walgreens is one of the nation's top employers of
8 pharmacists, and our pharmacists interact with
9 millions of patients every day.

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

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

25 Patients should not be unnecessarily

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

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

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

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

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1 information.

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

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

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

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

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1 different languages, depending upon patient need and
2 request.

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

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

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

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

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

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

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

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

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

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

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

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

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

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

25 You should know that to meet the current

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

11 Thank you very much for this opportunity.

12 We look forward to answering any questions you may
13 have.

14 CHAIRMAN SELIGMAN: Thank you for you
15 comments.

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

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

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

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

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

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

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

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

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

10 About -- I don't know -- seven, eight
11 years ago, the Office of Health Affairs was disbanded.

12 I don't know whether it was that useful. Maybe you
13 folks felt it wasn't and it cost too much to run, but
14 at least you got them there, and I think, you know,
15 most physicians belong to their medical specialty, and
16 that's where they go to learn about, you know,
17 practice guidelines or, you know, what the current
18 educational stuff is. Those are the organizations
19 that run meetings unlike the AMAs, which is primarily
20 a business meeting, you know, not really scientific
21 meetings.

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

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

8 We first made some of these suggestions in
9 2002. We subsequently made them in 2003, and I think
10 in 2004 as well, and nothing has really happened, and
11 so, you know, physicians need the information filtered
12 to them, I think, to some extent, and it also has to
13 be reinforced, and I know the idea of using the
14 detailed folks is probably pretty controversial, but
15 if you go back to the original work that Dave Warren
16 and others, you know, they're really successful at
17 promoting products and getting physicians to use them.

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

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

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

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

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

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

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

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

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

22 CHAIRMAN SELIGMAN: Any other comments,
23 questions? Nancy.

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

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1 a whole lot.

2 You said that the patients tell you that
3 they don't read the information, and I was wondering.

4 The work that you've done, is it qualitative? Is it
5 quantitative? Is it available to the public? Is it
6 something that you could put on the docket?

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

9 DR. OSTROVE: Oh, fantastic.

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

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

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

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

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

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

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

17 DR. OSTROVE: Well, thank you.

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

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

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

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

9 DR. OSTROVE: Right. Thank you.

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

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

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

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

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1 worked from the other way around.

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

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

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

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1 perhaps focused it on the audiences who we're
2 targeting at the information at the right level, is it
3 a patient piece and a health care professional piece?

4 And those are the two things that we need.

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

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

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

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

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

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

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

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

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

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

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

24 It would be really helpful to hear about
25 that.

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

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

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

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

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

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

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

10 Are there any specific examples?

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

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

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1 translate it to a lot of patients quickly.

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

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

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

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

24 MS. TOIGO: Thank you.

25 CHAIRMAN SELIGMAN: With that then let me

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

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

10 CHAIRMAN SELIGMAN: We're not picking up
11 the feed on that floor mic. So just give us a second.

12 Do you want to try again? Hold on. No, I don't hear
13 the one, two, three.

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

9 And finally, again, borrowing from the
10 private industry, the PDR as I said is useless, but
11 they've got other tools nowadays that are very useful.

12 One of them, and just one of them, is Hippocrates.
13 Hippocrates is a PDR-like database that provides
14 useful information for medication that provides weekly
15 updates, sometimes more often than weekly updates, and
16 that also provides a section of handouts to patients.

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

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

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1 It should be there.

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

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

13 thank you very much.

14 CHAIRMAN SELIGMAN: Thank you for your
15 comments.

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

18 (No response.)

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

21 Thank you.

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

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AFTERNOON SESSION

(1:06 p.m.)

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

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

DR. RATTO: Thank you.

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

My name is Nick Ratto, and I hold a Doctor of Pharmacy degree and clinical residency certificate.

My initial training was in pharmacy practice, was with the VA system providing direct patient care services as member of the medical and surgical care teams and also working in clinics in which we had prescriptive authority and counseled patients on a regular basis and interacted with providing drug information to the professionals.

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

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

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

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

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

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

25 The MedWatch monthly labeling changes are

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

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

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

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

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

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

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

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

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

25 I was pleased to note that without my

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1 prior knowledge, other than having looked at the NCPIC
2 information Dr. Bowman presented yesterday, I had no
3 knowledge of the other speakers' information, and I'm
4 pleased to see, again, there's probably a half dozen
5 of them have reinforced to one degree or another the
6 information I'm about to present.

7 FDA approved and authored patient
8 education, whether it be medication guides or PIS, the
9 patient information sheets, communicates risk
10 information effectively to those with a high degree of
11 medical literacy.

12 However, the sizable consumer population
13 that to one degree or another is not medically
14 literate is very likely to misinterpret risk
15 information as presented. This is a serious quality
16 of life issue, as such misinterpretation of the
17 information by a patient frequently results in lack of
18 adherence to the medication regimen or not taking the
19 medication.

20 For example, and I'm about to discuss the
21 Salmeterol PIS, but before I do that, I think I want
22 to emphasize one point. Medical literacy has nothing
23 to do with education level or intelligence. You can
24 have a Ph.D. in chemistry that is medically to one
25 degree or another illiterate or at least less than

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1 fully literate.

2 So we're not just talking about people
3 that have a very low education level or, you know,
4 that sort of thing. We're talking about large
5 percentages of population that can cross many
6 different socioeconomic and ethnic levels.

7 Now, back to the specific PIS that I
8 wanted to use as an example. There was a recently
9 created patient information sheet for Salmeterol,
10 which is a long acting bronchodilator for people with
11 asthma that relieves their wheezing. This sheet
12 begins with the following bolded information, and I
13 quote: "FDA alert. In some patients with asthma,
14 medications called long acting beta agonists may
15 increase the chance of death from asthma problems."

16 A couple of paragraphs later, "because
17 these agents, such as Serevent, may increase the
18 chance of asthma death in some people, the following
19 recommendations are made."

20 Now, if I'm a patient, I think anyone
21 could probably logically walk through this and say,
22 "Why take this medication if it can do more harm than
23 good?" There has been no indication within this
24 information of key information such as how often this
25 is occurring or any other details. It's basically

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1 just saying if you have asthma and you use your asthma
2 medicine, in some people with asthma they will
3 basically -- this medication may kill them.

4 Now, this is supposed to be emerging
5 safety information, and there's a disclaimer that's
6 included to indicate that it is emergent, newly
7 emerging information.

8 However, I would take issue with the fact
9 that it's actually useful partly because of the grade
10 level, but partly because I really -- as a health care
11 professional, I can understand what they're trying to
12 get at, but I don't think a patient necessarily would,
13 and I quote: "this information reflects FDA's current
14 analysis of data available to FDA concerning this
15 drug. FDA intends to update this sheet when
16 additional information or analyses become available."

17 I think you would agree that there is
18 probably a sizable number of people in the population
19 that would not necessarily understand that this is
20 preliminary data, and that's the double edge sword
21 here. You do want to communicate risk information.
22 You want to get the word out early so to speak, but
23 you also do not want to present this as gospel, and
24 typically what's read on Web sites related to the FDA
25 could easily be taken as definitive information, and I

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1 don't see that this disclaimer properly addresses the
2 fact that this information is, in fact, preliminary
3 and that people would really understand what that
4 means the way it's described here.

5 Salmeterol nonadherence could result in a
6 decreased quality of life due to poor asthma control
7 and needlessly restrictive physical activity because
8 of that poor asthma control. Salmeterol can
9 significantly decrease the number of asthmatic
10 episodes. It has been used for several years in many
11 patients and has been very effective, and there is a
12 paradoxical drug related wheezing effect that does
13 occur, and this is probably something that is related
14 -- that has been known for a while now, and this
15 probably could be something that's similar to this
16 report in terms of its etiology.

17 But this is an uncommon occurrence. No
18 one debates the point that communication of risk
19 information to consumers is important. However, all
20 too often, as in this case, FDA approved or authored
21 medication information is written by professionals
22 who have not effectively placed the drug risks into
23 proper perspective for those with to one degree or
24 another limited medical literacy, including little or
25 no attempt to present the drug benefit or quality of

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1 life information.

2 Now, at this point I think it's important
3 to define what benefit is, at least in my view of it
4 as a clinical pharmacist. Benefit in FDA terms in the
5 past from various documents essentially in terms of
6 medication information anyway has focused primarily on
7 how to get the most benefit out of the drug meaning do
8 you take it with food; do you not. Do you take it at
9 bedtime, that sort of thing?

10 And to me that's fairly low level benefit
11 or shall I say it's sort of the rudimentary issue of
12 benefit, but there's a much greater issue that needs
13 to be discussed in terms of quality of life, and that
14 would be what is the benefit of the drug for you in
15 terms of your overall disease and quality of life.

16 So, for example, with the statin drugs for
17 cholesterol, I've heard other speakers here, and I've
18 read information that says benefit is communicated
19 everywhere. Benefit is communicated, you know, all
20 over the direct to consumer advertising and all of
21 that sort of thing.

22 And, again, I'm not here by any means to
23 be a representative of the pharmaceutical industry.
24 We're an independent organization, and I'm speaking on
25 behalf of patient care. I don't think that saying

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1 that a medication will help control your cholesterol
2 is necessarily benefit information, at least not
3 complete.

4 What's more complete and what we state in
5 our information is that by decreasing cholesterol
6 levels, that you can help prevent heart attacks,
7 strokes, and other, you know, serious diseases. And I
8 think that is more of an incentive to patients to
9 understand as they're making an informed choice in
10 weighing risks and benefits. That helps them
11 definitely get more information related to the drug's
12 actual effect as opposed to some laboratory effect
13 perhaps.

14 Another factor to consider that has been
15 alluded to by a couple of other speakers is that no
16 one tracks the morbidity and mortality consequences of
17 noncompliance or nonadherence with drug regimens due
18 to excessive fears because the patients are to some
19 degree or another medically -- they're not fully
20 literate, and these spheres can be generated by poorly
21 communicated information.

22 But be assured that harm does occur. If
23 patient are not taking their medication for a
24 prescribed condition, assuming it was prescribed
25 properly, then if they stop taking it because of

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1 exaggerated fears or poorly interpreted information,
2 then harm certainly could occur.

3 I think the old saying is relevant.
4 Frequently it's not what you say, but how you say it.

5 So what might be a more effective way to communicate
6 he Salmeterol bronchospasm risk?

7 Here are excerpts from one of our
8 monographs as an example, certainly not the only
9 example, but an example of a more useful approach to
10 communicating risk information in a proper
11 perspective.

12 Now, again, I'll remind you of what was
13 said on the FDA alert. In some patients with asthma,
14 medications called long acting beta agonists may
15 increase the chance of death from asthma problems.
16 Now, what we've done to incorporate that basic
17 information, which by the way is related to
18 information showing that some patients when they're
19 using their inhaler have unexplained severe cases of
20 wheezing that can lead to death, and that, again, has
21 been to one degree or another for perhaps different
22 reasons has occurred in the past and has already been
23 noted, but now has been highlighted with this new
24 information, which is important to be highlighted.

25 However, what's lost in that is that the

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1 number of overall episodes is decreased, and certainly
2 not every patient by any means, since it's uncommon,
3 experiences this particular problem. So the large
4 majority do have significant relief of their asthma
5 symptoms if it's prescribed properly.

6 So our statement is rare, parenthetically
7 possibly fatal, asthma type breathing problems have
8 occurred with the use of products containing
9 Salmeterol. Do not stop your medications for asthma
10 or other breathing problems without doctor approval
11 since your condition will worsen if you suddenly stop
12 your treatment. Consult your doctor or pharmacist for
13 more details.

14 Now, we go on in our how to use the
15 medication section to discuss a number of issues
16 related to how to monitor, if you're using your quick
17 relief inhaler, which asthmatics automatically should
18 have had prescribed well before they receive
19 Salmeterol. We discuss how many inhalers they should
20 be using per month before they get concerned that they
21 are using too much.

22 We also indicate that using your quick
23 relief inhalers more often than the scheduled amount
24 may be a sign of worsening asthma in that it's
25 serious, and that if symptoms do not improve or if

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1 they worsen after using the medication, call your
2 doctor immediately.

3 So the key points here, we've noted the
4 rare incidence of the effects in order to help put
5 this in perspective. The importance of continuing
6 therapy - and this drug, by the way, again, having
7 already been on the market for several years.

8 The importance of continuing therapy until
9 you discuss the issue with your physician or
10 pharmacist is also emphasized. Practical advice to
11 mitigate risk is given in terms of proper dosing and
12 how to recognize and immediately report worsening
13 asthma or severe wheezing because that can be either
14 drug induced or it can be disease induced. They may
15 not be well controlled, but they need evaluation
16 quickly.

17 And the benefit is inferred by saying do
18 not stop the medicine or your conditions will worsen,
19 and of course, we're assuming that they're not having
20 a wheezing episode. We're trying to deal with the
21 fact that some patients may just read the information,
22 become frightened and then just stop their medicine.

23 Dr. Day yesterday gave medication guides a
24 good rating for communicating numbers of side effects
25 or whatever side effects they were addressing, and I

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1 think this information complements what she said, and
2 I think that she may very well be correct about that.

3 In reading them, there's clearly risk
4 information communicated in the med. guides, but what
5 the patient does with the information is what I'm
6 trying to emphasize, i.e., if the risk is communicated
7 without the proper perspective, then the medication
8 may go unused. The patient may stop their medicine.

9 The antidepressant drug class recently
10 received a labeling change regarding increased risk of
11 suicidality in teenagers and possibly adults using the
12 drugs. As an example, First DataBank responded to
13 this risk information with the following update to our
14 CMI, and again, I would expect that other private
15 sector information would be similar in many ways.

16 While antidepressants -- this is in the
17 warning section of our particular consumer information
18 -- while antidepressants can provide great benefits, a
19 small percentage of people taking these medications
20 for various psychiatric conditions have had a
21 worsening of depression or other symptoms, including
22 suicidal thoughts or attempts. However, depression
23 itself can sometimes lead to suicidal thoughts and
24 attempts as well in both children and adults.
25 Therefore, when medications to treat depression or

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1 other psychiatric conditions, parentheses,
2 antidepressants are used, the benefits and risks must
3 be discussed with the doctor.

4 And then we follow with a statement that
5 says, "Tell your doctor immediately if you notice the
6 following conditions," and we note more than a half
7 dozen of the cardinal symptoms that might occur that
8 would trigger concern, such as panic attacks or
9 trouble sleeping, impulsive actions.

10 Watch for these symptoms especially at a
11 time of antidepressant dose change or when an
12 antidepressant medication is being started. Close
13 quote.

14 This information provides the risk and
15 benefit data in perspective. In contrast, FDA's
16 response to this issue was a multi-page medication
17 guide which is almost completely devoted to this
18 uncommon suicidality issue, to the exclusion of other
19 adverse effects and to the exclusion of the proven
20 benefits of the drug.

21 Again, I'm not saying ignore risk
22 information, but it has to be put in perspective.

23 Further, a director within the CDER
24 division stated during a meeting that I attended that
25 while First DataBank -- the text may be true, FDA

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1 would never state that type of information, and he was
2 referring to the fact that the drugs can provide great
3 benefits.

4 Now, it has been well proven for decades
5 that antidepressants treat depression. The reason I
6 bring up that quote is that it indicates that at least
7 with some people in the agency there is a definite
8 level of aversion to benefit information that is a bit
9 stunning.

10 It's not difficult to imagine the amount
11 of fright that can be generated in a parent after
12 reading this medication guide with no other
13 information, looking at three pages, all related to
14 the suicide issues which, again, are uncommon. It
15 doesn't mean that they're not important, but they're
16 the total focus of this, and perhaps as you might
17 imagine, leading to them feeling as though they would
18 not want their child to take the medication.

19 So, therefore, you have in some cases
20 untreated depression, assuming that the patient should
21 have been treated in the first place. You have
22 untreated depression and potentially suicide from
23 untreated depression.

24 However, no one ever tracks that
25 information, or at least not typically. So I'm just

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1 trying to make the point that because it's not
2 tracked, it doesn't mean it's not occurring. As was
3 said in previous lectures, there is the issue of
4 information that -- there is the double edged sword
5 here. You can communicate risk information and you
6 can also cause harm as well as good, depending on how
7 you do it.

8 Antidepressants likely were overused in
9 adolescents, but let's not swing the pendulum
10 completely to the other extreme.

11 The other thing we do with our data that
12 can be helpful in risk communication is provide
13 prodromal symptoms as emphasized. In other words, the
14 early symptoms of whatever condition is arising, we
15 try to focus on those, and also alternate treatments.

16 There was some discussion this morning and
17 actually yesterday as well about the Women's Health
18 Initiative and hormone replacement therapy. In our
19 monographs, we indicate, as were discussed in the fact
20 that there are issues related to risks for hormone
21 replacement therapy. The fact that there's other
22 possible treatments for osteoporosis that could be
23 discussed with your physician or pharmacist, and we
24 give a couple of examples.

25 The bisphosphonate group with fosamax and

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1 reloxifene or Evista in order to give the patient some
2 other information to help make an informed decision
3 knowing all of the benefits and all of the risks that
4 are important.

5 I think just to reemphasize, we must make
6 the paradigm shift to address the general population
7 and avoid the understandable but problematic view that
8 everyone thinks like we do as professionals, and so
9 patients are going to look at information and
10 misinterpret it when it's presented out of perspective
11 or just as basic medical statements, such as I quoted
12 in that PIS for Salmeterol.

13 Now, related to the PIS, what is the
14 purpose of it? The PIS was supposedly for emerging
15 safety information and critical drug information. In
16 fact, there were statements made that it was not
17 supposed to stand alone, not be a complete CMI
18 document, and the PIS was intended only for those
19 selected drugs.

20 However, the agency now has revised this
21 plan, as was noted by other speakers, and at least on
22 paper has intended to produce a PIS for all drugs,
23 despite the existence of a complete CMI database among
24 a few different companies that already exist, in other
25 words, reinvent the wheel.

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1 CHAIRMAN SELIGMAN: Mr. Ratto, if you
2 could take a minute to conclude your remarks, please.

3 DR. RATTO: Okay. What standards for
4 patient education content and format will the PIS
5 meter exceed? The FDA has not been -- the standards
6 have not been applied for medication guides or PIS
7 that are applied to the private sector, and that's the
8 Keystone guidelines or the action plan, and they
9 should be applied to all equally.

10 What resources are available to FDA to
11 order to produce a PIS for all drugs, any surplus
12 resources must be relatively scarce, and at this point
13 there are some problems related to the professional
14 labeling, let alone attempting to start a new effort
15 in the consumer arena, and one example is the
16 hypotension effect that has occurred with Viagram and
17 nitrate heart medications.

18 The professional labels were looked at for
19 nine different nitrate products about a year after the
20 initial report of the fatalities and problems with
21 people having hypotensive episodes, and three of those
22 labels on the professional side had no information
23 whatsoever about that particular warning, whereas,
24 three had the outdated relative contraindication and
25 three more had the correct absolute contraindication.

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1 So if this type of situation exists with
2 professional labeling, it's difficult to envision the
3 agency assuming a new resource intensive role in
4 authoring and maintaining PIS.

5 Also, how will the usefulness of the PIS
6 be assessed and validated? Currently the FDA is
7 planning to formally assess private sector CMI in
8 2007, but no FDA authored or approved CMI has ever
9 been systematically assessed versus standards or
10 validated for usefulness in consumer testing, and we
11 feel that it should be assessed objectively with the
12 same criteria applied to the private sector.

13 From a consumer patient care perspective,
14 it's logical and responsible to propose that FDA use
15 resources they might use on creating PISes instead for
16 CMI consumer testing in cooperation with NCPIE, who
17 they have commissioned actually to work on the CMI
18 project so that the information can be improved.

19 This is despite flaws in the 2001 survey
20 that's been quoted. The private sector has been
21 working diligently with NCPIE objectively assessing
22 and enhancing CMI. So why reinvent the wheel? Why
23 not work together with the FDA in the consumer's best
24 interest by reviewing the data as it exists?

25 FDB, First DataBank, and other NCPIE

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1 stakeholders stand ready and able to work
2 constructively with the agency for the optimum benefit
3 of the consumer.

4 thank you.

5 CHAIRMAN SELIGMAN: Thank you, Dr. Ratto.

6 The next speaker is Wendy Jezarian from
7 Time.

8 MS. JEZARIAN: Good afternoon. Thank you
9 for having me here. My name is Wendy Jezarian, and
10 I'm from Time, Inc., and I'll be taking you through
11 portions of a research study that we conducted last
12 fall with Harris Interactive.

13 Our study was conducted on line in late
14 September, early October of 2004, and the study was
15 adjusted for the fact that it was conducted on line and
16 is representative of the U.S. adult population.

17 In this study, caregivers were defined as
18 someone involved in the care of an ongoing medical
19 condition of a family member or friend. Of our total
20 sample of over 3,500 respondents, 19 percent of the
21 population characterized themselves as caregivers.

22 This is a brief profile of caregivers. As
23 you can see, they are more likely to be female and
24 also to be a sufferer of some illness themselves.

25 In addition, more of them are taking

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1 medications and are taking a higher median number of
2 prescription medications. We've postulated that one
3 of the reasons for this trend is that caregivers are
4 under greater amounts of stress due to their
5 caregiving, and this takes a toll on their own health.

6 We found that caregivers are most likely
7 to be caring for a family member, their spouse or
8 partner in 44 percent of the cases, and almost a
9 quarter are caring for an elderly parent while one in
10 five are caring for a child.

11 Our study found that caregivers are
12 overseeing a variety of illnesses, almost all of which
13 require long-term treatment and management and which
14 may include a regimen of prescription medications.
15 Four of the top five conditions seen here,
16 hypertension, diabetes, cholesterol disorder, and
17 heart disease, are related to metabolic syndrome and
18 are on the rise in the U.S. due to lifestyle factors.

19 Here are the three main ways in which we
20 found that caregivers assist patients with their
21 medical conditions, and I'm going to go in more depth
22 about each of these in the next few slides.

23 First, let's look at different ways that
24 caregivers intervene with the patient's doctor.
25 Nearly nine out of ten caregivers go with the patient

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1 to see the doctor, and between 65 and 70 percent
2 encourage the patient to continue with the prescribed
3 treatment and/or talk to a doctor about their
4 condition. Sixty-three percent make the doctor's
5 appointments for the patient.

6 So we see that caregivers are influencing
7 the patient's actions and are a key to compliance.
8 Therefore, the caregiver needs to hear and understand
9 the benefits and risks of treatment options since
10 treatment appears to be a joint effort in many cases.

11 Now, let's examine how the 92 percent of
12 caregivers help with the patient's medications.
13 Nearly 85 percent help the patient by picking up the
14 prescription for them. About six out of ten help the
15 patient remember to take their medications and/or help
16 administer them.

17 These numbers are important because they
18 illustrate that the caregiver is interacting with the
19 pharmacist, is helping to administer medications and
20 can be a key to compliance. Therefore, in addition to
21 the sufferer, the caregiver needs to be made aware of
22 dosage information, side effects and risks, and
23 possible drug interactions.

24 As you recall, earlier I stated that 74
25 percent of total caregivers said they looked for

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1 information about the patient's medical condition, and
2 this slide looks at the information sources that they
3 used.

4 On the next slide, we'll look at
5 information sources they used to learn about
6 prescription medications. Here we see that health
7 care providers are the primary source of information
8 about the condition, at 86 percent. After health care
9 providers, we see about four in ten turning to the
10 Internet and direct marketing, nearly one third
11 turning to magazines.

12 These types of media suggest caregivers
13 are proactive searching for detailed information from
14 sources that can educate them and are turning to
15 written forms which could be passed along to their
16 patient.

17 We then looked to see if these sources
18 differed from the sources used by recent sufferers to
19 learn about their condition, and we defined recent
20 sufferers as those who have been doctor diagnosed
21 within the last two years.

22 We found caregivers to be significantly
23 more likely to use proactive sources of information,
24 such as health care providers, direct marketing, and
25 pharmaceutical company Web sites.

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1 We also found that they were significantly
2 less likely to use a passive medium, such as
3 television, as an information source.

4 This chart shows us the information
5 sources used by caregivers to learn about prescription
6 medications, comparing caregivers to the general
7 population. Caregivers are more likely to use the
8 majority of these information sources, significantly
9 so for health care providers, direct marketing, the
10 Internet, newspapers, pharmaceutical company Web
11 sites, and medical books and journals.

12 You'll notice that the media types that
13 are used as a source of information on prescription
14 medications are similar to the sources that caregivers
15 use to learn about the patient's conditions, sources
16 where they can be proactive and get detailed
17 information, and again, they're less likely to turn to
18 TV as a source.

19 Also noteworthy, other friends and
20 relatives are important sources of information,
21 building on the idea that the circle of people around
22 the sufferer are influential and should be informed
23 and communicated to.

24 In response to seeing information on a
25 condition or treatment option, caregivers are likely

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1 to take action. In fact, they're just as likely to
2 take action for a family member or friend as for
3 themselves, and of particular importance is talking to
4 a health care professional and looking for more
5 information.

6 In summary, our study found that
7 caregivers are very involved in the care and treatment
8 of their patient and, therefore, should be well
9 informed of the risks and benefits of treatments and
10 medications.

11 Also, in addition to consulting with their
12 health care provider, caregivers are likely to turn to
13 proactive written sources of information on their
14 patients' conditions, as well as on prescription
15 medications.

16 And caregivers are likely to take action
17 as a result of communications regarding conditions and
18 medications, including increasing compliance and
19 seeking out more information.

20 Thank you for your time.

21 CHAIRMAN SELIGMAN: Thank you.

22 Our next presenter is John Kamp from the
23 Coalition for Healthcare Communication.

24 MR. KAMP: Thank you very much.

25 Just quickly, the Coalition for Healthcare

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1 Communication is a coalition of trade associations and
2 professional communication companies that support
3 drug, device, and other companies in their
4 professional communication. We're not speaking today
5 for any of those specific companies or representing
6 PhRMA as an institution or any of the PhRMA companies.

7 Just sort of quickly, my major points are
8 we'll talk about the need for new policy; some of the
9 limits I think that we all are beginning to understand
10 from the two days of discussions; the need that I
11 don't think surprises you now after two days about a
12 clear distinction between professional and consumer
13 communication; some ideas about some of the court
14 requirements that we might all face; and a thought
15 that hasn't been discussed before about the protection
16 of the FDA jurisdiction in this area.

17 The existing policy problems, this has
18 been a fascinating discussion for the last two days,
19 and I thank you for our opportunity to participate in
20 this dialogue. I want to put sort of a finer point
21 about what we've been talking about and what we're
22 really talking about, and part of it is my point of
23 view because I happen to have gone to law school, even
24 though I try not to think like a lawyer all the time.

25 But there's really two different basic

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1 questions going on here, and the first one is fairly
2 simple, but still hard to execute, and that is the
3 general question that we were asking most of yesterday
4 about how do you do what we're doing now better,
5 you're actually at the end of the first panel this
6 morning.

7 What's the role in all of this though is
8 another question, and I raise all of this because I
9 think that the second question, what's the role of the
10 FDA particularly in consumer facing communication
11 about risk and other information may be a new question
12 and may have some legal aspects to it.

13 Essentially let's think about the question
14 about whether or not the FDA wants to get in the
15 business of doing consumer labeling as the gold
16 standard and the legal standard that virtually every
17 other organization that does consumer facing
18 communication about drugs has to follow, particularly
19 the regulated industry.

20 That is a fairly new idea. It's not a new
21 idea for the FDA to participate, to collaborate with
22 NCPIE, all the other organizations, and it's not a new
23 idea for the FDA to supervise the communication of
24 direct to consumer advertising by the companies, but
25 the idea that the FDA essentially take on the sort of

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1 super labeling notion for consumer facing
2 communication is a new idea, I think. It's an idea
3 that I fear that PhRMA lawyers might like too well.

4 And one of the discussions that I think
5 several people had over the last couple of days is
6 that one of the problems with professional labeling is
7 that it serves the legal community inside of PhRMA
8 companies perhaps too much, and in serving that
9 master, it doesn't serve the prescribers very well in
10 doing so.

11 And I fear that a similar thing might
12 happen if there is a gold standard by the FDA that
13 everyone has to follow, and so I think the suggestion
14 that I have is that you think about whether or not you
15 really want to go there or if the existing process
16 where you collaborate rather than create the gold
17 standard, if the existing process is broken or you
18 want to go and take on what I call the new
19 responsibility.

20 If you do that, I have a few notes from
21 the trenches about that for some things for you to
22 think about. Consumers are complicated. You know,
23 some folks think that consumer communication is not
24 rocket science and we can all do it, but I think what
25 we found out for the last two days is that it's a lot

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1 harder than we thought.

2 In fact, I think consumer communication
3 may be harder than rocket science. It may be harder
4 than medicine. I suggest that you may want to avoid
5 some of the mistakes that the PhRMA companies have
6 done in consumer communication over the last 15 years
7 since the explosion of DTC advertising.

8 Think about the PhRMA principles, PhRMA as
9 a self-regulatory volunteer process has essentially
10 developed some new principles about DTC that the
11 companies are all agreeing on, and one of the first
12 things that they're agreeing on in DTC advertising is
13 to focus again on the prescribers and make sure that
14 the prescribers get it first before they start rolling
15 out DTC.

16 They're also taking very seriously the
17 notion of risk communication and the discussion of
18 risk communications in ways that clearly can be
19 understood by consumers instead of putting them all in
20 the end in the mouse type or in the real fast type,
21 with maybe distracting things going on.

22 They also sort of got it, and they're no
23 longer going to put ED ads. during family time. Don't
24 upset the consumer unnecessarily. Don't create a
25 situation for yourself that you have to go back and

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1 fix.

2 I think these are some things that even
3 the FDA might have -- there might be some parallels
4 on.

5 I want to use an example of one of the
6 ads, what I think of as the post-PhRMA guideline ads,
7 but the PhRMA guidelines really don't go into official
8 effect until January, but just use one ad as an
9 example of the kind of things that the PhRMA companies
10 are now doing in their consumer facing communication
11 that I think are helping them communicate more
12 effectively.

13 The troperads (phonetic) -- and we're
14 going to look at one of them in just a moment --
15 there's a lot of focus on disease education. There's
16 a lot of focus on compliance by the patient. The
17 messages about benefits and risk are really very clear
18 -- and then the thing that I think is very hard for
19 us, and I'm a former government enforcement person --
20 I think it's hard for the government to do, engaging
21 creative.

22 The reason for the new approach, why in
23 hypertension area do we have to look at this
24 differently, Astra Zenica in this case? The high
25 rates of noncompliance. They jeopardize the patient's

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1 health. They make it more and more likely that very
2 expensive treatment for complication is going to come
3 later.

4 We heard some of the statistics yesterday.

5 The statistics sort of range across the basis, but
6 it's really appalling to think about of the people who
7 are treated for hypertension, somewhere between 30 to
8 60 percent of them are not compliant with the drug
9 regimen. This is a huge number of people.

10 We're not talking about the people who are
11 not yet even diagnosed, less treated. We're talking
12 about the people who are being treated. There's
13 clearly a problem here. Consumers aren't getting it.

14 And it's interesting in the research that
15 was done on this. Not surprisingly, here the patients
16 that are taking these drugs who have been diagnosed
17 with hypertension who are taking the drugs sort of
18 know that it's a bad thing not to be compliant, but
19 they think that it's bad thing for other people.
20 It's sort of like the early days of safety belts. All
21 of us thought it was a good idea to wear them, but
22 when it came to whether we need to wear them, they
23 weren't so sure. These very patients were the focus
24 of the ads.

25 So what did drug companies do in all of

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1 this? They've essentially first researched the
2 audience, and the research of the audience for these
3 people, what did they find out? Consumers respect the
4 doctors. The patient, and what the company found here
5 is that the model for this is the consumer-patient
6 dialogue.

7 They also found out that consumers really
8 want to understand the risk information, the
9 compliance information, but it must be very clear, and
10 it must not be complicated.

11 Also, it must be reassuring, not
12 frightening. Several other people have talked about
13 that today and yesterday. One of the suggestions
14 today, I think, by Dr. Goldhammer at PhRMA was that if
15 you frighten someone, you've got a much larger barrier
16 to get past to get them then to understand more about
17 what's going on and then particularly to be compliant.

18 And then I think, you know, it's
19 intuitive, but also supported by the research, the
20 physicians, whatever the communication is must support
21 the physician's discussions. Physicians themselves
22 like the kind of compliance messaging that we're
23 talking about here, and they like DTC campaigns that
24 support their messages, particularly on compliance
25 contraindication side effects and warnings.

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1 So let's take a look at it. Can we run
2 the ad right now? We'll just take one example of sort
3 of how it works.

4 (A video was played.)

5 MR. KAMP: This is the kind of
6 communication that I think works. In fact, I want
7 that doc. I think his raised eyebrow said more than
8 any of the contents said, and if he raised his eyebrow
9 at me, I'm going to take my drug.

10 The next thing that's going to happen with
11 this series of ads is to measure the results. There's
12 now in the field some measurement about what's going
13 on here. There's some measurement about most
14 importantly whether the patients really understand the
15 message, the black box warning kind of message,
16 whether patients intend to discuss it more directly
17 with their doctor at their next visit, whether they
18 intend to adhere to the drug regimen, whether they
19 really understand the value of compliance after seeing
20 one of those ads.

21 Actually they're going to do some tracking
22 study on this message understanding, and then more
23 important going directly to the question that Dr.
24 Smith asked yesterday, one of the things they're going
25 to be doing is looking to see about the behavior

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1 change. Do the patients actually make a change based
2 on this ad?

3 So, you know, again, it's just an example
4 or the kind of thing that has to be done to do good,
5 clear patient communication. It's the warnings. It's
6 the encouragement about compliance. It's the benefit
7 and risk information that's in this clear, realistic,
8 and fair, serious matter. It's about the availability
9 in this case they're working on their patient
10 assistance program, but it also entertains and engages
11 the patient in ways that I think at least when I was a
12 government employee trying to communicate with the
13 press and the Congress and the public, engaging the
14 consumer or the audience member was not something that
15 we were particularly good at.

16 With all of that aside, meanwhile let me
17 give, you know, some of our free advice about some of
18 this. I think that there is clear guidance that's
19 possible from the FDA that can help us all get where
20 we need to go.

21 More objective, predictable standards by
22 the FDA, maybe even a clarification about this notion
23 of whether the FDA, in effect, wants to take on this
24 role of being the creator of the gold standard in
25 consumer communication or wants the rest of us to do

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1 it as well as possible with the FDA giving very clear
2 oversight.

3 Some value of consistency from the FDA, of
4 course, would be useful. Respecting the differences
5 we heard from virtually all of the witnesses yesterday
6 about the difference between professional and consumer
7 communication.

8 I have to use this forum to talk again
9 about brief summary form. I think it's time for the
10 FDA in the context of DTC advertising, which is not
11 really the central focus of this, but we're talking
12 about essentially the same kind of information on the
13 patient package insert and elsewhere; we have to
14 issue, I think, the final guidance. We have to have
15 that guidance give us the ability to do clear,
16 uncomplicated messages and in a format that work.

17 And it's time. I notice that Bob Temple
18 is not here today. Bob Temple was the first one who
19 used what I thought was a fabulous analogy in 1995.
20 He said at that time at a DTC hearing that the brief
21 summary has no friends, and it's like the Holy Roman
22 Empire. It's not holy; it's not Roman; it's not an
23 empire. It's not brief nor a summary.

24 I think it's time for us, all of us, just
25 to blow away and sort of get on with it and get to a

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1 different stage.

2 This is some suggestions from us that if
3 you do make some very clear policy choices essentially
4 to take on officially this role to create an official,
5 gold standard labeling for consumer communication; if
6 you do that because of court requirements, there are
7 some things that need to be done.

8 And the first one, of course, is a public
9 record. The FDA, if it does decide to do some things
10 in there and, in fact, has limits on the commercial
11 speech of other players, even the PhRMA companies, it
12 must articulate the need for the new rules. It must
13 have evidence that the new policies or rules work. It
14 must have considered other alternatives, and it must
15 use marketing limits by drug companies or others. It
16 must use those only as a last resort because nothing
17 else would actually enable the agency to insure that
18 the safety information was understood.

19 I also suggested that I think that there
20 are some very interesting ideas that came out of the
21 last hearing, and they've been being kicked around,
22 and there are some things that I think we ought to
23 keep on the table and think about more seriously.

24 Peter Pitts on November 2nd in this room
25 suggested that maybe we ought to be looking at the

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1 idea of a permanent advisory committee in the
2 communication area or maybe another way of doing the
3 same thing would be to have an advisory committee
4 person in the other advisories, perhaps especially in
5 the new drug approvals, who was a communications
6 expert, and that the agency start developing a set of
7 social science, behavioral science standards that
8 people can know and understand just as it does in the
9 medical area.

10 If it's going to go there, if it's going
11 to take charge of these behavioral science issues, it
12 should put behavioral sciences in the places where
13 these decisions are made.

14 Again, a good, simple rule: high profile
15 enforcement when those rules are broken. It's good
16 for all of us, and use a public process.

17 I also want to put on the table something
18 nobody else has put on the table, but I think we all
19 have to fully understand right now. In these areas,
20 and it's not just the marketing jurisdiction; it's
21 sort of the whole labeling jurisdiction. It's the
22 reputation and the important understanding of the
23 agency as the gold standard in this area. The
24 agency's jurisdiction must be protected. It must be
25 protected not just for the sake of the agency, not

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1 just for the sake of the regulated industry. It must
2 be protected because the American public, citizens,
3 patients need it.

4 We must resist the incursions on the
5 agency's jurisdiction in these very important
6 communication areas by state laws, Attorney General
7 enforcement, state cases, state legislatures. We must
8 resist the private actions, plaintiff's cases on
9 failure to warn and false advertising kind of
10 theories. I think we must resist and work much more
11 carefully even with our own sort of inside the house,
12 the HHS IG and the Department of Justice as they
13 develop their own theories about what's legal and
14 what's legal by the regulated entity under the False
15 Claims Act and anti-kickback statutes.

16 So the summary sort of quickly. I think
17 we all need clear objectives about what the FDA is up
18 to, what it wants to do. If it wants to go in new
19 areas, it must proceed carefully.

20 I think we must separate the consumer and
21 professional warnings and risk communication. We must
22 follow the court mandates for due process, open
23 record, and other kinds of things, and for all of our
24 sakes, especially for the sake of the patients in
25 America, we must resist the attacks on the

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1 jurisdiction of the FDA.

2 Thank you very much.

3 CHAIRMAN SELIGMAN: Thank you for your
4 comments.

5 The next speaker is Dr. Susan Kleimann
6 from the Center for Plain Language.

7 DR. KLEIMANN: Good afternoon. Thank you
8 very much for this opportunity.

9 I must admit, however, that I do not come
10 to speak before you as a person who is a medical
11 expert. I come to speak before you as a person who is
12 a part of the communication field that is interested
13 in plain communication.

14 The Center for Plain Language is only a
15 recent coming together of people, of government
16 employees, of academics, and of private sector
17 consultants who really do wholeheartedly believe that
18 plain language, clear communication, and clarity is a
19 civil right that we owe to every single one of our
20 civilians in the United States.

21 Now, that is going to make me sound like a
22 very strong advocate, and I am, but I do want to be
23 clear that I'm advocating on the part of clear
24 communication.

25 For my own background, I do have a Ph.D.

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1 in composition and rhetoric, and in my business, when
2 I'm not wearing the hat of Director of the Center for
3 -- I can't even remember the name of our center --

4 CHAIRMAN SELIGMAN: Plain Language.

5 DR. KLEIMANN: -- Plain Language -- thank
6 you very much, that I am president of Kleimann
7 Communication Group and have over 30 years of
8 experience in working primarily with government
9 clients, such as VBA, the IRS, recently with the FDC
10 on privacy notices, and with HUD on the good faith
11 estimate.

12 So I've been doing a lot of work in this,
13 and I hope that you will appreciate the kind of very
14 narrow focus that I want to bring today.

15 I want to be able to focus primarily --
16 I'm not a mechanical engineer either. So I apologize.

17 I want to focus really very narrowly today on the
18 Adderall patient information sheet, and obviously I
19 want to talk about what is clarity and how do you know
20 when you have clarity.

21 As a very simple definition, I think that
22 we can say that consumers find the -- clarity is when
23 consumers can find the answers to their questions very
24 easily. As Dr. Ratto said, you know, we're not
25 talking about people who necessarily have a high level

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1 of education or have a high level of intelligence, nor
2 are we talking about the opposite when we're talking
3 about clarity.

4 What we're talking about is people who
5 have questions. That's how we read. If you look at
6 all of the reading research, what you're going to see
7 again and again is that when a consumer goes into a
8 document, they're really looking for only one thing:
9 the answers to their questions, not questions that are
10 necessarily in there, but the questions that brought
11 them to the document.

12 If they can find the answers to their
13 questions, they're very happy readers and we have
14 clarity. And if they can't find the answer to their
15 questions, they're going to do a couple of things that
16 are really quite unfortunate, especially when we're
17 dealing with health information, which is they're
18 going to one stop reading or, secondly, they're just
19 not going to understand what they read and perhaps
20 misinterpret and misindicate upon the information and
21 their misinterpretation.

22 So how do we do this? How do we find out
23 what consumers want to know about a particular
24 product, about a drug, about any of the myriad of
25 things that we want to give them information about?

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1 One is we have to figure out what those
2 questions are. So in preparation for today I did a
3 very, very quick survey asking my own staff. Gee, if
4 you were going to go look for information about a
5 drug, any drug, what are the questions that you would
6 want to have answered?

7 First question, nine out of ten people,
8 are there any side effects?

9 Secondly, will the drug react or interact
10 with other medications or vitamins I'm taking?

11 How long has this drug been on the market?

12 What do I do if I turn out to be allergic
13 to this drug? A very high percentage of people are
14 interested in that, perhaps our sample.

15 Where can I find the information about how
16 or whether this drug was tested?

17 Now, I'm not trying to claim that these
18 are all the right answers. Consumers are complicated,
19 but the point is that we really do need to know what
20 those answers are or what those questions are.

21 Clarity for the consumer is going to be
22 when we answer those questions, the questions that
23 they have. So what's on the information sheet when we
24 go out to the FDA?

25 Well, first, there's the usual FDA

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1 information. I was on the Web site. Dr. Anetta
2 Cheek, my colleague, spoke yesterday about the Web
3 site. So I'll refer you back to her comments about
4 that.

5 There is an FDA alert. There's a warning
6 about abuse, and then there are a series of questions
7 and answers. What is Adderall Rx? Who should not
8 take Adderall? What are the risks? Are there any
9 interactions? And how do I take Adderall?

10 So how did we really do? Well, the first
11 question my staff had is are there any side effects,
12 and it seems to me that the FDA alert and "are there
13 any interactions," both of those are going to get to
14 the consumer or allow the consumer pretty easily to
15 get in and get answers to their questions.

16 What about the second one? Will the drug
17 interact with other medications or vitamins that I'm
18 taking? Again, we have are there any interactions.

19 I will point out that all of the Qs and As
20 are on page 2, however, when you print this out. So
21 you have to delve a little bit into it, but you can
22 get to it.

23 What about how long has the drug been on
24 the market? Not so sure about that.

25 What do I do if I turn out to be allergic?

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1 We certainly have interactions again.

2 And where can I find out if the drug has
3 been tested? I would assume that we would find that
4 under what is Adderall XR or who should not take
5 Adderall or what are the risks. It's someplace in
6 there. I can't go directly to it.

7 Now, again, I'm not trying to say this in
8 a way of saying that that particular patient
9 information sheet is disorganized. My point is merely
10 to illustrate that when you are going to organize
11 information, you want to organize the information
12 around the questions that the consumer has. A sample
13 of ten is insufficient to really predict what the
14 basic questions should be, nor am I presuming that FDA
15 hasn't gone about and done this at some level, but
16 it's really that the consumer's questions need to be
17 able to drive the organization.

18 So if we can assume we can get to that and
19 we can assume that we can make those questions
20 prominent, we're at least part of the way along the
21 road to clarity. What's our next step?

22 Let's look at the language of the Adderall
23 alert, and from now on I'm just going to focus on the
24 little alert.

25 "Health Canada has suspended marketing of

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1 Adderall XR products from the Canadian market due to
2 concern about reports of sudden unexplained death
3 (SUD) in children taking Adderall and Adderall XR.
4 SUD has been associated with amphetamine abuse and
5 reported in children with underlying cardiac
6 abnormalities taking recommended doses of
7 amphetamines, including Adderall and Adderall XR. In
8 addition, a very small number of cases of SUD have
9 been reported in children without cardiac
10 abnormalities taking Adderall. At this time FDA
11 cannot conclude that recommended doses of Adderall can
12 cause SUD, but is continuing to carefully evaluate
13 these data."

14 I believe this is totally intended to
15 communicate to consumers. Let's go back and think
16 about the situation under which this came: a lot of
17 media coverage.

18 You're going to have the anxiety of people
19 going to this because, "oh, my God, my child is taking
20 Adderall," and, again, if we think that we have a very
21 large range of reading levels of people's medical
22 literacy, is this going to address what their needs
23 are?

24 I would argue probably not. Doing a
25 Flesch-Kincaid, we have a reading grade level of 16.7.

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1 Maybe we all have that, but I don't know about the
2 general population. I think we can assume that most
3 people will not have a reading level of 16.7.

4 I think we can also assume that reading
5 levels are kind of false measures. There's much in
6 the newspaper about children who graduate from high
7 school, which would put them at a 12th grade reading
8 level, and who actually can't function at that level.

9 So let's not assume that just because they're a
10 college graduate they're going to have a reading level
11 of 12.

12 Even if I take out the word Adderall
13 because readability formulas are based on some
14 combination of how big are the words and how many
15 words did you put into a sentence and how many
16 sentences do you have in the paragraph. It's a very
17 simplistic way of calculating how difficult something
18 is to read.

19 But even if I took out the word
20 "Adderall," it still stayed at 16.7. So this is a
21 fairly complex little passage that's giving an alert
22 about a drug that's been covered in the media. Again,
23 I think we have a problem.

24 But what I want to be clear about is that
25 readability is a function of so much more than simply

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1 how big are the words and how many words do we put
2 into a sentence and what is the sentence length. So
3 let's see what could we do with a rewrite.

4 In the rewrite that I'm going to be
5 showing you in a moment, it reduces the reading grade
6 level to 13.3. Well, guess what, folks. That's not
7 much better. But is it easier to read? And I'm going
8 to leave part of that to your decision to make.

9 I also, before I show it to you to protect
10 myself, I don't want to presume that this is a perfect
11 rewrite. I'm pretty sure it's not. There may be some
12 technical inaccuracies in it. I do believe that when
13 we're talking about readability and clear
14 communication, technical accuracy is paramount. So I
15 apologize again for my lack of knowledge if I have
16 perhaps not quite gotten the details right.

17 "Status. Health Canada no longer allows
18 marketing in Canada of Adderall XR products. Reason.

19 Some children taking Adderall XR have died suddenly
20 and without apparent cause. A sudden unexplained
21 death (SUD) has occurred with three types of medical
22 conditions: (1) in children with an abuse of
23 amphetamines; (2) in children with underlying cardiac
24 abnormalities and who are taking recommended doses of
25 Adderall and Adderall XR; and (3) in a very small

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1 number of children without underlying cardiac
2 abnormalities.

3 "The future. FDA is looking at these
4 data, but cannot conclude that recommended doses of
5 Adderall can cause SUD. FDA will update this
6 information when we learn more."

7 It's not perfect, but I will argue that it
8 is clearer. Now, why is it clearer? And, again, this
9 is going to speak to readability.

10 What would you rather I do? Should I
11 leave this up so you can follow along with the changes
12 or put my list of changes?

13 Response?

14 PARTICIPANTS: Changes.

15 DR. KLEIMANN: Okay. What did we do?
16 First we set up a predictable structure, a structure
17 that followed status, reason, the future. Not the
18 best words, absolutely not the best words.

19 Even as I was coming over, you know, it
20 could say "What? Why? What's next?" We could make
21 those words work better.

22 But what it does is it gives for an alert
23 a cognitive map for the reader. It allows the reader,
24 a consumer who comes to this, to be able to have a
25 predictable structure if all of them would be

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1 structured in this way.

2 In addition, it categorizes the
3 information according to consumer questions. We all
4 grew up with newspaper articles. Who, what, where,
5 when, why? Maybe those are not the right questions
6 here, but they're still the basic information that we
7 are going to want.

8 What's going on? Why is it happening?
9 And what's going to happen next? Those seem to me to
10 be very basic questions, and if we can group that
11 information for a reader, anticipating what the
12 reader's question is and then labeling it so that the
13 reader can find the answer to his or her question more
14 quickly, we have done a service around clarity and
15 around readability.

16 We simplify words. Let's see. I have to
17 find what the original was. Where the original is
18 talking about "has suspended marketing," well, it's
19 not that those are hard words, but it's a little bit
20 more direct to say it no longer allows marketing, and
21 again, I'm not trying to claim that I've got this
22 precise, but I want you to see the gist, the
23 illustration of the direction these types of alerts
24 could move in.

25 It breaks up long sentences. The first

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1 sentence in the original, "Health Canada has suspended
2 marketing of Adderall XR products from the Canadian
3 market due to concern about reports of sudden
4 unexplained death (SUD) in children taking Adderall
5 and Adderall XR." That doesn't trip off the tongue.

6 And if it is not quite accurate, it is
7 still closer to being controllable if we are saying
8 simply Health Canada no longer allows marketing in
9 Canada of Adderall XR products.

10 The other thing that I did in breaking
11 that sentence is that we separated what the status was
12 or what was going on from the reason.

13 It isn't that "because" is a terrible
14 joiner. It isn't that what comes after it was a
15 terrible sentence or clause. It's that together it
16 was very long, and we can simply split it apart and
17 then identify what the different functions of those
18 two sentences become, one status, what's going on, and
19 secondly, cause or reason.

20 We defined unknown words. I consider
21 myself relatively educated, and there's something
22 about the phrase "sudden unexplained death" followed
23 by an acronym that dehumanizes this. There's a way
24 that that -- there's something about that phrase, even
25 if it's a valid phrase, that just speaks of jargon.

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1 Now, what we did in the rewrite was say
2 children have died suddenly and without apparent
3 cause. Again, I'm not claiming that that's the best
4 or most solicitous, but it is also much clearer, that
5 it's children have died of X. Then due to concerns
6 about reports of sudden unexplained death in children.

7 Let's be more direct. Let's be more
8 focused. More direct. That's it.

9 We broke out the key three pieces of
10 information using numbers, one, two, three, who was
11 being affected, children with an abuse of
12 amphetamines, children with underlying cardiac
13 abnormalities, and a very small number of children,
14 they who do not have underlying cardiac abnormalities.

15 It breaks it out. It's visual. They can see it.
16 There are three instances. You're in one of those
17 three categories or you don't have to worry. Again,
18 it's a very visual way of talking about that.

19 In addition, I added information that
20 explicitly states that FDA will provide more
21 information. Did the original do that by
22 implication? Yes, I think it did. FDA is looking
23 into these data, but cannot conclude that recommended
24 doses -- no, I'm sorry. That's my rewrite.

25 At this time FDA cannot conclude that

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1 recommended doses of Adderall can cause SUD but is
2 continuing to carefully evaluate this data.

3 Notice that then big parenthetic comment
4 that isn't made is "and we'll let you know," and
5 that's what people are going to really want, is tell
6 us that you will let us know.

7 Now, this is very focused. It's really
8 looking at what was only a paragraph on that page, but
9 if we apply these same kinds of standards trying to
10 set up a very strong structure that a consumer can
11 recognize, the idea of what's happening, why is it
12 happening and what will happen next, that type of
13 basic plain language, technique can give us a clarity
14 that we don't currently have on these.

15 Clarity is not a simple quest. If people
16 are complicated, I assure you that coming up with a
17 rewrite of this, balancing all the different policy
18 issues that people have talked about and incorporating
19 some of these very basic, plain language techniques is
20 a lot more than rocket science. It is complicated.
21 It is difficult because we're not merely trying to
22 inform people, but we're trying to influence people.
23 At least the first step of this is to give them the
24 knowledge, give them the understanding, give them the
25 clarity around what this information is.

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1 The next step, getting them to act, is a
2 whole new kettle of fish and a big one at that.

3 How do you know if you've got clarity?
4 There's only one way of knowing. I can do all sorts
5 of things about this because I have a lot of plain
6 language techniques that I can bring to bear on
7 something. Experts can go through, and they can get
8 it technically accurate, but there's really only one
9 way of knowing and that is to test it and test it and
10 test it again because the ultimate judge of a
11 document's success is going to be the consumer.

12 Measure everything you want, but know what
13 the consumer knows, and I'm not talking about merely
14 doing surveys. I am talking about being able to do
15 usability testing, doing one-on-one conversations,
16 one-on-one tests with consumers to be able to
17 understand, to see if they comprehend and if they know
18 what it is that they need to be doing, if they know
19 what the consequences of inaction are.

20 This is how we're going to find out what
21 to do, and this type of ongoing, iterative testing can
22 be done in very small n's. It doesn't have to be 800
23 people or 1,000 people. You can get very valid
24 information by talking with seven consumers. Seven
25 consumers who can tell you where the sentence goes

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1 wrong, where the paragraph goes wrong, who can tell
2 you that "I don't know what that means," and who can
3 give you clues on how to fix it so that you can fix
4 it.

5 We have to ask about the consumer's
6 questions. We have to know what those questions are,
7 not try to guess what those questions are. We have to
8 know what the structures are that they want to hear
9 based on those questions, and we have to be able to
10 get the language right so that they can understand it.

11 Let me end with Frank Lloyd Wright. "Out
12 of clutter find simplicity."

13 Thank you very much.

14 CHAIRMAN SELIGMAN: Thank you very much.

15 I must beg everyone's permission. I'd
16 like to take a ten-minute break if I may. So we'll
17 reconvene at 2:30 with the last three speakers.

18 Please, I'd like to invite the four
19 speakers to remain on the panel so that you're
20 available for questions at the end.

21 So ten minutes. We'll reconvene at 2:30
22 with Peter Mayberry.

23 Thanks.

24 (Whereupon, the foregoing matter went off
25 the record at 2:21 p.m. and went back on

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1 the record at 2:33 p.m.)

2 CHAIRMAN SELIGMAN: Okay. Let's begin the
3 last session and then we will have some time after the
4 next few speakers to entertain additional questions.

5 Our next speaker is Peter Mayberry from
6 the Pharmaceutical Printed Literature Association.

7 MR. MAYBERRY: Yes, thank you.

8 I do have a prepared statement which I've
9 submitted for the record, and it's pretty short. It
10 basically just simply notes that in terms of the
11 electronic means that FDA has sought comment on, all
12 of them have their good points and their bad points,
13 but none of them did any good to folks who were
14 stranded in New Orleans earlier this year or people
15 who were living in the Super Dome.

16 The biggest benefit of PPIs and med.
17 guides, especially as FDA has done them with the
18 antidepressants, is that FDA has taken the med. guide
19 and married it to the concept of a unit of use package
20 such that rather than the manufacturer, shipping a
21 product in a bulk bottle, a bulk container of, say,
22 1,000 pills and leaving it up to the pharmacist to
23 take that product out of a big bottle and put it into
24 a smaller bottle and then print something off from
25 first data point and then give it to a patient, what

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1 FDA has said is here we're going to have information
2 that's prepared by the manufacturer, approved by the
3 agency, and it's shipped in the manufacturer's
4 original packaging so that the pharmacist can simply
5 take it off the shelf and give it to the patient.

6 Now, I am here today on behalf of the
7 Pharmaceutical Printed Literature Association, but
8 through the course of my career I've worn many hats,
9 and one of the hats that I've worn the longest that
10 I'm the most proudest of is I've developed quite an
11 expertise in the area of patient compliance, and I
12 believe that I probably read 90 to 95 percent of every
13 study that's ever been published on the issue of
14 patient compliance, and to my knowledge if there's a
15 study out there that shows that patients do not comply
16 with their pharmaceutical regimens because they're
17 afraid of the label, I am not aware of that study.
18 Perhaps such a study could be provided, but I do not
19 know of such.

20 Compliance is driven by a number of very
21 complicated factors. Antihypertensives are incredibly
22 difficult to insure compliance, but a recent study,
23 the most recent study, released in May of this year by
24 Ohio State University and funded by HHS, sponsored by
25 and funding from Representative Price of Ohio,

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1 basically found that when patients are given their
2 medication in the manufacturer's original package with
3 the compliance profiting feature and the bare minimum
4 amount of information needed to insure that they take
5 it properly, they get a higher therapeutic outcome.
6 In other words, patients, you have got their product
7 in the traditional cap and bioclosure had either no
8 reduction in their blood pressure or very minor,
9 whereas the people who got their product in the
10 special packaging had significant reductions in both
11 their systolic and their diastolic blood pressure.

12 Mr. Kamp said that we need to protect
13 FDA's jurisdiction. I agree wholeheartedly. But we
14 also have to keep in mind that FDA's jurisdiction by
15 and large stops at the manufacturer's door.

16 The gentleman from First DataBank said
17 should we be thinking about paradigm shifts. Most
18 definitely. We have to be thinking about getting
19 product not being shipped from the manufacturer in
20 bulk containers that have to be repackaged in the
21 pharmacy where errors happen, where product is
22 exposed, where all of the stability data is thrown out
23 the window and product cannot work 100 percent as it
24 was intended.

25 Plus we have the opportunity now, as shown

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1 through both the NSAIDs and the antihypertensives to
2 have information, reliable information, approved
3 information dispensed with medications every time a
4 prescription is filled.

5 That's my basic message. Thank you.

6 CHAIRMAN SELIGMAN: The next speaker is
7 Harry Sweeny from the Dorland Global Health.

8 MR. SWEENY: Thank you very much.

9 By way of background, I'm here. I'm the
10 chair of the Coalition for Healthcare Communication.
11 I also am an unreformed copywriter of some 40 years
12 standing in the business, and I wanted to, along with
13 several of the other speakers, compliment the FDA on
14 these last two days of hearings and, by the way, two
15 days a couple of weeks ago on DTC.

16 I think about the FDA like I think about
17 the Flying Wallendas, that famous circus act that
18 worked without a net all the time and managed to pull
19 off some amazing feats. I think that the pressure
20 that the agency works under sometimes served up by
21 people like me and by others, I think they function
22 very, very well. And as you'll hear later, I think
23 they do it under some constraints that we need to fix.

24 So here's the three topics that I would
25 like to talk about. I saw the questions that the FDA

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1 asked for, and I thought about the topic itself, and
2 so these are the three that I've lined up.

3 First, how safe are prescription drugs?

4 And what makes a prescription drug
5 different from an ordinary chemical?

6 And what steps do we need to take to help
7 assure an understanding on the part of the public
8 about the risks of prescription drugs?

9 Well, last Saturday night I was having
10 dinner with a long time friend of mine, a trial lawyer
11 who has survived two heart attacks and heart surgery;
12 his daughter who had a GI incident this summer where
13 they took out about half of her intestines; my
14 friend's wife, who is a cancer survivor and who is now
15 doing twice a week dialyses; my own wife, who is a
16 communications professional; myself, and two friends
17 of the daughter of my friend, one of whom was a
18 pediatric pulmonologist and the other of whom was a
19 dentist.

20 So there's seven of us sitting there, and
21 I said, "Look. Before we get rolling here, I'd like
22 to play a little game with you. Bear with me.
23 Imagine a line. At one end is a zero and at the other
24 end is a ten. So it's a ten-point scale. I'm going
25 to ask you a question, and I want you to put your

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1 finger on that line on the number where you think it
2 belongs."

3 And they said, "Well, what's the
4 question?"

5 And I said, "How safe are prescription
6 drugs?"

7 Now, before I give you their answers,
8 since it's after lunch and we're all having
9 postprandial meltdown, I'd like you to think about
10 that line, and where would you put your finger on that
11 line?

12 Okay. Now, everybody who put their finger
13 on four or less, less being dangerous or unsafe, show
14 me your hands.

15 (No response.)

16 MR. SWEENY: Nobody at all? Okay. How
17 about eight and above?

18 (Show of hands.)

19 MR. SWEENY: Okay. I'd say about a third.
20 Is that fair?

21 CHAIRMAN SELIGMAN: We're going to abstain
22 up here on the --

23 (Laughter.)

24 MR. SWEENY: Abstentions? All right.

25 Okay. So we had nobody below four. We

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1 had perhaps a third of the people eight and above. In
2 my little group of seven, we had two ones, a three, a
3 four, and let's see. That's two ones, a three and a
4 four, two fives, and one seven.

5 That's what we need to be doing on a
6 population basis before we do anything about risk. We
7 need to understand where people are in their
8 understanding of how safe they think prescription
9 drugs are.

10 There's a book by two fellows out of
11 Harvard, Center for Risk. Some of you may be familiar
12 with it, and in that book they distinguish two
13 polarized points of view which drive all conversations
14 about risk. All topics about this are very
15 contentious, and in fact, the authors write that you
16 can almost not have a noncontentious discussion these
17 days on any of these topics.

18 But they outline two principles, one
19 called Edmund Burke's precautionary principle, which
20 basically says that all technology is not to be
21 trusted and that you must prove it all. It's guilty
22 until proven innocent, versus a more contemporary view
23 that we've heard about in the last two days here about
24 trying to balance risks and benefits so that we get
25 some serious benefits out of it.

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1 How safe are prescription drugs? Well,
2 here's an example of the polarization. Safe enough to
3 make them the fourth leading cause of death, said the
4 head of the National Nutritional Foods Association a
5 couple of years ago, not a group that's very fond of
6 pharmaceuticals.

7 But Ropeik and Gray in their book on risk
8 attempted to do something that is maybe unprecedented,
9 and interestingly they did not do it for prescription
10 drugs, although they did it for some disease entities,
11 cancer and high blood pressure, I believe, and some
12 others. But you can't probably read it on the bottom.

13 They said we don't explain risks from drug reactions
14 which are so unique to each individual that the
15 discussion in the book about risk in general might, in
16 fact, be dangerous for the reader.

17 Now, if this is what a couple of experts
18 from Harvard believe about risk and they're dealing
19 with all sorts of risk, airplanes and, you know, all
20 of the rest of it that we know about, then how in the
21 world can we expect an agency to deal with the topic
22 in any sort of a meaningful way?

23 What makes a prescription drug different
24 from the chemicals? Information. We used to say a
25 prescription drug is a chemical poison wrapped in a

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1 protective capsule of information. The more
2 information you have about it and about its use and
3 about its risks, the better off you are.

4 What is the value of the information? It
5 separates reality from perception. It tells us what
6 we know versus what we don't know or what we're
7 uncertain about. It lets us make judgments about
8 what's safe and what's dangerous, what we need to be
9 fearful of and what we can be relaxed about.

10 But remember at the bottom of it all,
11 familiarity breeds contempt. That's why we have
12 campaigns like "Speed Kills," to remind us, and that's
13 the kind of thing that we need in relation to
14 prescription drugs.

15 There's another book that's out there now
16 that's on the best seller list that's called
17 Freakonomics. There's a very interesting set of
18 observations in there. Steve Levitt, the economist is
19 known for his in some cases bizarre applications of
20 economic analysis to problem solving in problems that
21 no one has approached before, and one of the things
22 that he's very clear about is information asymmetry in
23 the role of experts, and one of the only examples that
24 he gives in the book is that of a doctor who was a
25 cardiologist, interventional cardiologist, who was

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1 getting patients from people in the community, and
2 when he was asked why he was performing some
3 procedures that probably shouldn't have been
4 performed, he hesitated and then he said, "Because if
5 I didn't do them and I sent them back to the primary
6 care doc, they wouldn't refer patients to me anymore."

7 One of the things that hasn't been said
8 here today is that in this complicated world that we
9 work in, with all of the competing entities, it's
10 extraordinarily difficult to try and make a move
11 because it's a mexican standoff kind of a world where
12 any move on one part is going to affect a move on the
13 other part, and the unexpected consequences can be
14 severe.

15 The other point that I wanted to make that
16 Levitt talked about was about incentives. Now, the
17 incentives for the doctor that I just described was
18 clearly an economic incentive, but there are others.
19 There are social incentives, and there are moral
20 incentives, and in any given situation those are the
21 arguments that are going to be brought forward, and in
22 many cases that's what's going to be the decision
23 point.

24 So what steps do we need to take to help
25 assure an understanding of the risks? Well, my first

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1 recommendation would be start low and go slow. What
2 does that mean?

3 Well, a few years ago we made some
4 recommendations to the agency. One of them was for a
5 prescription drug warning box. If the problem is that
6 the general public believes that prescription drugs
7 are not potent, then we need to raise that awareness
8 so that they understand it.

9 And I know the arguments about warning
10 boxes on smoking, on tobacco and all of that business.

11 Whether that's worked perfectly or not isn't the
12 point. The point is that if you want to move the
13 needle and if you believe that the public thinks that
14 prescription drugs are trivial, then we need to move
15 that needle in the other direction and a warning box
16 might be a very good place to start.

17 We've heard also at this meeting about
18 standardized icons and at an outreach public health
19 program to inform the public as to what they mean. We
20 thought that would be an excellent step five or six
21 years ago, and we think it would be an excellent step
22 now.

23 What else? We need to understand the
24 barriers that consumers have to behaving the way we
25 want them to behave. About two and a half years ago I

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1 was asked to address a DTC conference on compliance,
2 and I looked around, and as our last speaker
3 indicated, there wasn't very much information on
4 compliance as a result of DTC, and I was extremely
5 frustrated.

6 So I typed this question in and I Googled
7 it. "Why don't people do what they're supposed to
8 do?" And I was amazed at the long list that I
9 received. But one of them was from a book by an
10 author by the name of Ferdinand Fournies, and Fournies
11 knows why people don't behave the way they're supposed
12 to. He's a consultant for some 30 years now. He was
13 a professor in his youth at Columbia. He did a 15-
14 year study of 25,000 employees, and then he wrote a
15 book called Why Employees Don't Do What They're
16 Supposed to Do and What You Can Do about It.

17 So I bought that book, and in there he had
18 16 different reasons, but I just picked these top ten
19 on why people don't do what they're supposed to do.
20 The first one, they don't know why they should do it.

21 They don't know how to do it. They don't know what
22 they should do. They think your way won't work. They
23 think their way is better. They think they are doing
24 it. They think they're going to be punished for doing
25 it. There are no positive consequences for doing it.

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1 It's beyond their personal limits. Nobody could do
2 it.

3 Think about these things when you get an
4 opportunity and think about relating them to some of
5 the health care decisions that have to be made.

6 But then I went further, and I found that
7 there was also interest in why physicians don't do
8 what they are supposed to do according to some others.

9 Cabana and his group sets forth a group of practice
10 guidelines here or -- I'm sorry -- the reasons that
11 doctors don't follow practice guidelines. A very
12 thoughtful analysis of why not, and here's why.

13 Lack of awareness, easily overcome. Lack
14 of agreement, more difficult. Lack of outcome
15 expectancy, it won't work. Inertia. Lack of
16 familiarity. Lack of self-efficacy or confidence, and
17 the external barriers. My partners will make fun of
18 me. They don't want to do it either. There's
19 restrictions for managed care.

20 The problem is pervasive among human
21 beings, not just doctors of patients. Patient
22 expectations in the clinicians' role was treated in
23 another article, and this goes back to the incentives.

24 This was an article about what doctors ought to do in
25 order to avoid litigation. It's stunning in its

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1 simplicity. They need to talk to patients. They need
2 to communicate better. What a surprise.

3 So we say start low and go slow.
4 Understand the barriers. Connect the dots, and then
5 what about risk perception itself?

6 Well, there's a fellow up at Rutgers. He
7 and his partner, Neal Weinstein, he invented and put
8 together a formula that he calls the risk equals
9 hazard plus outrage formula, where hazard is a product
10 of outcome severity and probability, and outrage is
11 the soft stuff, trust, shared control, fairness,
12 courtesy, all measurable.

13 And using this model for some 35 years, he
14 and his group up there have worked on things like
15 what's riskier, radon or radiation or nuclear waste,
16 and what's consumer perception? And how does that
17 industry communicate on that subject?

18 The risk perception people have a whole
19 literature of their own. It's somewhat less than
20 crisis management, but it's a lot more than the kind
21 of communication skills that many of us bring to the
22 party.

23 So we have those things, and what would
24 the last admonition be? This one comes from Professor
25 Bill Kissick at the University of Pennsylvania. He

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1 told a story at a meeting I was at. He said, "You
2 know, when I was a young doc," he said, "I used to lay
3 asleep at night worrying about all the problems I was
4 trying to solve, and I'd get up and I'd go charging
5 around in the morning," and he said, "I did that until
6 I got into my 40s."

7 And he said, "I got up one morning, and I
8 realized, do you know what? There's always going to
9 be a top ten cause of death." And he said, "I decided
10 I would just slow down and think problems all the way
11 through and not try to solve them so instantaneously."

12 Not a bad thought for what we're trying to
13 deal with here.

14 Last but not least, I think we ought to be
15 using the mental models approach. This one we've
16 heard now from at least five speakers over the last
17 couple of days. Remember Mrs. Robinson in the movie?

18 Remember what the famous word was from the uncle?
19 Plastics. Well, the word I'd like to leave everybody
20 with coming out of this meeting is research, research
21 before, research during, research afterwards. That's
22 going to be our way out of the jungle.

23 I'll be happy to answer any questions you
24 might have.

25 CHAIRMAN SELIGMAN: thank you very much.

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1 Our final speaker is Vanessa Cullins from
2 Planned Parenthood Federation of America.

3 DR. CULLINS: Thank you very much for
4 giving me the opportunity to speak on behalf of
5 Planned Parenthood Federation of America.

6 I was trained as an obstetrician-
7 gynecologist and practiced for over ten years. I'm
8 now Vice President for Medical Affairs for Planned
9 Parenthood Federation of America.

10 Planned Parenthood Federation of America
11 is the world's largest voluntary reproductive health
12 care organization. It was founded in 1916 by Margaret
13 Sanger, and now is composed of 120 affiliates plus the
14 national office. The 120 affiliates have over 850
15 health care delivery sites and it serves over five
16 million men, women, and teens each year.

17 The overwhelming majority of Planned
18 Parenthood's health care services are preventive, and
19 as such, we are striving on a daily basis to promote
20 understanding of risk and benefits of preventive care
21 activities. While most people we serve understand
22 that the benefits of preventive care vastly outweigh
23 the risk associated with preventive care, this
24 information is always competing with sensational
25 headlines about rare but expected adverse events and

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1 with unfounded myths that circulate within a
2 community.

3 PPFA's commitment is to advance consumer
4 understanding and control of personal reproductive and
5 sexual health care. So we find it imperative to
6 increase health care provider and consumer
7 understanding of individual and population risk
8 factors.

9 And the reason why we find this to be so
10 imperative is because a better understanding by both
11 provider and consumer of both individual risk factors
12 and population risk factors should serve to enhance
13 informed decision making about health care.

14 Now, whether we're imparting information
15 about immunizations, contraceptions, cervical cancer
16 screening, STI screening, diagnosis, and treatment, or
17 pregnancy options or any other preventive health care
18 option, we find that we're in the situation where no
19 medication and on intervention is without risk.
20 Nothing is perfect in preventive health care.

21 In addition, the statistical information
22 from the population based studies and also from the
23 clinical studies appears to be poorly translated into
24 individualized decision making, whether you're talking
25 about decision making that is being pushed by health

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1 care providers or clinicians or decision making that
2 is made in conjunction with the health care provider
3 and also the consumer.

4 In the interest of time, I'm going to
5 limit my remarks about the FDA informational documents
6 to those that are intended for consumers. My remarks
7 are based on Ortho Evra consumer information, FDA
8 News, FDA updates labeling for Ortho Evra
9 contraceptive patch, and questions and answers, Ortho
10 Evra.

11 The reason why I chose these three
12 documents is because we're now currently struggling to
13 help clinicians understand the new warning for Ortho
14 Evra as it relates to the pharmacokinetic data, and we
15 understand that the providers need to be able to place
16 this warning in context in order to convey the
17 information appropriately to consumers, to the women
18 that they see that want to either initiate Ortho Evra
19 use or continue Ortho Evra use.

20 In all three documents, the actual content
21 that was covered was very good. However, as many of
22 the speakers have already mentioned, the reading level
23 and also the medical literacy level is very high.

24 These and other consumer information
25 documents would benefit from a section that generally

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1 and briefly outlines issues that the consumer in
2 consultation with the health care provider might
3 consider when trying to decide whether a risk, whether
4 we're talking about a side effect or a serious adverse
5 event, is worth taking because the risk-benefit
6 balance in terms of whether or not you're going to
7 start a medication or continue a medication or start a
8 preventive activity and continue a preventive activity
9 is based on individualized decision making that should
10 take into account not only what that particular
11 individual is at risk for as it relates to their
12 population, their demographic characteristics, but
13 also their personal behaviors and their personal
14 medical risk factors, and personal medical risk
15 factors including risk factors based upon behavior.

16 So the type of conversation that would
17 need to occur is actually alluded to within one of the
18 documents. It's actually within the Q&A. In the Q&A
19 about Ortho Evra, there is a question: what should I
20 tell my health care provider?

21 And there's another question: what are
22 some possible side effects?

23 Now, missing is an explanation that such
24 information should be used by the consumer in
25 conjunction with the health care provider to make the

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1 health care decision that this is information that
2 will help to inform the risk-benefit equation for that
3 particular individual.

4 Now, interestingly and appropriately, a
5 specific example of risk-benefit consideration is
6 found in the November 10th, 2005 FDA News, FDA updates
7 relating for Ortho Evra contraceptive patch.
8 Paragraph 3 gives balance and allows for
9 individualization of the product through this
10 particular statement.

11 Furthermore, women taking or considering
12 using this product should work with their health care
13 providers to balance the potential risk related to
14 increased estrogen exposure against the risk of
15 pregnancy if they do not follow the daily regimen
16 associated with typical birth control pills.

17 Because Ortho Evra is a patch that is
18 changed once a week, it decreases the chances
19 associated with typical birth control pills that a
20 woman might miss one or more daily doses.

21 Now, a similar helpful statement is found
22 in a document titled "Questions and Answers, Ortho
23 Evra." In this document it states, "When thinking
24 about prescribing or using Ortho Evra, health care
25 professionals and women need to balance the increased

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1 exposure to estrogen against the chance of pregnancy
2 if a birth control pill is not taken daily."

3 Now, granted, the sentences are too long.

4 There isn't much clarity as we learned from our
5 previous speaker, but the content is correct. The
6 approach is correct.

7 What we need to be able to see is more of
8 this approach in order to help both consumers and
9 providers understand risk and benefits and determine
10 that individualized risk-benefit balance.

11 What the speakers have conveyed today is
12 that that information needs to be clearly understood
13 and, therefore, the issues about research, testing,
14 developing of tools, we're all in agreement or at
15 least I'm in agreement and PPFA is in agreement that
16 that work definitely need to be done.

17 At PPFA we applaud the FDA for having this
18 public hearing specifically to receive comments on
19 risk communication tools. PPFA, and I personally hope
20 that this is the first of a more expanded process
21 where the public will be invited to continue to
22 participate and there will be focus group testing of
23 tools that are developed by the FDA.

24 It's important that we use every day and,
25 to quote our previous speaker, plain language and that

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1 we begin to use comparisons that resonate with the
2 individual learner, the individual decision makers,
3 educational, cultural, social, personal health, and
4 personal behavioral context.

5 Now, this implies that there is audience
6 segmentation of messages designed to inform about
7 risk. No one document is going to do it for every
8 single audience, and that also was spoken to by
9 earlier speakers.

10 To move in this direction regarding
11 messaging of risk, many must be involved in first
12 deconstruction and then the reconstruction of risk
13 messaging. PPFA, Planned Parenthood Federation of
14 America, offers its input and assistance in this
15 effort, especially as it relates to reproductive and
16 sexual health risk.

17 PPFA has already begun to work to improve
18 clinical messaging about risk. Planned Parenthood
19 Federation of American in partnership with the
20 Association of Reproductive Health Professionals,
21 which is usually called ARHP, is launching a multi-
22 phased educational program designed to provide health
23 care providers and consumers with improved
24 understanding of risk associated with hormonal
25 contraception.

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1 Now, ARHP, Association of Reproductive
2 Health Professionals, was founded in 1963, and it is
3 an international nonprofit association of health care
4 providers, researchers, educators, and other
5 professionals. ARHP serves as an information and
6 education resource for health care providers, the
7 public, policy makers, and the media on a full range
8 of reproductive and sexual health issues.

9 Our program is entitled "Putting Risk into
10 Perspective, Making Informed Health Decisions." Now,
11 we hope that we will be able to have this program
12 ongoing for years and years because it is our intent
13 to tackle various topical areas in preventive health.

14 We hope to be able to have a module on
15 immunizations, a module on laboratory screening tests,
16 nonhormonal contraception, unintended pregnancy and
17 child birth.

18 Also, we want to be able to address the
19 myriad of preventive health measures and interventions
20 that, while associated with small, measurable health
21 and well-being risks, are extremely important for both
22 individual health and also population public health.

23 We at ARHP and also PPFA would welcome
24 further collaboration with the FDA and with others
25 that have spoken, both today and also yesterday, as we

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1 embark on this multi-phase project.

2 thank you.

3 CHAIRMAN SELIGMAN: Thank you, Dr.
4 Cullins.

5 We'll turn to the panel to see if there
6 are any questions. Yes, Nancy.

7 DR. OSTROVE: Mr. Ratto, and I apologize
8 if I missed this because you had a lot of information
9 out there. Now, your group actually puts together the
10 information, the CMI. Can you speak more to what do
11 you do?

12 I mean, what we heard here is research,
13 research, research, test, test, test. You don't need
14 to have large groups. How do you test the
15 information?

16 I mean, you believe that your information
17 is consistent with the Keystone criteria. How do you
18 make that determination? What do you do to test with
19 consumers? What can you tell us that might be helpful
20 for us in terms of looking at our tools in that sense?

21 Can you give us more kind of specifics
22 about that?

23 DR. RATTO: There haven't been any formal
24 tests with our data, and I'm not sure about other
25 providers as well, and that's why we're looking for

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1 some collaboration via NCPIE since FDA has
2 commissioned NCPIE to work on this CMI project in
3 order to do research on this topic.

4 There have been a number of discussions
5 and attempts to get funding, and at this point what
6 we've done, we certainly have had input from our
7 customers. We have millions of patients that are
8 receiving our documentation, and we get pretty much
9 daily feedback from the field from pharmacists and
10 physicians about information. That's clearly not
11 testing, but it is information that tells us areas
12 that might be perceived as problematic in some way,
13 and we certainly answer all of that in terms of
14 research.

15 We use basic information. We have a
16 detailed policy that we use, and basic information in
17 terms of clarity and sentence structure and that sort
18 of thing, and I think every one of our group has a
19 considerable amount of clinical experience in working
20 with physicians, patients, and other health care
21 professionals, and it's based a lot on personal
22 experience in terms of what works in terms of
23 educating patients.

24 But we definitely feel that there needs to
25 be more work done in this area. We've also been

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1 involved with the NCPIE group in constructing a guide
2 to the Keystone guidelines, essentially a working
3 document from which we can essentially use as a way to
4 operationalize the Keystone guidelines. We came up
5 with that through the NCPIE criteria committee, and we
6 certainly abide by some of those, all of those types
7 of guidelines.

8 FDA has issued their own version of this
9 with not as much detail or not as much concreteness to
10 it, if you will, and so we've submitted that
11 information quite some time ago to FDA in terms of
12 that particular piece of data on the interpretation of
13 Keystone.

14 So we're also looking basically to
15 collaborate with the agency on this sort of thing in
16 terms of getting a systematic approach to research
17 established and the logical vehicle would be through
18 the NCPIE organization.

19 Does that answer your question, Nancy?

20 DR. OSTROVE: Yes. Thank you very much.

21 DR. RATTO: Okay.

22 CHAIRMAN SELIGMAN: I had actually a
23 question really more for point of clarification. In
24 your presentation, Mr. Kamp, as well as in yours, Mr.
25 Mayberry, you talked about conservatisms related to

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1 the protection of the FDA jurisdiction. I wonder if
2 you could just say a little bit more about what you
3 mean by that protection and what the nature of your
4 concern is in that realm when it comes to
5 communicating safety information.

6 MR. KAMP: There seems to be a panoply of
7 "wanna be FDAs" out there. Most importantly I see it
8 in state legislatures, state Attorney Generals using
9 their consumer protection area, perhaps most
10 dangerously for the drug companies, plaintiffs'
11 attorneys bringing cases on against drug companies on
12 failure to warn.

13 California is one of the states that have
14 had state laws that essentially require warnings that
15 are inconsistent from the warnings of the FDA. That
16 was a case actually that the General Counsel's Office
17 of FDA intervened in, and in that case the drug
18 company had to make a choice whether it followed the
19 federal law or the state law.

20 These kinds of incursions on the
21 jurisdiction of the FDA, I think, are very dangerous
22 for all people involved, as I said, because I think we
23 need one regulator that's professional, that knows
24 what it's doing. The FDA is the right one, and that
25 the FDA General Counsel's Office and others inside the

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1 FDA must, I think, be very careful to insure that
2 their regulations are understandable, have the
3 reputation in the world as the gold standard or in the
4 United States as the gold standard, and essentially
5 through law and its prestige cause the rest of them to
6 go away.

7 CHAIRMAN SELIGMAN: How would you apply
8 that to information that in large measure we're
9 talking about today that isn't really formally part of
10 the label but is, you know, information about emerging
11 risks, things that go out to consumers or to patients
12 or to health care providers, you know, related to
13 appropriate use of medications, concerns about on
14 label or off label use.

15 I'm trying to sort of put it in the
16 context of the discussion you've been having in the
17 last couple of days, your concern about what various
18 Attorneys Generals and state legislators are doing.

19 MR. KAMP: It's about the professional
20 labeling part where the FDA -- the FDA's job in
21 approving drugs is essentially the chemical entity
22 approval and the communications envelope around it.
23 When other entities get into the business of deciding
24 what should be in that communication envelope that
25 surrounds the drugs, you create a very difficult

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1 situation for drug companies that want to do right.
2 They just want to do it right, but it also adds to the
3 confusion.

4 Now, my comments about that were not about
5 the stuff that we talked about much of yesterday
6 where, you know, how can we make our Web site more
7 consumer friendly. That's not the issue. It's sort
8 of the legal requirements of what an entity, most
9 specifically the drug companies who are the regulated
10 kind of companies, what kind of safety warnings they
11 must have in order to follow the FDA regulations and
12 to insure as much as possible that the professionals
13 and consumers know what they need to know in order to
14 take a drug safely.

15 DR. TRONTELL: We've talked today about
16 communicating. We talked as well yesterday, and I
17 think we've had, in my opinion, some implicit
18 assumption that we're talking about risks where we
19 have some degree of confidence that they're real. We
20 believe that there's a degree of certainty attached to
21 them.

22 I'd appreciate hearing from all of the
23 panelists, from their own perspective, from the
24 stakeholders that they represent's perspective. What
25 is the best mechanism to describe risks that might be

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1 classified as uncertain, where there's a glimmer or
2 signal where telling people too much information might
3 have unintended consequences of frightening them when
4 it's not a certain risk, but where failure to warn
5 might be considered paternalistic or less than fully
6 transparent about what risk information is available,
7 since a lot of safety information falls into this
8 region at least for a period of time, until the risk
9 is fully clarified.

10 Can you speak to how do we warn people
11 when we're not quite sure what we're warning them
12 about?

13 CHAIRMAN SELIGMAN: Dr. Cullins.

14 DR. CULLINS: First, I think that you're
15 not warning people. You're informing people when you
16 don't know that a particular adverse event is
17 necessarily correlated to actual use of a medication,
18 and I think that's the way to look at it, that there's
19 a certain amount of information that people have a
20 right to have, and the information as outlined by our
21 previous speaker in that the main thing the needs to
22 know is that the FDA is watching this. And the FDA
23 will inform providers and consumers if anything
24 different needs to be done as it relates to their
25 individual health care.

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1 I think people need guidance. Providers
2 need and want guidance in terms of how they should
3 really be processing the information, and that's some
4 of what has, I think, been missing.

5 And I can understand the reluctance of a
6 governmental agency to move in that direction, but if
7 we're really talking about helping both providers and
8 consumers to put the potential risk into context,
9 there's guidance associated with that, and I think
10 actually the sticking point is going to be in terms of
11 how much guidance you can really give.

12 CHAIRMAN SELIGMAN: In that vein before we
13 go on, I would be very interested, Dr. Cullins -- I
14 know you talked about Ortho Evra -- the degree to
15 which you or your association or your organization who
16 can provide specific comments to us about those
17 materials in way that will allow us to approve either
18 the questions and answers or the alerts that will
19 provide that kind of context will be much appreciated.

20 DR. CULLINS: I will.

21 MR. MAYBERRY: To my mind it gets really
22 to the role of FDA and what your jurisdiction is, and
23 the fact that the biggest tool that you have is the
24 CGMPs in my mind, and you know, these are prescription
25 drugs. They are only dispensed pursuant to a

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1 prescription. So that implies a learned intermediary,
2 you know. A doctor is going to inform you of anything
3 that the doctor is aware of, and the pharmacist
4 certainly plays a huge role in the learned
5 intermediate growing role as well.

6 But, now, for FDA's side, to my mind, it's
7 your responsibility to publish what is known without a
8 doubt and what is largely suspected. That's what your
9 job is, is to make those determinations.

10 And I know that Mr. Kamp will tell you
11 that, you know, everybody is going to get sued and all
12 drug businesses, all of the pharmaceutical
13 manufacturers are going to go out of business, but at
14 the end of the day, these are prescription drugs, and
15 they all have some inherent amount of risk to them
16 because they're prescription drugs.

17 CHAIRMAN SELIGMAN: Comments from the
18 other side? Yes.

19 MR. KAMP: Yeah, I'm not sure everyone is
20 going to get through. I think that Dr. Trontell asked
21 a very good question, and I think I'd like to separate
22 it out in two different things.

23 The most important one and the one that's
24 central to the FDA is to decide when there's enough
25 information to say something definitive about a risk,

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1 and that's the job of the FDA. The FDA is and should
2 continue to be the gold standard on the making of that
3 judgment using the scientific evidence it has before
4 it.

5 Now, I think there are going to be some,
6 of course, who are dissatisfied with the Adderall
7 message. We're watching it, but we don't know. But
8 that is the answer. That was exactly the answer that
9 the agency in an expert judgment came to at the time,
10 and that's exactly what you should do, you should
11 continue to do.

12 I don't have any idea what the right
13 answer is on those kinds of things as they go forward.

14 I trust the FDA to make the right decisions.

15 The other half is the one that we talked
16 about today. Once you have made those decisions, once
17 the decision is made that additional information needs
18 to be out about possible new risks and situations like
19 that, then it's a behavioral. It's a consumer
20 communications issue.

21 My thought if I were in your position
22 would be essentially to do the best job you can,
23 explain it to the professionals, and then let the rest
24 of the world, all those other folks who have a stake
25 in this, the drug company itself, the pharmacists and

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1 all of the other health care providers and supporters,
2 the press and whatever, to do with it what they will.

3 But if you give the best information
4 possible, you make the judgment you make, you explain
5 them as well as you can, particularly to the
6 professional community that needs to know them the
7 best, then that's pretty much your job and you've got
8 it done.

9 DR. RATTO: I would say that for the
10 emerging safety information, one thing to do, adding
11 onto the Planned Parenthood comments, would be move
12 the disclaimer up to the top of that particular
13 documentation and indicate clearly that it is
14 preliminary information.

15 If the first thing you see which is the
16 current situation is the bolded information about the
17 fact that this drug can kill you if you're asthmatic,
18 and you already are asthmatic, I think that's a
19 problematic issue in terms of information that clearly
20 is emerging and not proven.

21 CHAIRMAN SELIGMAN: Others wish to
22 comment?

23 DR. KLEIMANN: Yes. Again, a very simple
24 way of thinking about this, and I'm not trying to
25 gloss over the complexities of this, but label it.

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1 Maybe there is something that says we don't know,
2 something that doesn't make people process through the
3 sentences, process through the language, process all
4 the way through the this hand and on the other hand
5 and on this hand, but simply gives them the bottom
6 line very simply up there.

7 Now, I know that that is complicated to do
8 it simply, but, again, I think we see again and again
9 that people need the label, the label that sums up,
10 the label that directs them, that helps them know
11 exactly what it is is being said, not simply having to
12 process through all of the language themselves.

13 MR. SWEENEY: you asked the question
14 yesterday about the role of the FDA, and I think this
15 part of the meeting gives an opportunity to sum that
16 up as the most trusted source of this kind of
17 information. I think the rest of your role flows from
18 that.

19 You are the consumer advocate and
20 protector. You are the convener of experts. You are
21 the consensus former. You are the information
22 clearing house, and then you become the disseminator
23 of information, and I think when we talk about the
24 dissemination, some of the ideas that we've heard to
25 set up some templates so that consumers can become

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1 accustomed to dealing with this information in a
2 readily understandable format, a road map of the
3 information, if you will, that's what we do in the
4 rest of the world and it doesn't make sense that we're
5 not doing it for drug information.

6 CHAIRMAN SELIGMAN: Thank you for that
7 comment.

8 Any other questions or comments from the
9 panel?

10 (No response.)

11 CHAIRMAN SELIGMAN: Is there anyone else
12 remaining in the audience who wishes at this time to
13 say anything or make a statement?

14 (No response.)

15 CHAIRMAN SELIGMAN: Before I conclude, let
16 me remind everyone that is here that we are, indeed,
17 accepting statements and comments to the docket.
18 Clearly many of the panelists have already provided
19 their statements, which we already have, and I thank
20 you for those.

21 Let me just simply add in conclusion then
22 that I really appreciate not only this particular
23 panel, but everyone who participated and contributed
24 to our meeting in the last couple of days. I think
25 everyone has been not only blunt, but fair, but also

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1 very constructive in their comments, and particularly
2 because I think at the end of the day, we all share
3 ultimately the same goal, which is to insure that
4 information that is provided out there to all of
5 those, since we all at one point in our lives are
6 either patients, consumers or in some cases, even
7 health care givers; indeed, this information be given
8 in a fair and constructive way, and that it be
9 accessible and available to all.

10 Clearly, I've heard lots of messages about
11 the way the FDA faces the world and I've heard a lot
12 about our Internet site. We've also heard a lot about
13 the panoply of messages and communication tools that
14 we use as an organization, and the desire amongst many
15 who have spoken here today about trying to certainly
16 at least reduce that number or simplify them or at
17 least certainly make clear what the purpose of these
18 various tools are.

19 I've heard a lot about the importance of
20 partnerships and about collaboration and about
21 interaction and, you know, the needs to really engage
22 not only the health care professional community,
23 whether they be physicians, nurses, pharmacists or
24 other organizations, as well as the specialty health
25 care organizations.

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1 I've heard a lot this last couple of days
2 about the importance of standards and consistency and
3 the need to insure that we not only have consistent
4 approaches, but that the standards that are used for
5 the development of this information be well and
6 clearly understood.

7 And then finally, if I didn't say the word
8 research, it's clear that we all need to not only
9 understand the scientific underpinnings of good risk
10 communication and clarity, but also that we need to
11 have the kinds of resources that would allow us to
12 both pretest, test during, and test after the
13 development of many of these messages.

14 It was a delight, and I again thank you
15 all for taking the time to be here, for traveling, for
16 preparing your presentations and your submissions to
17 the docket. It really left me with a profound
18 appreciation as well as respect for not only the
19 breadth of the community out there in this world that
20 are interested in effective and valuable risk
21 communication, but also a profound respect for the
22 tremendous amount of expertise that's out there. It's
23 certainly my hope, and I hope I speak on behalf of the
24 other members of the panel that we can work together
25 in the future to corral this tremendous amount of

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1 energy and expertise and caring that exists out there.

2 So with that, thank you and I will close
3 the proceedings on that note. Thank you all.

4 (Whereupon, at 3:27 p.m., the meeting was
5 concluded.)

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