

1 don't believe it has any relationship, I don't believe it
2 has any relationship, to the use of your drug but, because
3 of the legal system in which this product has to be
4 marketed, people are saying, "We are going to cover our
5 backsides and put information in there that is, arguably,
6 misleading from a medical, physiological perspective but is
7 probably quite good from a legal perspective."

8 I think this is the point Janet was bringing and
9 this is what worries us, that it is the tail wagging ^{the} ~~to~~ dog,
10 that is this really a medium to get good communication to
11 the health-care practitioner on how he or she should use
12 this drug effectively in a patient, then that should be our
13 focus.

14 If we have to deal with the liability, perhaps
15 there are other ways of doing it.

16 Janet or Bruce, do any of you have any comments?

17 DR. WOODCOCK: I couldn't agree with you more. I
18 think we all are going to have to compromise on some of our
19 favorite hobby horses if we are going to have a document
20 that actually communicates information because we couldn't
21 have gotten a clearer message that the practicing physician
22 at the point of prescribing does not want to plow through,
23 for example, a description of the pharmacokinetics of the
24 drug even though that is an icon to many people in drug
25 development.

1 Similarly, the legal issues are going to have to
2 be solved some way or we are not -- and, in fact, we have
3 heard a lot of opinion and information on the use of the
4 Brief Summary as it currently resides in advertising. We
5 are not going to be able to have it both ways. We are
6 either going to have something briefer or we won't.

7 So the legal folks, if we are going to
8 communicate, are going to have to come to peace somehow with
9 this. Similarly, within FDA, there may be things that we
10 hold very dear about information that really isn't that
11 useful from the perspective of the prescribing physician.

12 DR. BURLINGTON: When we started talking about
13 this, we also envisioned the full information being there in
14 every package insert in every PDR label so that what we have
15 talked about to date is the Brief Summary that goes up
16 front. But sitting behind this is all the information that
17 is currently in a label and that that would help address the
18 question about liability.

19 MS. MARTIN: It crossed my mind with the Summary
20 Section, thinking -- I am an attorney, so thinking along
21 those lines, someone might only read the Summary Section and
22 might not necessarily go to the remainder of the insert and
23 what would that mean in terms of liability for the company.
24 That goes beyond, probably, our discussion here today but,
25 obviously, those are company concerns.

1 DR. LUMPKIN: I guess part of it has been, to
2 answer that -- what we were hearing is that as it is
3 configured today, they are not reading it at all. The worry
4 was -- and it was one of the questions asked -- that if you
5 had a summary, would you then go the rest of it. What we
6 were hearing was that, particularly if it is a summary that
7 directs you where to go in the rest of it, it would be a
8 more helpful document than just this layout of information
9 that we have now that is very hard to wade through.

10 Lou, you had something you wanted to say.

11 DR. MORRIS: Actually, I wanted to follow up on
12 what you just said, Mac, and that is an awful lot, I would
13 think, of the analysis about liability would have to do with
14 how physicians actually use labels now and to what extent
15 physicians actually read them and how they read them.
16 Certainly, if you all have any data that is old and you
17 don't mind sharing, we would love to see that because I
18 think that would help us resolve some of these issues.

19 If Mac's point is correct, because it is so
20 uninviting now that physicians don't use package inserts
21 because they have such a difficult time navigating through
22 them and/or learning from them, then some advantage of
23 making more useful information, pulling out useful
24 information, might actually help in a legal analysis. But,
25 certainly, that is up to the attorneys.

1 MS. PARKER: I think the problem is pinpointed up
2 from ^{it} that the package insert has many different uses. Maybe
3 the physicians don't read the whole package insert but the
4 defense attorneys do. So I think that maybe including some
5 attorneys in some of your focus groups might be a good idea.

6 Thank you.

7 DR. LUMPKIN: Thank you. Are there other
8 thoughts? Please.

9 DR. HORN: Mark Horn from Pfizer and PhRMA. I
10 think, and just making one specific comment about what we
11 talked about this morning, there is one section of the
12 proposed labeling that I think is mislabeled and is
13 potentially confusing, and that is the New Information
14 Section. I think it is confusing because the people who are
15 the audience for this, the practitioners, are not generally
16 aware of the often arcane contortions that one must go
17 through to change a drug label.

18 What they are going to think when they see New
19 Information is that this is, indeed, new information when,
20 in fact, it is nothing of the kind, it is a labeling change.
21 If, in fact, someone looks at this and expects to see that
22 which they recently saw in The New England Journal or The
23 Annals of Internal Medicine and, instead, does not see that,
24 then it is confusing because what you say to yourself when
25 you are there is, "Why is that information which I have been

1 seeing in The New York Times and on the news and in my
2 journals not in the section in the label that says, very
3 explicitly, New Information.

4 So I think your idea is a good one, to call
5 attention to labeling changes. But I think that you have
6 got to call it what it is which is Recent Labeling Changes,
7 or something like that, because otherwise you will be
8 confusing the practitioner and defeating the purpose.

9 Then I will put on my practitioner's hat for just
10 one moment, and this is my practitioner's hat, to respond to
11 some of the other comments. I think that, in many cases,
12 the discussion that we have had this morning reflects a real
13 confusion about how these labels are used. And I will just
14 give you an anecdote.

15 When I am in my clinic, and I am there once a
16 week, and I go to the PDR for information on how to use a
17 drug which I may not have prescribed, I care about very
18 little. I have got about 30 seconds and I want to know
19 whether it is a pill or a capsule. I want to know if it is
20 given once a day or twice a day or four times a day.

21 I want to know what the dose is. And I want to
22 know that information which is necessary so that I don't
23 cause harm to the person for whom I am prescribing it.
24 Basically, what I need, are the contraindications, the drug
25 interactions with drugs that the patient is likely to be on,

1 and anything that is warning in a box. That is what I want
2 to know.

3 At that point in time, although I might like to
4 know a lot of other things, I don't have time or the
5 inclination to know those other things. I think that that
6 is probably the typical situation. Think of managed care.
7 Think of eight minutes a patient, ten minutes a patient.
8 Think of a doctor who has to make a decision and get that
9 patient in and out quickly.

10 That person is going to that book because they
11 need to know some information that is important to them. If
12 you give them too much, or try to make it a CME experience,
13 you will lose the benefit of that interaction and
14 ultimately, I think, potentially cause harm to patients
15 because that person wants information.

16 They are highly motivated to do the right thing.
17 Help them to do the right thing.

18 MS. CRISTY WYATT: Cristy Wyatt with Hoechst
19 Marion Russel. I had a question about the Summary and then
20 a question about the format. You proposed some specific
21 criteria for how to condense the side effects for the
22 Summary Section. But I noticed that the major toxicities,
23 the precautions and the drug interactions are also
24 condensed. What criteria did you use or would you use?

25 DR. OSTROVE: These are bound to be judgment calls

1 in some cases. The major toxicities that are in there were
2 taken straight from the label as it currently exists. And
3 an analysis was made of what is important for the physician
4 to know at the point of prescribing so that, as Dr. Horn
5 mentioned, you can prescribe the drug safely.

6 I think that that will probably end up being --
7 may end up being -- a point of contention between the Agency
8 and the manufacturer, certainly, as to which one should be
9 included and which one should not. Then you end up getting
10 into issues of liability, et cetera, et cetera.

11 But right now, the best I can say is that it is a
12 judgment call. It is very difficult to lay out specific
13 criteria that were used.

14 MS. WYATT: As a follow up, in your survey and
15 your focus groups, you talked a lot about the type size and
16 about the highlighting. Can we expect to see those details
17 of the format specified in your proposed rule?

18 DR. OSTROVE: Certainly, I think that it is
19 something that we want to consider. Obviously, no hard and
20 fast decisions have been made up to this point, but type
21 size is certainly -- what we have heard is that it would be
22 a lot easier if people could read it. You saw, just in the
23 demonstration of how brief summaries have changed over the
24 past years, that, in the past, 1972, you could actually read
25 the Brief Summary without a magnifying glass whereas,

1 nowadays, with the changes in leading and kerning or
2 whatever those things are, it is very difficult to read it.

3 I think that we probably will want to consider and
4 are likely to consider some kind of a minimum type size.

5 DR. BURLINGTON: I wonder if there is any comment
6 from the audience about how broadly this initiative ought to
7 extend in order to move forward. For instance, in the
8 Center for Devices, we have issues about durable medical
9 equipment, imaging and monitoring the equipment, where the
10 person operating the equipment is quite different from the
11 person who orders its use.

12 Do we need to extend this sort of brief-summary
13 information to the person ordering the use. Similarly, for
14 in vitro diagnostics, laboratory tests, the laboratorian
15 gets the label. The ordering doc doesn't. Should that be
16 part of this initiative or are those separable issues?

17 For vaccines, they are commonly administered in
18 clinics. Commonly, the labeling is not there on a patient-
19 by-patient basis. It is rather there more to inform the
20 decision made to use a vaccine or not. Any sense of the
21 breadth, or whether this is and ought to be principally a
22 pharmaceutical therapeutic initiative?

23 [No response.]

24 Don't everybody speak at once. Well, maybe you
25 can think about it and get back to us.

1 DR. LUMPKIN: Bob, are you going to talk about
2 devices?

3 DR. TEMPLE: New subject. You didn't get any
4 response on that, as probably you noticed. Lou, you
5 provided some interesting history, namely about how the
6 Brief Summary was designed to give you information -- was
7 intended by Kefauver et al. to give information about how
8 the drug worked and all that stuff.

9 Of course, the one section you are allowed to
10 leave out, the two sections you are allowed to and regularly
11 do leave out of the Brief Summary, are the Indication
12 Section and the Clinical Trials Section.

13 Are you thinking that in some new version of a
14 Brief Summary, the whole Brief Summary would be required, or
15 those parts in particular would have to be included?

16 DR. MORRIS: Clearly, any decision would have to
17 be worked out. But I think from the historical perspective,
18 as I understand it, and, again, just from a brief reading of
19 some records, at the time there was a concern that in the
20 promotional material the use might be misrepresented or
21 exaggerated in some form and that there needed to be a
22 statement that a physician could rely upon where the use was
23 not exaggerated.

24 Therefore, it literally was a balancing function
25 where the truthful statement of the indication was important

1 so physicians wouldn't be misled. I think we would have to
2 look and to see to what extent we believe that that truthful
3 statement of indications is necessary in light of the
4 oversight we give now, in light of the types of claims that
5 are being made.

6 So I think that that would go into our analysis,
7 but whether we could leave it out of a Brief Summary --
8 whether it needs to be changed, because physicians may use
9 brief summaries differently than they do labels, is another
10 issue that I think we might have to think about. Maybe it
11 has to be adapted in many other ways.

12 Clearly, liability is a whole other issue. We
13 haven't really thought through this from the standpoint of
14 advertising implications but I think it is important for us
15 to start doing that.

16 DR. TEMPLE: The current arrangement is quite
17 inconvenient. If you want to put information in the form of
18 a limitation of use as opposed to a warning, you have to
19 simultaneously write in your approval letter that this is a
20 reminder that this information must always be included in
21 the promotion, which is a big pain in the neck. It would be
22 a lot simpler if the important parts of labeling were
23 routinely part of the Brief Summary and the unimportant
24 parts weren't.

25 MS. TONI STIFANO: Toni Stifano, Center for

1 Biologics. Just an interesting point when you were talking
2 about the indications being included as part of the Brief
3 Summary. Some of the products that have come in as part of
4 the Center for Biologics tend to be tomes. They are
5 extremely long, multiple indications.

6 There is a provision in the Regulation that will
7 allow you to do an indication-specific Brief Summary. I
8 have been asked, on several occasions, to work with
9 manufacturers in doing that. I think it is a point that
10 really does need to be considered. Also, just a question
11 that crossed my mind for devices; there is a lot of
12 publicity as far as the harmonization for international
13 markets and what that means in terms of submissions. How
14 are you going to handle the labeling with the harmonization?

15 DR. BURLINGTON: To our knowledge, the Europeans
16 don't regulate device labeling in any systematic way. It
17 is, in fact, the province of every notified body, and there
18 are many of them, 25 or more.

19 MR. PARKER: Jonathan Parker, Rhone, Poulenc,
20 Roher. Going through this prototype that you have here, one
21 thing does stand out. As mentioned previously in the
22 discussion, the insert typically is a long accordion-like
23 device. What we have here when we look at it is a little
24 more than seven and a quarter pages.

25 As you look at it, too, as you look at the point

1 size, I am sure the point size isn't any more than, say,
2 five or six point. Would it be your intention that a
3 booklet would come with every bottle?

4 DR. LUMPKIN: I think the point, again, that we
5 were trying to make at the beginning of this is looking at
6 it from a conceptual basis from the idea of using white
7 space, from the idea of using minimal point size. This was
8 not really thought of as being the example of how it should
9 be all the way through.

10 I think the point that Bruce made earlier on in
11 relation to the litigation was that we fully realized this
12 is not going to shorten the label from what we have right
13 now. That was never its intent because we knew that we
14 would never, ever, get it past the lawyers to get it much
15 shorter than what it is right now, but a way of trying to
16 segregate the information, as it were, into the information
17 that one needs to know on kind of an on-time basis in order
18 to use the product effectively and safely, and then the more
19 comprehensive information that exists about the product that
20 is there in a way that somebody can go and find the bits and
21 pieces that they need.

22 So, if anyone has this illusion that this is going
23 to shorten the labels, let me dispel that. That was never
24 the intent. It really was the intent to try to organize it
25 in a better way by having the two sections.

1 MR. PARKER: To follow up on that, there is an
2 initiative right now with patient package inserts. I was
3 just wondering if you would be following with that
4 initiative that, perhaps, having the patient package insert
5 also follow a similar format and style.

6 DR. LUMPKIN: You asked the ultimate question;
7 right? It was on everybody's mind and he was the only one
8 who would come forward and ask it. I think, as many of you
9 realize, when many of us have been talking about labels over
10 the years, there have been people, including myself, that
11 had talked about a tripartite label, that you would have the
12 Summary, you would have Encyclopedic Information and then
13 you would have the information for a patient in lay language
14 so that he or she understood how they needed to use the
15 product with their health-care practitioner's help.

16 At this point in time, as all of you are aware,
17 the patient package-insert regulation is going down its own
18 track. We have decided to decouple this particular
19 initiative from that initiative because we didn't want them
20 to get interlinked and not go to fruition because one or the
21 other started interfering with the other initiative.

22 So we see this as really an initiative to deal
23 with the ^{professional}~~patient~~ labeling as we know it today to add the
24 Health-care Practitioner Summary at the beginning and to
25 deal with issues that we have talked about today. If, years

1 and years later, we finally come to the consensus on the
2 patient package insert, if ultimately it can dovetail in as
3 a third form, we will cross that bridge if and when we ever
4 get to it.

5 DR. MORRIS: Just to say that, at least in the
6 current version of the labeling, if an approved PPI does
7 exist, there is a requirement to reprint it at the end,
8 reference it in the Patient Information Section and reprint
9 it at the end. Whether that should or should not go on in a
10 revision is something that we are considering the comments
11 about. But, at a minimum, our^r thought is that physicians
12 should have access to the patient information that does
13 exist.

14 In terms of your question about format, I guess my
15 question is what format is going to work best for what
16 audience and we should try to optimize it. We may need to
17 think of different formats because of different expertise,
18 different ways of thinking about different decision that
19 need to be made.

20 So, personally, I don't see why we would have to
21 be locked into one format for both types of audience.

22 MR. PARKER: I wouldn't say that you would locked
23 into it. One of my thoughts is -- I am a practicing
24 pharmacist. A lot of times pharmacists do include the whole
25 PI when they give it to a patient when, actually, sometimes

1 it is dangerous. But when they do, obviously, it would be
2 easier for the patient, if they do have questions with their
3 patient side of the information, to be able to, then,
4 reference information medically.

5 DR. MORRIS: Good point.

6 DR. OSTROVE: I would also point out that one of
7 the other things that we heard in the initial focus groups
8 was that, with regard to the patient counseling section,
9 that a number of the physicians said that they would really
10 like to have patient information at the end of the package
11 insert so that they could take it out, xerox it, and give it
12 to their patients, that there were a number who basically
13 said they would really like to have that information.

14 They didn't necessarily need it in the summary,
15 but they would like to have it in the comprehensive label.

16 DR. LUMPKIN: As we are getting close to the lunch
17 time here, are there any other comments or questions people
18 would like to make? If not, in closing, the one thing that
19 I would like to say, as we close, just in response to one of
20 the questions made about whether, indeed, this should be
21 entitled new information, I thought that was a very, very
22 interesting comment.

23 I got back earlier this week from Germany where I
24 was working with some of my ICH colleagues on safety
25 reporting. One of the big issues there deals with what

1 defines a core datasheet as far as expectedness for
2 reporting safety issues. It was interesting that, in the
3 process, people talking about arcane procedures, it was one
4 of the times that we, here, at the FDA got good comments
5 because it was pointed out that, even in Europe, you can't
6 even add new safety information without preapproval whereas,
7 at least here in the United States, clearly you can do that.

8 I think it is interesting, though, when you talk
9 about -- we all realize that the labeling, itself, the
10 actual text as it has been used in the past on paper, has
11 not been the mode for disseminating new information, and
12 particularly new information that needs to be disseminated
13 quickly, if there really is a very important safety issue.

14 We do have other means for doing that but I think
15 we do see this as a way of highlighting for practitioners
16 when they go to labeling of information getting to a point
17 where it has been verified to the perspective that now it
18 can be included in the labeling. Or, if it is new safety
19 information, that the company has deemed it necessary to put
20 it into the label.

21 I would be interested to hear what people have to
22 say about what they might want to call this. That was a
23 very interesting comment, and we would be interested in what
24 you have to say.

25 It is now about 25 after. Why don't we plan to

at

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1 regroup here at 1:30 and we will start hearing what our
2 reactor panel has to say at that point in time.

3 [Whereupon, at 12:30 p.m., the proceedings were
4 recessed, to be resumed at 1:30 p.m.]

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

2 [1:30 p.m.]

3 DR. LUMPKIN: Before we get started with the
4 afternoon session, I realize a fair number of people here
5 today went to the various restaurants around so I am sure
6 there will be people trickling in as we go on.

7 **REACTOR PANEL**

8 As we said this morning when this morning began,
9 we have a real special opportunity this afternoon to hear
10 from seven individuals who represent the major professional
11 organizations that are involved in prescribing prescription
12 drug products here in the United States. We are very, very
13 appreciative of these people taking their time to come this
14 afternoon and to give us their perspectives on this
15 particular initiative.

16 As I said this morning, several of these
17 individuals have been involved, to a much greater extent in
18 this initiative, than have others here. So I think we are
19 going to get a little bit of a mixed perception here from a
20 time perspective as far as people's involvement with this
21 process.

22 What we thought we would do this afternoon is
23 simply go down through the seven individuals that we have
24 and give them an opportunity to share with us their views on
25 this initiative, things that they think are heading in the

1 right direction, things that they think are, perhaps, there
2 are better ways of doing. Then, following their
3 presentations, we will have our final open session here for
4 questions and thoughts from any of you to discuss with
5 anyone here in the front of the room.

6 As you can tell, the panel members are sitting to
7 my right here. The first individual who will be talking
8 with us this afternoon is Dr. Donald Bennett who, as Nancy
9 pointed out earlier, during his time on this initiative, was
10 representing the AMA, but this afternoon, he will be
11 representing the United States Pharmacopeial Convention.

12 **DONALD BENNETT, M.D.**

13 DR. BENNETT: Thank you, Dr. Lumpkin. I had some
14 prepared remarks, but I have decided to put those away and
15 simply react to some of the things I have heard this
16 morning. Some are sort of housekeeping items in one sense
17 of the word. Some are more important concerns and there are
18 one or two new things that I would like to bring up.

19 First of all, the whole process the FDA used in
20 this evaluation, I felt it was very fair, a very accurate
21 accounting, this morning, of what had taken place. I only
22 attended the early focus groups and I can honestly say that
23 -- and wrote a trip report on it and mine matched exactly
24 what they provided to you this morning.

25 So, overall, I support the whole change in

1 labeling just as a generalization. I would like to make one
2 point of clarification. On the proposed label, itself, I
3 had an item in my prepared remarks which said what it isn't.
4 I thought I don't really need to say that, but after this
5 morning, I would like to reinforce it. It isn't a
6 comparative evaluation of all labeled and unlabeled uses for
7 the practicing physician or the health-care professional to
8 make a prescribing decision.

9 This mockup truly determines that -- is based upon
10 the fact that the prescribing decision has already been
11 made. I thought the Indications and Dosage Table were very
12 good. It was taken out in the copy that I have that I
13 received on Thursday, but it was in some prior copies that I
14 had at home, so I was glad to see that the one I really
15 wanted to see up there on Capoten was up there.

16 I wasn't sure when Dr. Lumpkin mentioned side
17 effects and, perhaps, a cutoff at 1 percent, whether he
18 meant minus a placebo rate or an active drug. But I think
19 that ought to be clarified.

20 I am not as worried as Dr. Woodcock was about drug
21 interactions, a listing of them, even. Perhaps, if I could
22 use a different analogy just because it is easy; when I was
23 looking at the Capoten sheet which we have used as a
24 prototype, I saw hepatic failure. In fact, I was reading it
25 in the clinic one night, and I didn't remember that at all.

1 I turned to hepatic failure quickly in the
2 prototype and suddenly realized that the minute I saw the
3 word "rarely," I almost didn't read any further. But the
4 important thing was it forced me to take a quick look. I
5 think there will be that aspect of it even if it is only a
6 listing at times.

7 I thought Mark Horn's comment about the New
8 Information Section and changing that to a Recent Labeling
9 Change was excellent. That just makes good sense.

10 Now, some of my concerns. Is this going to be
11 adequate information for direct-to-consumer. I think you
12 have to be a little bit careful here. There is a lot more
13 negative data in there than there is positive data. I have
14 been associated with IRBs since 1980. I have been the
15 Chairman of one for the last ten years. I think we need to
16 take a lesson there.

17 We try and get in as many benefits as we can risks
18 in the informed consent because there is a natural tendency
19 to include everything that is sort of bad, or ugly, if you
20 will. In fact, we just had a major meeting of the Annual
21 IRB Boards in Boston. They take up a lot of issues there.
22 One of them was that we have all watched them grow from two
23 sentences up to about anywhere from five to ten pages, now.
24 Is that good?

25 In fact, there was a lot of discussion about the

1 retention of information versus the understanding and that,
2 therefore, outcome studies are needed for understanding. I
3 think the analogy, the lesson to be learned here, is that
4 the Agency really needs to measure did we achieve a desired
5 outcome fairly soon. I was pleased to hear that there will
6 be an additional 500 physicians studied before this all goes
7 to a final notice of publication in the Federal Register.

8 What is important? That concerns me. I think
9 there we need to take a lesson from MedWatch. I can
10 remember how everyone agonized over what "serious" means.
11 It is hard to define. But the Agency finally, either
12 themselves or through comment period or something, came up
13 with six criteria which defines "serious," the serious
14 adverse drug reaction.

15 It is really nice, now, after a year or two, to
16 see that not only have the number of reports increased but
17 the ratio of serious to total numbers of reports have
18 increased. So I think that is important. In fact, one
19 would hope that in this comment period that we have got
20 coming up that there will be, in fact, some really good
21 suggestions for those kinds of criteria.

22 With regard to patient counseling. I may be a bit
23 confused on this subject, myself, but I don't view it as the
24 same thing as information for the patient at all. And I am
25 still not sure where we are going here. For me, the Patient

1 Consulting Section is the more critical information for the
2 patient which encourages the physician to verbally reinforce
3 and expand, if necessary, the written information provided
4 to the patient.

5 Whereas everyone here knows what information for
6 the patient is, a lot of organizations, and I think USP is a
7 good one, publish a great deal on that. Here we have some
8 differing opinions even within USP. One view recommends
9 that an abstract or, depending upon space, at least a
10 listing of those critical items in a section on patient
11 counseling be restored to the summary. There is that view.

12 Another view, in our own organization, says that
13 this section sets a standard of care which is not supported
14 in the current regulations for labeling. Because the
15 section could adversely affect physician liability, it
16 should be removed from the label. So we are still debating
17 and considering exactly what posture we might take and
18 written information is likely to be forthcoming.

19 In summary, the technology is going to lag behind
20 with regard to the computer. It just doesn't take a second
21 with hypertext and a good computer situation to go from
22 "hepatic failure" to "rarely hepatic failure is seen," et
23 cetera, et cetera.

24 I work with 30 residents in a family-medicine
25 program at the present time, and we always have the problem

1 of not only, as Mark points out, do you have eight minutes
2 per patient but, if those residents get behind, you get a
3 little apprehensive as well, and trying to get everyone
4 happy including the patients is very difficult. But until
5 we have the kind of computer technology that is available
6 today, sitting right there with that kind of drug
7 information on it, I think we have got a ways go to yet.
8 But this is a great start.

9 Thank you.

10 DR. LUMPKIN: Thank you, Dr. Bennett.

11 The next person we will be hearing from is Dr.
12 Joseph Cranston representing the American Medical
13 Association.

14 **JOSEPH CRANSTON, Ph.D.**

15 DR. CRANSTON: Thank you, Dr. Lumpkin. First of
16 all, I would like to commend the Food and Drug
17 Administration for undertaking this initiative that,
18 hopefully, will result in a more useful and user-friendly
19 professional labeling for the prescribing physician.

20 I was added to the FDA's Project Advisory Group
21 only about two months ago after Don retired, so my
22 historical perspective on the project is somewhat limited.
23 But I would like to offer about eight comments on the
24 prototype that was discussed this morning.

25 First of all, the FDA has conducted two focus

1 groups already as well as a physician survey and listed an
2 intent, this morning, to do additional research in the area
3 in the future. So I think the Agency is pursuing this
4 project in a careful way. And the prototype that you saw
5 today probably does, in fact, represent something that the
6 physician would desire; a Short Summary, a numbered Table of
7 Contents and a reordered package insert to reflect their
8 needs.

9 To date, the FDA's focus has been on revising the
10 package insert to make it more useful and user friendly for
11 physicians as they care for their patients. I would hope
12 that this remains the focus as opposed to letting liability
13 concerns take over. In that regard, I believe that the
14 summary, as seen in the prototype, should have space
15 limitations. The half page is probably a good size. A
16 consistent message from physicians to the FDA has been to
17 keep the summary short.

18 A third point. The numbering system for major
19 headings -- that is Indications and Usage, Warnings,
20 Precautions, and so on should be standardized across all of
21 the products. This would make the new PI much easier to
22 access, particularly amenable to computerization.

23 Fourthly, the new PI summary should replace the
24 currently Brief Summary that is required in advertising. I
25 believe it will be much more useful.

1 Fifth, the addition of the New Information
2 Section, and I agree with Don that Dr. Horn's recommendatio.
3 is probably a very good one. I think it would be very
4 useful especially if the PIs are available by on-line
5 databases.

6 Sixth, the inclusion of Drug Interactions as a
7 major heading would be welcomed by physicians especially as
8 they become more involved in perspective drug-use review at
9 that point of prescribing.

10 So I think, in summary, a summary adds value to
11 the PI from the physician perspective because they will be
12 more readily able to access that information and save
13 valuable time. However, I think there are a couple of
14 concerns that need to be raised. One; will the physician
15 fall into a false sense of security with the summary and
16 fail to access the full text of the PI when it is necessary
17 to do so.

18 For example, a patient may have renal dysfunction
19 that makes a particular drug interaction more clinically
20 relevant, but the interaction may not be of sufficient
21 importance to be included in the summary on the list. Can
22 this type of problem be avoided in some way by carefully
23 constructing the summary -- so that is not going to be a
24 problem.

25 Will FDA being doing additional research to test

1 the physician's ability to perform tasks of the new
2 prototype. The other concern is related -- it was brought
3 up this morning to some extent, and was brought up in the
4 Project Advisory Group -- and that is the issue of
5 effectiveness. Clearly, we don't expect to see comparative
6 effectiveness among products in PIs or summaries, although
7 that would be, certainly, useful to prescribing physicians.

8 However, more and more products are being approved
9 for indications when their actual effectiveness may not be
10 all that great. That is particularly true with some
11 accelerated approvals. The examples that come to mind are
12 Tacrin for Alzheimer's and some of the antiretroviral agents
13 for HIV. It would seem to me that either more clinical-
14 trial information about effectiveness needs to be in the
15 summary under these circumstances or, alternatively, there
16 must be some way to clearly signal to the physician or
17 reader to refer to the relevant section of the PI for more
18 detailed information.

19 So I guess I would like to conclude by stating I
20 believe the FDA is on the right track in terms of making the
21 PI more useful and user-friendly for physicians. I believe
22 some additional research should be done in the prototype.

23 Thank you.

24 DR. LUMPKIN: Thank you, Dr. Cranston.

25 The next person we will be hearing from is Dr.

1 Cheryl Graham from Biometric Research Institution,
2 Incorporated.

3 **CHERYL GRAHAM, M.D.**

4 DR. GRAHAM: Thank you, Mac. First of all, as
5 with my colleagues, I really appreciate the opportunity to
6 be on this panel today. This has been a long-term
7 relationship with this project and I really value my
8 colleagues' ability to keep me on the panel and continue
9 with my interest in this area.

10 I am going to take a somewhat different viewpoint,
11 only to be controversial maybe, but also to get some
12 comments from you folks in the audience who have been very
13 quiet up to now. I would like to say it in one sentence.
14 "One size may not fit all."

15 Let me tell you why I am concerned. From my
16 viewpoint, product information goes through a life cycle
17 very much like the product, itself, does. It starts
18 basically in the marketplace with a launch program. It
19 becomes a more mature product with a fairly constant flow of
20 the same kind of information and it eventually goes into an
21 end stage, maybe a long-term life in the market.

22 Each of these cycles takes somewhat different
23 information. I think that the Brief Summary, as we have had
24 it presented today, speaks quite eloquently to a mature
25 product and one that has been on the market for probably

1 greater than six months, maybe a year, and that the PDR,
2 itself, is really reflective of that.

3 However, the ability to get the appropriate
4 information for products which may be early in cycle, who
5 are new products, or old products that are still being used,
6 or for many of the other products for which there is not a
7 PDR; devices, many of the parenteral products. There are
8 whole host of therapeutic products now for which there is no
9 PDR and there is no really ready source of information.

10

11 So what I guess my bottom line here is that I
12 think we not only have a brief-summary problem but we also
13 have a dissemination problem with respect to overall product
14 information for various other products that are not really
15 being addressed here today.

16 Getting to the notion of the Indications Section
17 and the clinical trials, I would suggest that early in the
18 product-information cycle, during the launch period, there
19 is a fairly heavy burden to educate the health-care
20 practitioner community into using the product correctly and
21 that consideration should be made as to whether a Brief
22 Summary during that period of time really would be
23 appropriate.

24 Much of the marketing materials, at that point in
25 time, are really a reiteration of the scientific data on

1 which the product was based. Consequently, some
2 consideration may want to be given to at what point in the
3 product cycle you actually add the Brief Summary and allow
4 it to become a primary focus for accessing maybe the more
5 detailed information.

6 Finally, one last parting thought. There is
7 probably a need, and it gets to the legal liability here a
8 little bit, in the use of actually something speaking to the
9 audience about the utility of the information that they are
10 actually getting. For instance, something to the effect
11 that if you are a first-time prescriber of this product,
12 this Brief Summary information may not be adequate
13 information, as opposed to saying something more derogatory,
14 just being more helpful in saying there is additional
15 information located someplace else and directing -- in this
16 real-life situation that we have right now, we are not all
17 computerized yet, in that the actual direction to additional
18 paper and additional sources of information may be the key
19 to making the Brief Summary, as proposed, to be more
20 palatable to the entire community.

21 I look forward to participating and hearing more
22 feedback from all of you in this process as it goes along.
23 I think this is a major undertaking by the Agency. I think
24 it has long-term implications both within companies and
25 within FDA with regard to the burden of regulatory oversight

1 and, I think, the detailing and updating that will be
2 necessary to make this project entirely viable.

3 Thank you very much for inviting me.

4 DR. LUMPKIN: Thank you, Dr. Graham.

5 The next speaker on the panel is Mark Horn whom we
6 have heard from some during the discussion. Dr. Horn is
7 representing the Pharmaceutical Research and Manufacturers
8 of America.

9 **MARK HORN, M.D.**

10 DR. HORN: As many of you probably know, PhRMA
11 represents an array of companies. As this process is a
12 process in evolution, I think it would be inappropriate to
13 have a PhRMA viewpoint at this time because I don't think
14 there is a PhRMA viewpoint.

15 On the other hand, the industry has historically
16 reacted in certain ways to the kinds of proposals that are
17 put forward here. I certainly feel comfortable reflecting
18 some of the values that PhRMA brings to the table in
19 discussions like this one.

20 I think I agree with everyone so far at being
21 impressed at both the motivation for this effort and its
22 quality. I guess that is where I will start. I think that
23 it would be a shame, having gone this far, to not take the
24 input from the physicians that you have so carefully gone to
25 talk to. You have identified your customer. I think you

1 have chosen well. You have asked your customer what he or
2 she wants and they have told you, in no uncertain terms.

3 I think that it is flattering, always, to be in a
4 situation where somebody is actually seeking your piece of
5 information out. The doctors are telling you they are going
6 to these books. In the clinic where I work, it actually has
7 to be nailed to the wall or otherwise it will be stolen.
8 And they want the information that is there.

9 But they don't want all the information that is
10 there acutely. They only want some of it. They want to
11 know the indications. They want to know the dose. They
12 want to know how the medicine is supplied, what the
13 dangerous drug interactions are, what are the key side
14 effects, whether pregnancy is an issue, and to what degree
15 it is an issue, and any specific instructions that are
16 needed that are pertinent to the immediate safety of the
17 product.

18 And they are asking you to tell them that, and
19 tell them that, succinctly. Clearly, and I am certain here
20 that my PhRMA colleagues will agree, it is critical that the
21 entire document be provided. It is also critical, and here
22 the liability issue either gets dealt with or it doesn't get
23 dealt with, that somehow the fact that what the prescriber
24 is looking at is a succinct Brief Summary, and is not meant
25 to be anything more than that, has to be clearly stated.

1 My supposition would be that there is a very
2 legitimate way to deal with that and handle the liability
3 issue. If there is, this is a doable project. If there
4 isn't, then industry is not going to support it. That is
5 something that the lawyers have to sit down and work
6 through.

7 That said, I also would suggest that a lot of the
8 discussion that has dealt with exactly what should be in the
9 summary and what shouldn't clearly is going to be product-
10 related. Here, the manufacturers ought to be engaged to
11 work with FDA to help you determine, on a product-by-product
12 basis, what belongs in the Brief Summary and what does not.

13 I would encourage you to do that and I would
14 anticipate that the industry response would be enthusiastic.

15 Someone mentioned this morning about the mechanism
16 for introducing this, that there was a supposition it would
17 immediately take place with the newly approved products and
18 then move, ultimately, to involve the 200 or so most widely
19 prescribed products. I don't have a position on that today
20 except I would say that the fact that you have the ability
21 to introduce this slowly allows you to do the experiment and
22 evaluate the results.

23 I would say that one of the key problems with
24 health-care as it is evolving is people jump in and do
25 things and only later on worry about the effectiveness of

1 what they have done and thing about the problems that they
2 are going to have measuring it.

3 Here, you have a chance to deal with that in
4 advance. I would suggest that part of this process ought to
5 be that the evaluation arm should be built in from the
6 beginning. You should know exactly what you are going to
7 measure, who you are going to ask, how you are going to
8 measure it. I would introduce it in a way that allows you
9 to get good data on the effectiveness and safety of this
10 process before you go the 200 most widely prescribed drugs
11 in the country. That is a fairly significant movement and I
12 think you can probably do it much more comfortably once you
13 have good information.

14 Someone mentioned this morning that there was a
15 possibility this would increase the flexibility and
16 usefulness of promotion and the ability to promote with a
17 little more facility. Certainly, the industry would be very
18 comfortable with that.

19 I have one additional comment on the issue
20 regarding the New Information Section that we alluded to
21 this morning. It sounds like there is general agreement
22 that, perhaps, the labeling of that section needs to be
23 changed.

24 I would also want to just mention one more
25 concern. There is no objective reason to have this concern,

1 but it makes me nervous, nonetheless. Nature and package
2 inserts abhor vacuums. When you have a space in the package
3 insert that talks about something new, there is going to be
4 a desire to fill it. I think we have to be careful, given
5 that this is primarily going to be, I imagine, a safety-
6 focus issue, that we not change at all the standards by
7 which new safety information gets into the package insert
8 out of a desire, and out of a sudden availability of this
9 new space in which to advertise it.

10 I think that reality being reality, that could
11 occur. I just raise it now as something that ought to be
12 part of the deliberations going forward.

13 Lastly, I know that many of the people in the
14 focus panels talked about cost information. Here, I will
15 diverge briefly from my other views. I think cost
16 information in the current environment is not scientific
17 information. It is business information. It changes based
18 on a lot of issues that really are not related to things
19 that ought to be in the package insert. As much as
20 providers might like to have it, I don't think that this is
21 the place where it belongs.

22 Thank you.

23 DR. LUMPKIN: Thank you, Dr. Horn.

24 The next individual that we will hearing from is
25 Dr. Calvin Knowlton from the American Pharmaceutical

1 Association.

2 **CALVIN KNOWLTON, Ph.D.**

3 DR. KNOWLTON: Thank you. The APHA, like others,
4 is delighted that we are asked to participate. I think we
5 have, perhaps, a little bit different perspective
6 representing practicing pharmacists. I would like to share
7 two points explicitly. However, before I do that, because
8 we are coming from a bit of a different perspective, I think
9 I need to spend a couple of minutes with a prelude to those
10 two points.

11 I will start with that. The first prelude is that
12 our perspective, or the perspective that we were struck with
13 when we looked at this, is that prescribing goes beyond just
14 physicians. It just seemed to me that it was a unilateral
15 or unitary focus on physicians from this morning and from
16 what I have read. I think we need to, perhaps, revisit or
17 consider revisiting that from a health-care practitioner
18 viewpoint.

19 The second thing is, as a prelude, is that this
20 morning I was struck with two things. One, someone said
21 that information business goes beyond drug prescribing. We
22 believe that that is a core value. The second was that drug
23 use goes beyond mere prescribing. We believe both of those.

24 Let me get to my point of the prelude. The recent
25 studies that have come out over the last five or six years

1 have shown to Pharmacy at least that there is another drug
2 problem in our society, and it is the problem of not
3 optimizing drug use. Pharmacy has made a decision about
4 1989 that we were going to try and attack that and we were
5 going to try and enter a new role, a societal role, for
6 pharmacists.

7 This is the third time we have done this in the
8 last 300 years since we have been around. We were first
9 apothecaries. We were then compounders for a number of
10 years, for over 100 years compounding medications. For most
11 of this century, we have been distributors of medications.
12 We believe that it is time to go into a fourth phase over a
13 third threshold, as I mentioned, into the era that we have
14 termed pharmaceutical care which is an era that has been
15 decided internationally in Pharmacy that pharmacists will be
16 entering that.

17 It has to do with pharmacists getting involved in
18 the management and monitoring of drug therapy with a goal of
19 optimizing outcomes -- not particularly talking about giving
20 up the distribution of drugs but getting involved in the
21 ongoing management and monitoring of drugs because it is
22 clear from some of the studies -- the Bootman study that
23 came out a couple of weeks ago and the Col study back in '89
24 and a number of others -- that we have a substantial problem
25 in the misuse of medications. No one is really adequately

1 monitoring and managing it and someone needs to step up to
2 the plate to do it, not as a substitute to physicians, NPs
3 or PAs but, indeed, as a complement.

4 Once they have worked up a patient and given an
5 initial care plan, then someone would provide the ongoing
6 pharmaceutical care. That is where we position pharmacists.

7 I say all that to then get to my two points. The
8 first point is that I think it is time, or APHA believes it
9 is time, for us to consider changing the Warnings and
10 Precautions Section, that type of section, to more of
11 explicit monitoring parameters. There are really no
12 explicit monitoring parameters in the insert. Lord knows,
13 with the research that is out there, that is where people
14 are getting tripped up right now when there is not explicit
15 notions of, "When do I do this?" "When do I do that?" "How
16 do I monitor for this drug?" and "How do I monitor for that
17 drug?"

18 What should be assessed when, what clinical
19 things, what adherence type parameters should be assessed.
20 So we believe that there is a real need for someone to come
21 up to the plate with some explicit monitoring parameters
22 somewhere in there. Now, they are laced throughout, but we
23 believe they need to be pulled together.

24 So somebody could use the hypertext when a patient
25 comes in and say, "These are the ten things I need to make

1 sure I am looking at."

2 The second point that APHA would make is, as Dr.
3 Bennett did, that we would caution also on the last section
4 of Patient Counseling because we, too, believe that it is
5 time to move beyond a drug product focus in counseling and
6 move into a patient focus. It is real difficult to do that,
7 obviously, with a drug-product monograph for labeling.

8 The nature of the material presupposes patient
9 empowerment which is not there. Not to pick on this
10 prototype, but just look at the first couple of paragraphs
11 under Patient Counseling. "Patients should be advised to
12 immediately report something." "Patients should be told to
13 report." "Patients should be advised not to use potassium-
14 sparing diuretics."

15 It presupposes, I think, a lot of empowerment that
16 is not quite there. We believe this should be something
17 between the health-care practitioner and the patient and
18 that, perhaps, some bullets there of items could be worded
19 somewhat differently. We would be happy with that.

20 Please don't let that douse, though, the overall
21 mission. We believe that you have done a marvelous job
22 here, that it is timely, it is on target, and we applaud
23 your efforts.

24 Thank you.

25 DR. LUMPKIN: Thank you, Dr. Knowlton.

1 Clearly, our data suggest that the PDR is the most
2 commonly used drug reference by PAs, as it is for
3 physicians. Over the past several years, there have been a
4 variety of other drug references developed and produced,
5 some specifically for PAs which are very highly used as
6 well. But, clearly, the need for drug references are very
7 important.

8 Having said all that, I think we support strongly
9 the efforts here of the summary information as it has been
10 presented. The use of a very brief summary with what I
11 would call "steered references" is, I think, a very
12 effective way to deal with a very large amount of
13 information as seen in the prototype.

14 I think it is also important, and I think this is
15 reiterating what Dr. Horn said earlier this morning, that,
16 at least in my perspective, the PI, itself, is rarely, if
17 ever, the sole bit of information that determines what
18 specific drug a prescriber is going to write for.

19 I think what a prescriber is looking for when they
20 look at the PI, when they look at the expanded PI in terms
21 of what is in the PDR, is some very concise information
22 about a product presumably they know a fair amount about
23 already.

24 Again, the decision to prescribe that particular
25 product should, I think, be based on a lot of other

1 information and to look to the labeling, itself, as exactly
2 why this one particular product is used, I think, is
3 overstating the importance of the labeling.

4 I think it is also fair to say that, generally
5 speaking, most clinicians have a relatively small stable of
6 products that they use, let's say, to use the example here,
7 of ACE inhibitors. They don't have to know all of the
8 information about all six or eight ACE inhibitors available,
9 but they will be using a relatively small number so that,
10 again, the product label information is to help them with a
11 product they may not be very familiar with but just to look
12 for the particular contraindications, et cetera, et cetera.

13 Also we would strongly support, which has been
14 mentioned several times, the change of the category from New
15 Information to Recent Labeling Changes. I think that is a
16 very good one. Finally, the patient counseling information
17 -- I am differing a little bit with what Cal just said, but
18 we feel that PAs particularly have a strong role in patient
19 education and patient counseling and I think that
20 strengthens these documents to include a specific reference
21 to that sort of information.

22 Thank you.

23 DR. LUMPKIN: Thank you, Mr. Thomas.

24 The last individual you have on the Reactor Panel
25 this morning is Dr. Jan Powers from the American Academy of

1 Nurse Practitioners.

2 **JAN TOWERS, Ph.D., RNC**

3 DR. TOWERS: I hope this is last but not least.

4 DR. LUMPKIN: Absolutely.

5 DR. TOWERS: Not having been a part of the process
6 that has gone on, I do feel a little like someone who has
7 been shown a new house that has been newly decorated and
8 they say, "Here it is; what do you think?" I do get the
9 sense that there is some room for movement. I also get the
10 sense that maybe I had better make a couple of comments
11 about nurse practitioners since my colleague from the
12 physician-assistants group pointed out that not everybody
13 yet realized that we do, indeed, prescribe.

14 We are about 32,000 strong, make up a variety of
15 specialties that mirror the specialties of the primary-care
16 groups of physicians so that we are framed in primary-care
17 activities primarily in the area of family, pediatric,
18 adult, women's health kinds of care. Prescribing is a major
19 part of our activity along with the other things that we do
20 in providing primary care to the patients that come to us.

21 We find ourselves utilizing the materials that are
22 under discussion a great deal, so I do have some comments
23 related to what has been presented to us so far. Because we
24 are new to this particular process which looks like a very
25 well thought-out process with focus groups, et cetera, I

1 would like to speak to three areas: first, the concept;
2 next some current suggestions related to the current
3 document; and then a few additional things to plant as seeds
4 that, perhaps, can be looked at further in the future.

5 The concept, of course, as everybody else has
6 said, is fine. It is very nice. One of the things that I
7 do want to point out is that we do feel very strongly,
8 however, that a Summary standing alone is, certainly, not
9 enough, that the larger document that comes with the drugs
10 and is printed in the PDR has very useful information that
11 is very necessary for understanding the ins and outs of
12 particular medications that are used on patients.

13 In looking at this, I reviewed, sort of thinking
14 how the physicians were interviewed in their focus groups,
15 the materials in that context and identified, with some of
16 our people, what are the things that we most use in these
17 documents. Of course, it came out to be very similar to
18 that of the physicians; the dosage administration, the
19 contraindications, the warning, the adverse reactions and
20 the precautions.

21 One other piece that came up with us that we feel
22 very strongly about is that we really do value the
23 description of the drug actions, the clinical pharmacy
24 pieces of this. One of the things that we have found is,
25 like physicians, nurse practitioners do have their own

1 favorite group of drugs that they prescribe and they always
2 know those very well and utilize them.

3 The other thing is that nurse practitioners often
4 deal with vulnerable populations who are transient patients,
5 who are poor, who are uninsured, who are elderly people,
6 many of whom have multiple health and medical problems.

7 I work, in addition to my activities with the
8 Academy, in a homeless clinic one day a week. When I see
9 the patients that are coming to me who have been seen in a
10 variety of emergency rooms all around the Washington-
11 Baltimore area who have moved from clinic to clinic and come
12 in, sometimes with a list of drugs that they have taken,
13 sometimes with a bag full of bottles of drugs that they have
14 taken and have been prescribed to them, trying to sort out
15 the multiplicity of treatments that have been instituted
16 with these patients can be a very time-consuming process.

17 Understanding the drugs that these people are
18 taking and how they may be interacting with each other
19 becomes a very important part of my role in helping them to
20 get the kind of continuous care that they need in order to
21 manage the chronic problems with which they deal. The
22 information related to packaging and in the PDR becomes very
23 valuable in that framework.

24 What we find is that patients often are on
25 multiple drugs doing the same thing. They are often on

1 incompatible drugs and are having side effects that they
2 have no knowledge of. Some of this comes from the fact tha
3 they go places where they really are not in a position where
4 they can give -- or their complete histories are necessarily
5 being taken -- that they are often treated with what is on
6 the shelves because people know that they will not be able
7 to go out and get the prescriptions filled.

8 All of these combinations of things lead us to
9 some very complex problems when you are dealing with these
10 patients.

11 In the current documents, the thing that probably
12 was most exciting was to find the Index. The biggest
13 problem that anyone has, as I think you have become aware,
14 is that finding information that you need, pertinent
15 information that you need when you need very specific
16 information, can become difficult when you are working in a
17 very busy clinic or a practice situation.

18 In looking at the short form -- actually, I looked
19 at two short forms. One was called a short form and one was
20 called a moderate short form, so I guess the first one was a
21 short short form. At any rate, it is clear that the short
22 form was easier to read. You could get pertinent data
23 related to that. Having those kinds of summaries can be
24 very useful.

25 One of the things that I did find, however,

1 knowing the kinds of things that we look for, is that the
2 moderate form did a better job than the short short form in
3 terms of giving you enough data that you understood what you
4 were reading. Some of the bullets in the very short form
5 were so short that you really would have to go to the large
6 document and check things out further to understand what
7 some of them meant.

8 They did have a tendency, sometimes, to be code-
9 like. I guess my comment there, as has been said by other
10 people, is beware of being too brief, that that can, indeed,
11 lead to difficulties in utilization of the data that is
12 there.

13 Other suggestions that we would have that parallel
14 very much what has already been said, I think, is that the
15 summary of the drug action at the beginning could be useful.
16 I think this is something that wasn't mentioned by any of
17 the other groups, that having something that introduces the
18 drug at the very outset of the summary would be a very
19 useful thing that helps to orient the person to determine --
20 particularly if you are trying to determine what a drug is
21 that a patient is taking that is not in the particular
22 framework that you are prescribing.

23 Another thing that if you read it, having the How
24 Supplied right next to the dosage is very useful. Right
25 now, the sample that we were shown has it separated. One of

1 the things that you do is you figure out the dosage and the
2 next thing you do is you figure out how it is supplied in
3 order to write your prescription.

4 When those things are separated, that, again,
5 takes some time to try to locate those pieces. Wherever
6 they placed in the document, it would be wise to keep them
7 together as they are currently, I think, in the PDR plate.

8 We, too, think that a separate category for drug
9 interactions is very valuable. The other thing that we
10 would caution about, also, is that the Patient Counseling
11 Section as it is stated in the current document that is
12 being shared with us really is not a patient handout. As we
13 were talking about how this is to be used with patients,
14 those kinds of things should be taken into consideration.

15 There are some guidelines there for providers, a
16 checklist as to what they should be remembering to say to
17 patients. That is one thing. But to make copies of it in
18 its current format is probably not the most appropriate
19 thing for patients and that needs to be thought through.
20 Truly, having something for patients is very appropriate,
21 but that particular piece may be a little inappropriate at
22 this point in time.

23 We, too, would like to have a section on cost even
24 though we know that that seems to be a problem because being
25 reminded of what drugs cost is extremely important not only

1 from the standpoint of capitated care but when you are
2 dealing with vulnerable populations, as so many of us are,
3 knowing what the cost is going to be for the patient or for
4 the clinic or whoever is providing the medication does have
5 to enter into your decision making related to drugs.

6 The last issue for consideration that I would like
7 to raise with you all is one that does not seem to be
8 present in anything that has been shared with us so far and
9 I think it is something to think about, and that is that in
10 the PDR currently, and in the drug information that is
11 currently given, the dosages and indications for children,
12 for pediatric dosing and for adult dosing, are separated.

13 One of the things that we are increasingly finding
14 as the population gets older is that there really needs to
15 be careful consideration given to how we are dosing the old
16 elderly and the frail elderly who really react to drugs much
17 differently than the average middle-aged adult. One of the
18 things that we would like to see is more attention being
19 given to how to dose that particular population.

20 It slips in and out of this somewhat when you are
21 talking about the relationship of drugs with chronic disease
22 and certain kinds of pathologic conditions that people have,
23 but the whole issue of geriatric therapy, I think, is
24 something that is going to need to be addressed even more in
25 the future and this might be a good place to start.

1 Thank you.

2 DR. LUMPKIN: Thank you, Dr. Towers.

3 I think, obviously, from the comments that we have
4 heard, there are a lot of other areas people have cited as
5 areas that we might think about trying to bring in in some
6 way into this particular document.

7 **AUDIENCE FEEDBACK**

8 I would like, at this time, to open the floor for
9 comments, questions that any of you guys might have for our
10 panel, for any of us from the FDA or just any comments that
11 you might have having been through this program today on
12 things that you think are good, bad or indifferent about
13 this process.

14 While you guys are thinking about your questions,
15 I have one that I would like to pose to the panel. This
16 morning, I think you probably heard by listening to some of
17 the people from the Center for Drugs that were talking on
18 the issue of the Indications and Usage Section and the
19 Dosing Section about whether this needs to be a bulleted
20 summarized part of the summary or whether, indeed, these are
21 very special parts of the document, whether they need to be
22 verbatim, the complete text, in the summary.

23 Particularly those of you who are involved with
24 groups that are involved in clinical practice, do you have
25 any thoughts on that particular issue that you could share

1 with us?

2 DR. CRANSTON: I guess I raised the very same
3 issue in my comments. I think that if the bullet is going
4 to mislead the prescriber about the actual effectiveness of
5 the product, then you have got a problem. I am not sure how
6 you are going to get around that. If you put it in
7 verbatim, you make these so long you'll turn them off from
8 using them.

9 On the other hand, if there is not some clear way
10 to convey that information or get them to the full text,
11 then medically you could have a problem.

12 DR. HORN: I will make a brief comment on this but
13 preface it by saying that this, as best I know, has not been
14 discussed yet within any of the halls of PhRMA, so this is
15 surely not a PhRMA view. But it strikes me that you have to
16 think about why the practitioner is looking at this section
17 in this document. Someone alluded to it, but generally the
18 physician is looking up a drug that they have already
19 decided to prescribe for additional information on that
20 drug.

21 So if you are looking up an ACE inhibitor, there
22 is something about the clinical condition of that patient
23 that makes you want to use that ACE inhibitor. I don't
24 think that they are looking at this to be educated. I think
25 they are looking at this to make sure that they are right,

1 that the drug is indicated for this particular indication,
2 to verify that, perhaps, they are right in thinking it is
3 not indicated and they need to tell the patient that they
4 are giving them -- to protect themselves, they want to know.
5 They want to be able to tell the patient, "Well, I am giving
6 you this. It has been used, but it is not formally
7 indicated by FDA for this."

8 There are a variety of reasons that people would
9 want to access information like this in kind of outline
10 form. I think that we shouldn't lose sight of the fact that
11 this is a summary of an attached document that has the
12 information in full. If everyone would feel more
13 comfortable, as I certainly would, with a statement that
14 says that because, as I said before, you are going to need
15 that to settle the liability issue anyway.

16 I think there is something important that is
17 gained by summarizing it succinctly that is lost by simply
18 reproducing the document in its entirety. The question, I
19 suppose for you, and I don't know the answer, is how
20 important is that gain. My personal view is there are
21 situations and individuals that occur not uncommonly where
22 you want to know this and you want to know it quickly and
23 you don't need to whole thing.

24 If it can be structured in such a way that that
25 information can be provided with appropriate caveats to make

1 both the lawyers comfortable and the practitioners
2 comfortable -- and I don't mean that cynically at all; those
3 things must be accomplished -- then it is better to leave it
4 in this form.

5 DR. TOWERS: One of the things that I noticed in
6 looking at this is that it is nice to have that little thing
7 to check at the beginning. But if you set up your complete
8 prescribing information in a way that you can find those
9 indicators as you have here right in the beginning so that
10 it is easy to read, they can, indeed, use the complete
11 prescribing piece as an outline and, if they choose to read
12 any further, they can.

13 For instance, if you look under 3.1, 3.2, 3.3. and
14 3.4, the very things that are in the indicators are there
15 but they are bolded in a way that they are very easy to see.
16 One of the things that has always been a problem with all of
17 the materials that are either in the PDR or otherwise are
18 that it is hard to read quickly unless you have a setup that
19 allows you to pick out those things and then choose to read
20 if you want to.

21 There may be ways to combine this so that you
22 don't necessarily have to have things printed up two or
23 three times and still make it easily accessible to people.

24 DR. LUMPKIN: Mr. Thomas, what do you think from
25 the PA perspective.

1 MR. THOMAS: I think Dr. Horn said it more
2 eloquently than maybe I did when I made my comments earlier
3 that, again, I don't think that the PI is the source of
4 education of what product to use. Furthermore, as I took
5 notes from this morning, Indications and Usage was ranked
6 sixth in order of what to focus group was looking for in
7 this information. So I think that sort of, again, answers
8 the question.

9 So I would support the abbreviated bulleted text
10 there.

11 DR. BENNETT: I thought Dr. Graham answered the
12 question; "One size doesn't fit all." If it is a new drug,
13 then, in fact, I think you might ultimately decide that
14 there will be more information on indications than you would
15 normally have for a drug that had reached its asymptote and
16 was on the way to obsolescence because it is, perhaps,
17 better known.

18 Maybe she doesn't quite feel that way, but I think
19 that is the logical answer. It isn't just for the first-
20 year residents. Sometimes they know a great deal more
21 because they have been close to medical school, the
22 residents; they are into the literature, as opposed to
23 someone who has been so busy practicing he hasn't kept up
24 with it, out there for 15 years.

25 So you could subset it not only by whether it is a

1 new drug or an old drug, you could subset it by physician.
2 But I think the important thing, if it is a new drug, then,
3 in fact, it requires that there be more information in the
4 Indications Section.

5 DR. GRAHAM: Was any consideration given to
6 potentially putting another section in there about the
7 actual population intended for use as opposed to this more
8 generic kind of indication. It is lifting the words out of
9 the current Regulations but, in fact, drugs are developed
10 and focussed in a fairly specific target population and
11 maybe that is the kind of information that would be more
12 useful in that particular section than the sort of generic
13 indication that we end up with.

14 DR. LUMPKIN: How about from the audience, now
15 that you have had time, thought about questions? Anything
16 you would like to propose?

17 MR. RON LIEBERMAN: Ron Lieberman from FDA. I
18 would like to just take maybe a minor exception to something
19 that was said here about -- that the PDR is not the place --
20 I am not sure if I am paraphrasing this correctly -- where
21 we would want to find out about which drug to use. I think
22 that I would like to pose the proposition that I think it is
23 possible to provide information about front-line drugs. I
24 think that is a very important issue.

25 I don't know why the PDR cannot address that,

1 particularly hypertension and congestive failure. You could
2 go on for serious infections. You could go all the way dow
3 the line. Certainly some feeling about whether this is
4 front-line therapy or some word -- I would say that this
5 would be the place that I would want to look. Where would
6 you find this?

7 You can look at the textbooks of medicine and they
8 are out of date, and that is controversial. There are other
9 places, obviously, but I am not so sure that it couldn't be
10 in there or some help.

11 MR. THOMAS: I guess that was directed to me?
12 Again, maybe I didn't state that as clearly -- I think that
13 when you have assessed a patient and made a diagnosis --
14 let's use hypertension -- and have determined that an ACE
15 inhibitor is the class of drug of choice, I don't think you
16 then go to the PDR and use it to determine which specific
17 product you are going to write.

18 I think that, as I hope I said clearly, that most
19 clinicians have a stable of products that they use that they
20 are very familiar with and the PDR or the PI or any other
21 drug reference is used if you are adding another product on
22 top of that or if you are dealing with a patient who has
23 been prescribed something by someone else that you just want
24 some quick information about. I don't see that for the
25 textbook of medicines to determine that.

1 MR. LIEBERMAN: I think that both points are
2 viable. Certainly there are certain kinds of drugs where it
3 is quite common to have comparative information built in,
4 certainly in terms of efficacy, antibiotic therapy, many
5 drugs are tested in an active controlled trial so that you
6 do have information in there.

7 I understand what you are saying, now, about the
8 specific -- you are fortunate if you have six or eight or
9 ten members of a particular class, but the question is that
10 you are going to have some comparative information in there.
11 Maybe it is going to be safety. Maybe it is going to
12 efficacy. Maybe it is going to be both.

13 Now, the question is do you just state that and
14 let the prescriber decide for himself or do you extract any
15 interpretation beyond -- if it looks like one drug maybe has
16 a better profile; equal efficacy but less toxicity, and it
17 is clearly true. Or more efficacy and equal toxicity, and
18 it is clearly true -- based on the data.

19 Now, the problem is it is limited information. I
20 don't know how far you would want to go.

21 DR. BENNETT: Ron, I would agree with you if you
22 could assure me that most physicians know exactly which six
23 classes of drugs are used for Parkinsonism, exactly which
24 eight classes of drugs are used for hypertension, the twelve
25 classes of drugs that are used for acne.

1 I think the danger is that you don't look at what
2 is on the gourmet table, what is available to you, when you
3 are looking at the PDR. If it is first drug you can think
4 of, and that is the one you use, I don't think that patient
5 has received full value for his dollar.

6 But if you know that beta blockers are useful,
7 then you can start looking through and picking out maybe one
8 beta blocker over another. It would be a lot of reading
9 but, nonetheless -- I think that the danger is that you
10 don't hit all the things that are truly out there.

11 DR. LUMPKIN: I have another question that I would
12 like to pose to the panel. I thought it was particularly
13 telling what Dr. Horn said about trying to organize this
14 initiative in such a way that, at the end of the day, we
15 can judge whether this has been worth the effort or not if
16 we go forward with it.

17 With that in mind, if you were designing the
18 protocol, as it were, to judge the success or failure of
19 this effort, what would be the outcomes that you would want
20 us to look at as a group to see at the end of the day
21 whether, indeed, this has been helpful or not -- other than
22 just the gestalt that we like it or not? There has got to
23 be something a little more solid than that.

24 DR. TOWERS: Peace is always a nice feeling. If
25 you have something that is a reassuring document that you

1 can use and providers are happy with it, that is probably a
2 significant thing. The kinds of outcomes you think about
3 are, do you have less mortality and morbidity for your
4 complications. That really gets into a very complicated
5 method for evaluating when you are testing things out in
6 terms of what is the hard result that you get.

7 Does it indeed make a difference in what we do
8 with our patients and how they manage using the old system
9 and using the new system. I think that what you are doing
10 here is something that is a little softer than that and it
11 is going to make it very difficult to evaluate. But
12 provider satisfaction should go a long way toward
13 facilitating that.

14 The other piece you have is that if providers are
15 misusing this, if they are using this as a crutch to have a
16 cookbook that they can fast look up drugs and get their
17 patients out in eight minutes, I am not sure you are going
18 to have the kinds of outcomes you want.

19 Likewise, if they are able to access information
20 so that they can do a better job in those eight minutes, you
21 may. But I think it is going to hard to evaluate.

22 DR. GRAHAM: There may be some lessons to be
23 learned from the effort that has been on the CME area trying
24 to understand what effect continuing medical education has
25 on prescribers and providers because it is a very difficult

1 area to get down to what you really want to know which is
2 did you make a difference in the patient's outcome.

3 Insofar as one might be able to incorporate this
4 kind of information transfer into a more total program, you
5 might, in fact, be able to see real benefit to the patient
6 because, in fact, the information is more accessible. It is
7 more utilizable and there are fewer needs for corrective
8 action on the part of other people who get involved in the
9 process whether it is a pharmacist or a nurse or somebody
10 else having to say, "Oh; but that is the wrong dose," or,
11 "This doesn't come in that size," or however fundamental the
12 questions might be, that the value of the document could be
13 measured somehow by the ability to facilitate not having
14 these other interferences along the way.

15 Again, though, that is a fairly ambitious program
16 because there are not very many randomized controlled trials
17 of CME programs in the literature.

18 MR. JONATHAN PARKER: Jonathan Parker, Rhone,
19 Poulenc, Roher. I do have a suggestion that follows along
20 that line, too. If you do want to evaluate the success of
21 this, I would suggest that you actually stick with, say,
22 perhaps, one therapeutic class rather than to go with all
23 new products. That is a helter-skelter approach that you
24 won't be able to measure versus older products or new.

25 If you stick with a certain indication or a group

1 of products, that way you would be able to measure outcomes
2 specifically within that group of products

3 Secondly, to kind of shift gears a little bit,
4 throughout the day, we have been talking about changing the
5 professional package insert. I just have one comment
6 because I have heard various opinions. I think one thing we
7 really have to think to ourselves is what is the package
8 insert supposed to be?

9 Is it a minimum information the prescriber needs
10 to prescribe the product? Is it a full educational service
11 for the physician? That defining mission statement for a
12 package insert will help to focus exactly what you want to
13 get out of it. But until you do that, until you say what it
14 is and really define it, I think you can always come up with
15 the ideals.

16 DR. LUMPKIN: Good point. Thank you. Anybody on
17 the panel? Anybody else?

18 MR. STEVE JACOBS: Steve Jacobs, Otsuka
19 Pharmaceuticals. I actually have one question and one
20 suggestion in reference to what my colleague just said. I
21 am also a registered pharmacist. One thing that struck me
22 from the very beginning of the program, in about the first
23 15 minutes but I didn't want to bring it up because I wanted
24 to go lunch early, was why was it, in those focus groups, at
25 the very beginning that there were no nurse practitioners or

1 physician assistants or pharmacists involved.

2 That is kind of a key point. That kind of leads
3 me into the second thing. I will give you a quick anecdote.
4 My wife, the other day, had an allergic reaction to a sulfa
5 drug. Because of the allergic reaction and the fact that I
6 was so close to the situation that I didn't realize what was
7 going on, we went to the emergency room.

8 The doctor was in that situation where he,
9 apparently, only had eight minutes and we saw a nurse
10 practitioner. She gave us some information about two new
11 drugs that she was going to give to us. We went to the
12 pharmacy. This was a late pharmacy, and the pharmacist, who
13 apparently was not really stressed out at the time, threw
14 the prescription over the counter and actually some nice
15 people at the register handed it to me and went to sell it
16 to me.

17 The key to that whole thing is that the nurse
18 practitioner didn't give me all the information. We didn't
19 see the doctor. And the pharmacist was, apparently, too
20 busy to do anything really helpful. So the information that
21 is actually passed on to the consumer has got to be key.
22 That was an affront to me as a pharmacist when I actually
23 had to turn to that person and say, "Give me more
24 information on this."

25 That is when I start to feel like a customer.

1 That kind of upset me. And that is something that I really
2 feel needs to be addressed sometime soon, whether it is in
3 patient package insert or in the package insert or whatever.

4 I was wondering if you were going to include all
5 the rest of those groups coming up in your future studies
6 before anything takes action on this.

7 DR. OSTROVE: I appreciate your comment with
8 regard to that. When we first started planning the
9 research, this was something that we considered. We know
10 that physicians are not the only groups out there who are
11 prescribing drugs for the population, who are prescribing
12 medications. We knew that there were nurse practitioners,
13 that there were physician assistants and that pharmacists
14 are very much involved, especially in the interaction where
15 the product goes from the mind of the prescriber to the
16 actual body of the person in which it is going to be
17 working.

18 We had to make some kind of logistical decisions
19 as to how best to do this. Physicians are kind of the major
20 source of prescribing. If we had unlimited resources, I
21 think we would look at every single group, but our thought
22 was that pretty much everyone was going to work the same way
23 in terms of the way that they used.

24 We didn't have anything to base that on, I admit,
25 but that was basically our thought processes is that the

1 physicians that prescribe are probably going to use the PI
2 pretty much the same as the nurse practitioners who
3 prescribe and the PAs who prescribe, and the nurses who, in
4 some cases, prescribe as well.

5 We were pretty sure that there were going to be
6 some differences with pharmacists but we had limited funds.
7 We had to figure out how we were going to do it, so it
8 really came down to a logistical decision. This is one of
9 the reasons why we brought in other groups to be on the
10 Reactor Panel today is to make sure that we are not coming
11 across as not thinking about everyone who is using this
12 particular document.

13 Again, I think that logistical considerations, to
14 some degree, are going to drive certain of our research to
15 go. But, hopefully, we will --

16 DR. MORRIS: Just as an aside, or in addition to
17 what Nancy said, we would be very happy to make our
18 moderator guides and work with whomever want to do
19 additional studies to do them. I think it is important when
20 you do a focus group, per se, to have a homogenous group, so
21 it would be appropriate to do a group of pharmacists, nurse
22 practitioners, physician assistants, et cetera.

23 We would be very happy to work with the
24 organizations to help us to get additional feedback. It is
25 really an resource issue for us. We would be very

1 appreciative because, indeed, it may that there are other
2 views that we do need to take into account and maybe will
3 really help us, if people could help us out. Now that there
4 are prototypes freely available, we would be happy to make
5 all our research forms available if anybody wants to follow
6 through to contact us.

7 We would be not only very happy, but really would
8 appreciate working with you.

9 DR. LUMPKIN: Other comments?

10 MS. IMOGENE RODGERS: My name is Gene Rodgers. I
11 am from PETA. Mostly, nobody has spoken about the use of
12 the PDR, and the information that will be in it, by the
13 consumer. I have seen a number of reasons to be concerned
14 by that. I think it is particularly in your Warnings and
15 Precautions if people who are not trained -- and I am a
16 Ph.D. in pharmaceutical chemistry -- they get their hands on
17 that material, they see the long laundry list, and it is a
18 case where somebody told me a long time ago, "Gene, you are
19 either saying too much or too little."

20 They look at this and it frightens them off. I
21 get these calls all the time. I say, "Please, see your
22 physician," knowing he will probably give her 30 seconds
23 because he is so rushed. This, I think, is an opportunity
24 with the summary to give people who really don't know how to
25 use the PDR and are using it for other purposes a little bit

1 of a feeling of the risk communication that is involved in
2 that section.

3 I would really sort of plead that we do. Thank
4 you.

5 DR. LUMPKIN: Thank you.

6 MS. SHERYL SILFEN: My name is Sheryl Silfen. I
7 am from Solvay Pharmaceuticals. I just had a comment about
8 the efficacy parameters for the endeavor that you are
9 undertaking. Since your goal is to create a more user-
10 friendly document, go back to the users and see if it taught
11 them anything or helped them in any way in prescribing drugs
12 because, to get to the real health outcomes is, like, too
13 far-reaching, but you can look at the goal that you set up
14 for yourselves.

15 DR. LUMPKIN: Thank you.

16 DR. KNOWLTON: I would concur. The outcome from
17 morbidity and mortality and things like that are too far
18 out. But with pharmacists, per se, I think one parameter
19 might be just utility because right now, to be real frank
20 with you, pharmacists generally do not use the package
21 insert. They either use the USP, the PI, or the American
22 Hospital Formulary Material or the Drug Facts and
23 Comparisons because it has kinetics in it and it explicates
24 nicely the drug interactions and all that other kind of
25 stuff.

1 So there may be some utility. If this hits home
2 and some pharmacists start using it, at least from the
3 pharmacy perspective, that might be one measure of success.

4 DR. LUMPKIN: Thank you.

5 MR. MATT BIONDI: Matt Biondi, Abbott
6 Laboratories. I was wondering if you could, perhaps, give
7 more thought to which adverse events would be in the
8 summary. Picking greater than 1 percent works well for a
9 product like captopril, but some of the neuropharm products
10 and some of the other products, you could fill up a half
11 page easily with one percent -- perhaps the top five or
12 something more realistic for that.

13 DR. LUMPKIN: I think you bring up a very good
14 point about how the Adverse Reactions Section could be put
15 together here. We used the 1 percent because, as you say,
16 it worked nicely for the example we had there. I think
17 there are several issues that are going to have to be taken
18 into account. It deals not only with this document but even
19 with the overall adverse-reactions document.

20 As you are aware, if you go and look at the PIs
21 that exist right now, even though this thing is entitled
22 adverse reactions, you find the complete listing of every
23 adverse event that happened during the clinical trial,
24 whether it has any physiologic relationship to the drug one
25 way or the other, in some.

1 In others, you find things that are much more
2 compatible with the idea of an adverse reaction. In some
3 you find it divided between clinical trials versus Phase-I
4 trials versus post-marketing experience. In others, you
5 find them all jammed together where it makes no sense to put
6 post-marketing experience in with clinical trials and then
7 you put some kind of a percentage on it with that kind of
8 data.

9 Clearly, we have got to have some -- it is a
10 larger problem than just this one here. I think that is one
11 of the things that we are looking at with the individual
12 parts of the adverse-reaction section.

13 MR. BIONDI: I think it would be great to have the
14 top five or something, tell your patients the one you could
15 expect.

16 DR. LUMPKIN: Good point.

17 DR. TOWERS: I have a question related to that.
18 My recall is that currently in the PDR you have the
19 comparisons with the placebo effects and they are not in
20 your prototype here. Are you thinking about taking it off -
21 - because that comparison helps a great deal.

22 DR. LUMPKIN: I think you bring up a very good
23 point. Unfortunately, I wish it were true that in all of
24 our PIs it was consistent whether we put the placebo in or
25 not. But I would venture to say it is not, that it varies,

1 probably, from Division to Division and, perhaps, even
2 product to product within the Divisions.

3 That is a very good question and it is one that I
4 think we would have to have for consistency. What I am
5 hearing from you and from other people today is that many of
6 you feel that when you do have a placebo controlled trial
7 that having either the difference from placebo or actually
8 having the two columns is helpful.

9 Anything else that people would like to bring up?

10 DR. TOWERS: I have one more question, and that is
11 where do you plan to go from here?

12 DR. LUMPKIN: What we had said earlier this
13 morning, the plan from this point is that the official
14 docket, as it were -- in other words, the opportunity for
15 people to submit written comments on this particular
16 prototype will remain open officially until January. What
17 we will be doing in the meantime is taking comments that
18 have already come into the docket plus the comments that we
19 have received from this public workshop here today to try to
20 revise what we gave out as the prototype today.

21 What we would like to do is to, then, go in the
22 early part of next year to a formal rulemaking process, to
23 change our labeling regulations in drugs, as it were, from
24 what we have now to incorporate this kind of an idea.

25 In order to do that, we have to go through the

1 Notice and Comment Rulemaking. We can't just say, "It is
2 now changed and this is what it is." So we will put out, a
3 that point, then, a Notice of Proposed Rulemaking which will
4 have a revised prototype based on the comments from today
5 and the comments that we receive in the period between now
6 and January.

7 That will, then, also have a comment period that
8 people can respond to the revised prototype. Then we would
9 go to implementing it. I think, as we mentioned earlier
10 today, there are issues of how to implement it, how to have
11 a program in place to judge whether this effort is of value
12 or not of value as we go into it, and we would like to have
13 both of those as part of the Notice of Proposed Rulemaking
14 so people would understand how we are going to proceed along
15 those lines.

16 I will tell you, and I hope people will take this
17 back, if you think that this is something that is important,
18 is something that would be helpful to your communities,
19 please let us know. As you can well imagine, there are as
20 many initiatives on the FDA's plate right now there are
21 people to think them up. Things have to get put into some
22 kind of a pecking order.

23 For things that people feel in the community that
24 this is exciting, I hope that you take from this today that,
25 at least in the Centers, that were represented here today,

1 at the upper levels of leadership in those Centers, people
2 are very excited about this. They think this is very
3 important, that this is something that will matter in the
4 real sense to our practitioners and to the patients.

5 We would like very, very much to see this come to
6 a very good fruition. The three Centers are willing to push
7 that through. But any help that people out there who also
8 feel that this is a good idea can give in terms of writing
9 and encouragement would go a long way to help prioritize the
10 initiatives. It really would.

11 MS. KAREN PERSINGER: My name is Karen Persinger.
12 I am from Otsuka Pharmaceuticals. I just have a question
13 about the Adverse Reactions Section, also. You indicated
14 that you -- I know; can you tell I am in safety? One of my
15 questions was, you were saying that you would list those
16 events that were felt to be possibly related.

17 I just would like for you to clarify whether you
18 are meaning the drug relationship from the principle
19 investigator during the clinical trial or whether or not you
20 are meaning a company assessment, whether they have taken
21 these events and looked at the investigator's assessment and
22 then made their own assessment.

23 DR. LUMPKIN: I think in a lot of the
24 international discussions that we have been in on safety
25 reporting, the answer that has come long those lines is

1 either -- when you have got a situation where you have got a
2 principle investigator who is assigning the fact that he or
3 she believes that it is possibly related, that counts, then.

4 If, on the other hand, you have got a company who
5 is looking at a series of things that individual
6 investigators might not have thought but, from the
7 perspective of a company who might see it happening at Site
8 A, Site B, Site C and say, "You know, this really might be
9 related," because of our overall perspective, then that
10 counts, too.

11 But it is not that one can overrule the other, as
12 it were, on that.

13 If there are no further questions, let me thank
14 our panel members for being here today, all of you for being
15 here today. Thank you very, very much for your comments and
16 I am sure we will be hearing from you in the days to come,
17 and months.

18 Thank you very much, again.

19 [Whereupon, at 3 o'clock p.m., the proceedings
20 were adjourned.]