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DEPARTMENT OF HEALTH AND HUMAN SERVICES  
FOOD AND DRUG ADMINISTRATION  
CENTER FOR DEVICES AND RADIOLOGICAL HEALTH

MEDICAL DEVICES DISPUTE RESOLUTION PANEL  
OF THE MEDICAL DEVICES ADVISORY COMMITTEE

Tuesday, October 31, 2000

1:00 p.m.

Room 020B  
9200 Corporate Boulevard  
Rockville, Maryland

MILLER REPORTING COMPANY, INC.  
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## PARTICIPANTS

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 Panel Executive Secretary: Les Weinstein

## Panel Members

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 Hector H. Gonzalez, Ph.D., R.N., Consumer  
 Representative  
 Judy Gordon, D.V.M., Industry Representative  
 Scott D. Ramsey, M.D., Ph.D.

## FDA

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P R O C E E D I N G S

**Introductory Remarks**

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2  
3 MR. WEINSTEIN: Good afternoon. My name is Les  
4 Weinstein. I am the CDRH Ombudsman and Executive Secretary  
5 of the newly created Medical Devices Dispute Resolution  
6 Panel which is having its very first meeting today. The  
7 purpose of the meeting is to introduce the panel members and  
8 for them to hear from FDA and from the public some  
9 background and views on the resolution of scientific  
10 disputes concerning medical devices in general and on the  
11 role of this panel, in particular.

12 Pursuant to the authority granted under the  
13 Medical Devices Advisory Committee Charter dated October 27,  
14 1990 and as amended on August 18, 1999, FDA has appointed  
15 Drs. Harold C. Sox, Mark D. Carlson and Scott D. Ramsey as  
16 voting members of this panel, Dr. Hector H. Gonzalez as the  
17 non-voting consumer representative and Dr. Judy F. Gordon as  
18 the non-voting industry representative for this panel.

19 I would like to thank these panel members for  
20 their interest in and willingness to serve on this important  
21 new panel. I would also like to thank all those persons who  
22 recommended and nominated the many outstanding candidates  
23 from which these panelists were selected.

24 Please note that each time the panel meets to hear  
25 a specific dispute, three additional members will be

1 appointed as temporary voting members to participate in the  
2 review of that particular dispute only.

3 Normally, at the beginning of FDA panel meetings,  
4 the Executive Secretary of the panel reads into the public  
5 record a conflict-of-interest statement. However, because  
6 the panel will not be hearing and voting on any disputes at  
7 today's meeting, no conflict-of-interest statement was  
8 required.

9 Now, Dr. Harold Sox, the panel chair, will call  
10 the meeting to order.

11 DR. SOX: I will call to order this open public  
12 meeting of the Medical Devices Dispute Resolution Panel. I  
13 would like to begin by asking the members of the panel to  
14 introduce themselves. We will start with you, Scott. When  
15 you do that, would you designate your specialty, your  
16 position or titles, the institution you represent, your  
17 status on the panel, whether you are a voting member,  
18 consumer member, and so forth, and give a brief statement  
19 about why you accepted the invitation to be on the panel.

20 DR. RAMSEY: My name is Scott Ramsey. I am from  
21 Seattle and I have appointments at the Fred Hutchinson  
22 Cancer Research Center and the University of Washington. I  
23 am an associate member at the Fred Hutchinson. I practice  
24 as a general internist and I have expertise in technology  
25 assessment and cost-effective analysis.

1 My interest in devices stems from my very first  
2 faculty appointment when, at the request of the State of  
3 Washington, I put together a task force to develop  
4 guidelines for technology assessment of medical devices for  
5 the State of Washington. At that point, I spent time  
6 learning about the FDA process for evaluating devices.  
7 Before that time, I didn't know about it.

8 I found it fascinating, and I found the world of  
9 medical devices very interesting. As a result of my  
10 experience on that panel, I learned that there were many  
11 different stakeholders with often conflicting views, and I  
12 found it interesting to see how those issues could be  
13 resolved.

14 So, when this opportunity came along, I thought it  
15 would be an excellent chance to continue my interest in the  
16 area.

17 DR. SOX: Hector?

18 DR. GONZALEZ: My name is Hector Gonzalez. I am a  
19 registered nurse. Currently, I am Professor Emeritus from  
20 San Antonio College in San Antonio, Texas. I hold a part-  
21 time position because I do intend to stay retired, a part-  
22 time position as the chief executive officer for the San  
23 Antonio Chapter of the Hispanic Nurses Association.

24 My reason for being on the panel, what I hope to  
25 achieve as a consumer rep--you know, I have always felt that

1 consumers don't have to have anyone speak for them because  
2 they are mostly able to speak for themselves. However, they  
3 sometimes need guidance and information to guide that input  
4 a little better.

5 So what I hope to be is a conduit for consumers,  
6 take their input and then use it accordingly on this panel.

7 DR. SOX: Thank you.

8 Judy, would you introduce yourself, please?

9 DR. GORDON: I am Judy Gordon. I am a  
10 veterinarian by training but the clinical trialist by  
11 profession. I have spent the last eighteen years doing,  
12 managing clinical trials and the regulatory process for both  
13 medical devices and pharmaceutical products. I have  
14 experience in Class I, II and III products and have taken  
15 through the process enough PMAs and NDAs to feel that I can  
16 contribute.

17 I have a longstanding commitment to working  
18 closely with FDA and making this process a good one for  
19 companies and for the agency. I hope to continue in that  
20 mode as the industry rep to this panel.

21 DR. SOX: Mark?

22 DR. CARLSON: My name is Mark Carlson. I am from  
23 Cleveland, Ohio. I am Associate Professor of Medicine at  
24 Case Western Reserve University and the Vice Chairman for  
25 Clinical Programs at University Hospitals in Cleveland. I

1 am a cardiac electrophysiologist by trade. Because of that,  
2 I have been utilizing devices all of my career.

3 I have been involved in designing and implementing  
4 clinical trials of devices and drugs and have a keen  
5 interest in seeing that they are safely utilized and brought  
6 to market in a timely fashion. I am one of the voting  
7 members.

8 Thank you.

9 DR. SOX: My name is Harold Sox. I am a general  
10 internist, as is Scott, and I am Chair of Medicine in the  
11 Department of Medicine at Dartmouth Medical School, and  
12 Dartmouth Hitchcock Medical Center.

13 I am the Chair of this committee and, as such, I  
14 vote only in case of a tie. The background behind my  
15 joining the panel is that I have been involved in evaluating  
16 clinical evidence for the purpose of developing clinical  
17 guidelines with the American College of Physicians and with  
18 the United States Preventive Services Task Force, which I  
19 chaired, and with the Institute of Medicine and most  
20 recently with the Medicare Coverage Advisory Committee which  
21 I also chair.

22 Each one of these experiences has been a growth  
23 experience for me. It was really in that spirit and in the  
24 spirit of public service that I accepted the invitation to  
25 be on this panel.



1 several years ago, charged us with developing a robust  
2 process of resolving disputes.

3           This panel is one of the mechanisms, perhaps one  
4 of the ultimate mechanisms, of having disputes addressed, in  
5 fact having the opportunity to have those disputes addressed  
6 in public. One of, I think, the great strengths of the way  
7 that FDA functions as a consumer protection agency is with  
8 the transparency of its processes and the way that it lays  
9 out the evidence on which it makes its decisions and our  
10 willingness to present those in public.

11           We value all of the advisory panels that work with  
12 us to evaluate evidence and, in general, we take overruling  
13 a panel recommendation very seriously. Because you will  
14 often be asked to look at situations where we have, in fact,  
15 have agreed to disagree with a panel or with a company or  
16 some variations, you are probably wondering what our stance  
17 will be for matters brought before you.

18           I think that, in general, we will look at the  
19 decisions that you come to in your processes as ones that  
20 have a very high burden on us to establish a good reason to  
21 overrule. We realize that many of the cases that will be  
22 brought for you to consider will be close calls and, if we  
23 are not able to make the case in a way that convinces the  
24 panel to agree with us, then, in almost all cases, we will  
25 accept your advice.

1           As you know, the system of advisory panels for all  
2 of FDA is that they are advisory, that we still have the  
3 final decision and, in fact, there are times when an issue  
4 not brought before the panel becomes a deciding factor for a  
5 completely different reason than the reason considered.

6           But I wanted to address this point because it has  
7 been asked by some, what is the point of having another  
8 panel if you are willing to overrule the first one? You  
9 will just overrule the second one. That is not our  
10 intention to do that.

11           I would like to make some broad comments about the  
12 dispute resolution process and our philosophy towards that.  
13 As we have written about this, we have tried to emphasize  
14 the importance of problem solving and we have tried to  
15 develop a large number of mechanisms that, if there is an  
16 issue or a dispute on which the development of the product  
17 is stuck, that there are ways to get the process unstuck.

18           This is a function that is imbedded in many of the  
19 offices that do the day-to-day work. We also have an Office  
20 of Ombudsmen which has been created within the last year  
21 that Mr. Weinstein heads that is there essentially to help  
22 do problem solving.

23           We value speed in this process. We value getting  
24 back to the work and identifying the disputes and getting  
25 our hands around them and moving on from them.

1           One of the perceptions when we actually wrote the  
2 first draft of a guidance was that it sounded like you had  
3 to go through about forty-seven steps to ever get to this  
4 panel. That was not our intent. Our intent was to actually  
5 identify all the different ways in which you could reenter  
6 the system and actually work up through the chain of command  
7 and get appeals.

8           There are times when it is appropriate to skip  
9 steps, to collapse mechanisms and to do things at once.  
10 Again, our goal, really, is to get the quickest way to get  
11 an agreed-upon resolution to a dispute.

12           One question which also comes up is what types of  
13 things do we expect you to review. Some of them will be  
14 appeals for products that are fairly along in their  
15 development, in fact where the manufacturer may feel that  
16 they have collected all the evidence that is necessary to  
17 establish that it should be marketed, but there is a  
18 disagreement over that.

19           There may be appeals of a prior panel decision or  
20 there may not be. We will not always require that a  
21 decision have gone through another panel in order to be  
22 brought to this group.

23           There also will be times, though, when there will  
24 be disputes about the standards or evidence that are  
25 required to get a whole new product area started. There

1 have been examples in the past of deliberations on the level  
2 of evidence that would be appropriate for some new  
3 technologies and where we and the sponsor seem to be at an  
4 impasse, this panel may be able to provide useful  
5 recommendations to move some of that forward.

6           So, at today's session, as Dr. Sox, you have  
7 mentioned, this is an opportunity for the panel to ask FDA  
8 more questions about our processes and about your function.  
9 It is an opportunity for you to hear from the public and  
10 from interested parties from industry on what they expect  
11 this process will do and how it will help in the process of  
12 providing timely access to new therapeutic medical devices.

13           So, again, let me welcome you and thank you. I  
14 don't know if you will have questions for me or if it is  
15 better to actually hold some of those until we get into some  
16 of the more detailed presentations later. But, again, let  
17 me thank you.

18           DR. SOX: Thank you very much, Dr. Feigal. Are  
19 there any immediate questions, clarifications? In that  
20 case, let's go on. The next FDA speaker will be Mr. Les  
21 Weinstein who is the CDRH Ombudsman and the Executive  
22 Secretary of the Dispute Resolution Panel.

23           Mr. Weinstein?

24           MR. WEINSTEIN: Thank you, Dr. Sox.

25           [Slide.]

1           The Food and Drug Administration Modernization  
2 Act, known as FDAMA, which was passed in 1997, introduced  
3 many significant changes to the regulation of medical  
4 devices. One of the provisions of the new law, Section 404,  
5 on dispute resolution, is designed to insure that FDA has  
6 effective processes to resolve scientific disputes that  
7 arise between FDA and its regulated industry.

8           Essentially, FDAMA directs FDA to use the  
9 independence and expertise of clinicians and scientists from  
10 outside FDA to advise the agency on issues where industry  
11 and FDA differ. There was and is already a wide array of  
12 mechanisms by which the device industry could obtain  
13 reconsideration of FDA decisions and actions.

14           Some are informal, such as appealing up the  
15 supervisory chain in a particular office. Others are more  
16 formal, such as evidentiary public hearings and hearings  
17 before the FDA Commissioner. We always encourage use of the  
18 more informal means, at least initially, to try to resolve  
19 disputes early on.

20           [Slide.]

21           FDAMA added to this array a new option by  
22 directing the agency to insure that a medical-device  
23 sponsor, applicant or manufacturer could obtain independent  
24 review by a scientific advisory panel of a scientific  
25 controversy between that person and FDA.

1           The Congressional intent here was to provide that  
2 scientific issues would receive appropriate attention from  
3 independent scientists who could bring a fresh perspective  
4 to assure that industry received a fair, impartial and  
5 timely hearing and that FDA received sound recommendations  
6 and advice.

7           [Slide.]

8           To implement this new provision, FDA amended its  
9 regulations and 21 CFR 10.75 to clarify the availability of  
10 review of scientific disputes by an advisory panel of  
11 experts when circumstances warrant. CDRH, in turn, created  
12 a new advisory panel, the Medical Devices Dispute Resolution  
13 Panel which operates now under FDA's Medical Devices  
14 Advisory Committee.

15           On April 27, 1999, FDA issued a draft guidance on  
16 resolving scientific disputes concerning the regulation of  
17 medical devices for public comment. This draft guidance  
18 document focuses on the new panel and it provides the  
19 framework for my remarks today.

20           You should keep in mind, as I will mention a  
21 little later, this guidance document may be changed in some  
22 degrees when it is put into final. But, before that final  
23 version is issued, the panel will function under the draft  
24 guidance document.

25           When we issued it for public comments, we received

1 three letters of comment and are currently revising, as I  
2 said, the document and looking very closely at those  
3 comments with a view toward being responsive to them  
4 wherever possible.

5 [Slide.]

6 In addition to serving as a useful forum in which  
7 scientific disputes, in general, can be erred, the panel  
8 will implement four provisions of the Federal Food Drug and  
9 Cosmetic Act, Section 514(b)(4) regarding performance  
10 standards, Section 515(g)(2)(B) regarding appeals of  
11 premarket approval applications and PDP, product development  
12 protocol decisions that the panel heard about this morning  
13 in their training, and Section 522(b) which was added by  
14 FDAMA when there is an order, an appeal of an order, to  
15 conduct postmarket surveillance for more than thirty-six  
16 months--the panel also heard from Dr. Kessler this morning  
17 on this particular area--and Section 562, also added by  
18 FDAMA, which talks about the review of scientific disputes  
19 regarding medical devices including by a scientific panel  
20 but only to the extent that the Act or regulations did not  
21 already provide a right of review.

22 Now, FDA believes that its existing procedures  
23 already provide methods to obtain review of most scientific  
24 disputes. The establishment of this new panel provides an  
25 additional, more focused, option for the timely review of

1 those disputes.

2 Let me give you a definition of scientific dispute  
3 or controversy. A disagreement with a science-based  
4 decision which bears on a regulatory matter pending before  
5 FDA or an appeal arising from a science-based decision which  
6 served as the basis for a regulatory or public-health  
7 decision or action by the agency.

8 This term excludes matters relating to potential  
9 criminal activity, intellectual or regulatory bias or FDA's  
10 designation of a particular center to regulate a combination  
11 product.

12 [Slide.]

13 The panel is--I can say "is;" for months I have  
14 been saying "will be," but now I can "is"--is comprised of  
15 eight members, five standing members appointed to four-year  
16 terms, somewhat staggered initially, including a non-voting  
17 member representing consumer interests and a non-voting  
18 member representing industry interests, and three temporary  
19 voting member, as I mentioned earlier, appointed to  
20 participate in the review of a particular dispute. One of  
21 the standing members, Dr. Sox, in this case, serves as the  
22 chair.

23 [Slide.]

24 A party may request review by the panel of a  
25 decision or action by submitting a written request to the

1 ombudsman within 30 calendar days following the decision or  
2 action that is disputed. The panel will hear requests from  
3 sponsors, applicants or manufacturers of a particular  
4 device.

5 [Slide.]

6 In that request, the sponsor, applicant or  
7 manufacturer has to indicate their standing to request  
8 review, a summary of the scientific issue in dispute, the  
9 results of any efforts to resolve the dispute elsewhere  
10 within the agency such as going up that supervisory chain,  
11 and then a summary of the arguments and the data and  
12 information that it wishes the panel to look at.

13 [Slide.]

14 In addition to requests coming from a sponsor,  
15 applicant or manufacturer, FDA, at its discretion, could  
16 refer a dispute to the panel without an industry request.  
17 So, at FDA's option, on its own accord, FDA could initiate  
18 panel review if the interests are the interests of a party  
19 outside of FDA, are, or are likely to be, adversely affected  
20 by an FDA decision or action.

21 [Slide.]

22 Procedures after the agency receives the request;  
23 upon receipt of the request for review, I will make a  
24 preliminary review of the request to determine whether it is  
25 appropriate for this particular panel to review. After I

1 make a the preliminary review, I consult with the panel  
2 chair and an appropriate deputy center director, and then  
3 make a determination within thirty days regarding whether or  
4 not to grant panel review or deny panel review or to ask the  
5 requestor if they would be willing to participate in  
6 mediation during which I would serve as the mediator between  
7 the agency and the applicant.

8 This is an option that I can offer, as I said, to  
9 the requestor, but one that the requestor can reject and say  
10 no, that they would prefer to go to panel.

11 [Slide.]

12 All meetings of this panel will be governed by FDA  
13 regulations and 21 CFR, Part 14, regarding hearings, and all  
14 panel meetings will be open to the public as provided by the  
15 Federal Advisory Committee Act and FDA regulations, except  
16 that portions of the meeting may be closed to the public.

17 The requesting party will be given the right to  
18 speak first and present its views after which the FDA  
19 representatives and other affected and interested parties  
20 may address the panel. Each party may be accompanied by  
21 scientific experts, health professionals, legal counsel and  
22 other technical experts.

23 Members of the panel may question the parties  
24 directly. There will be no questioning by or debate between  
25 the parties during the hearing. Once deliberations have

1 been completed, the chair will determine if a consensus  
2 exists among the members and, if not, call for a vote. The  
3 chair votes only in a tie, as was mentioned earlier.

4 [Slide.]

5 Within thirty days of the panel meeting, I will  
6 then prepare a statement of findings and recommendations  
7 summarizing the panel's recommendation including any  
8 minority views, and will provide a copy of the statement of  
9 findings in draft form to the panel chair and to each  
10 dispute resolution panel member for their input. The panel  
11 chair will sign the final statement of findings and will  
12 then forward it to the CDRH director.

13 [Slide.]

14 Upon receiving the statement of findings, the CDRH  
15 Director shall take one of the following actions, normally  
16 within fifteen days, accept the panel recommendations,  
17 accept the panel recommendations with modification or not  
18 accept the panel recommendations.

19 The Ombudsman then notifies the parties, and by  
20 parties I mean the requester and the agency, of the decision  
21 and will also inform the requestor of any appeals processes  
22 that might be appropriate to appeal the decision by the  
23 Center Director.

24 Thank you very much. Any questions?

25 DR. SOX: Any questions from the panel?

1 MR. WEINSTEIN: Thank you.

2 DR. SOX: The next FDA speaker will be Mr. Phil  
3 Phillips who is the Deputy Director for Science and  
4 Regulatory Policy in the Office of Device Evaluation of  
5 CDRH. Mr. Phillips?

6 MR. PHILLIPS: Good afternoon.

7 [Slide.]

8 My name is Phil Phillips. I am the Deputy  
9 Director for Science and Regulatory Policy within the Office  
10 of Device Evaluation. On behalf of our entire office, I  
11 want to welcome each of you to this particular panel. I  
12 think that the roles that you serve or will serve are going  
13 to be of a tremendous amount of value to us as well as to  
14 the regulated industry.

15 I will say that probably most of the disputes that  
16 you will be handling will result from issues that arise in  
17 our organization. Now, that is not as a result of any  
18 scientific deficiencies that we have but simply because of  
19 the amount of workload that we have.

20 We generally issue thousands of decisions each and  
21 every year so the chances are that many of the disputes that  
22 you will hear will probably be coming from the Office of  
23 Device Evaluation.

24 [Slide.]

25 Over the next fifteen minutes or so, I am going to

1 really be talking about three particular topics, one of  
2 which is the evidence required in device submissions. I am  
3 going to talk a little bit on industry, the internal agency  
4 review process that Mr. Weinstein also just mentioned a  
5 moment ago, and then end up talking about some of the least  
6 burdensome provisions of the FDA Modernization Act of 1997.

7           Let me just indicate that I think that one of the  
8 roles that you will have will only be really fulfilled if we  
9 provide relevant information to you at the time that you  
10 actually are involved in looking at different types of  
11 disputes. The reason that I mention that here is, for  
12 example, the evidence required for device submissions.

13           That evidence required will vary tremendously  
14 depending upon the particular dispute that is before you at  
15 any point in time. So, therefore, I think it is important  
16 for whoever it is that would be presenting information to  
17 the panel to make sure that you do have information  
18 regarding all of the pertinent regulations and policies and  
19 precedents, et cetera, that pertain to the particular  
20 dispute in question.

21           [Slide.]

22           As far as the evidence required in device  
23 submissions, let me just indicate that I believe that most  
24 of the disputes that you will encounter will probably be  
25 related to either the 510(k) program, the premarket approval

1 of the PDP program, as well as reclassification activities.

2 If we focus specifically on the 510(k) program,  
3 keep in mind the statutory criteria for decision making is  
4 known as substantial equivalence. We could spend an entire  
5 afternoon defining exactly what substantial equivalence is.  
6 It sort of illustrates the point that I had mentioned just a  
7 moment ago.

8 If you have a dispute that relates to substantial  
9 equivalence, there is a wealth of information that I think  
10 needs to be brought to the panel's attention regarding how  
11 the agency has approached those particular terms in the  
12 past.

13 If we focus on the premarket approval area or, as  
14 of lately the product develop protocol program that we have  
15 up and running, both of these programs apply to class III  
16 devices. The statutory criteria for making decisions is  
17 reasonable assurance of safety and effectiveness.

18 [Slide.]

19 Lastly, if we focus on reclassification  
20 activities, and, again, I think that as we go forward, there  
21 are probably going to be more and more reclassification  
22 petitions submitted to the agency as well as some  
23 reclassification activities that are actually undertaken by  
24 us in the future.

25 I would imagine that there will probably be some

1 disputes as we get involved in this particular area as well.  
2 Again, the evidence here is that we have to know that  
3 general controls provisions of the Act--these are  
4 prohibitions against adulteration and misbranding, et  
5 cetera--there is a whole series of general controls that  
6 apply to class I devices--or that general controls combined  
7 with special controls--these are for class II devices--will  
8 provide, again, reasonable assurance of safety and  
9 effectiveness. So that is, again, the statutory criteria  
10 there.

11 [Slide.]

12 When we talk about actual determinations of safety  
13 and effectiveness, what I will do is call to your attention  
14 12 CFR 860.7--this is entitled Determinations of Safety and  
15 Effectiveness--there are certain relevant factors that we  
16 are, by regulation, told to focus on whenever we make  
17 determinations of safety and effectiveness.

18 Basically, we are talking about looking at the  
19 particular patient population, looking at the conditions of  
20 use, looking at probable benefits from use of the device  
21 versus the probable risks of illness or injury as a result  
22 of the use of a product, as well as the reliability of  
23 devices. Those are the factors that we look at when  
24 determining safety and effectiveness.

25 [Slide.]

1           We are also instructed, whenever we make  
2 determinations of safety and effectiveness, to focus on what  
3 is called valid scientific evidence. If you go to the  
4 regulations--and, again, this is 860.7--what you will find  
5 is that valid scientific evidence is evidence from well-  
6 controlled investigations, partially controlled studies,  
7 studies and objective trials without matched controls and  
8 reports of significant human experience.

9           Likewise, from the opposite perspective, the  
10 regulations tell us that valid scientific evidence does not  
11 include isolated case reports, random experience, reports  
12 lacking sufficient detail to permit scientific evaluation  
13 and unsubstantiated opinions.

14           I think it is important to also point out that  
15 when we get marketing submissions, keep in mind there is  
16 quite a diverse amount of information that is generally  
17 submitted. Some does meet the definition of valid  
18 scientific evidence. In other cases, you will find that it  
19 is also laced with things that we would say, according to  
20 the regulations, do not meet the definition of valid  
21 scientific evidence.

22           We are instructed that we can entertain all of the  
23 information that is presented, but we are supposed to be  
24 relying on valid scientific evidence for our decision-making  
25 authority.

1 [Slide.]

2 Mr. Weinstein mentioned the fact that we do have  
3 internal agency-review procedures that we use quite  
4 frequently within the Office of Device Evaluation. This is  
5 under 21 CFR 10.75, and the part is actually defined as  
6 internal agency review of decisions.

7 This is so-called supervisory review. You will  
8 find that, as a supervisor in Office of Device Evaluation,  
9 that if any one of my subordinates makes a decision, I have  
10 the right, according to regulation, to go back and to  
11 revisit any decisions that are made by those individuals.

12 Generally, this is done with consultation between  
13 all of the interested parties and/or the review of the  
14 administrative file. Generally speaking, if you go back and  
15 look historically, it is quite unusual that we just simply  
16 make a decision by looking at the actual paper that is  
17 provided. There is usually interaction between all  
18 interested parties in making these different types of  
19 decisions.

20 It is also important to understand that 12 CFR  
21 10.75 can also be requested by someone outside of the  
22 agency. It is generally an affected party. A device  
23 company who has an objection with one of the decisions that  
24 we have made can request, through the normal supervisory  
25 channels, a review of any of the decision-maker's

1 authorities.

2 10.75 goes all the way to the Commissioner's  
3 level. In other words, there is no one to go with, under  
4 10.75, once you get to the Commissioner of Food and Drugs.  
5 It stops there.

6 Keep in mind that it is important, when we use  
7 these particular procedures, that the decision that is  
8 rendered must be based on the information that is included  
9 in the administrative file. If anyone disputing under 10.75  
10 comes in with additional information, according to  
11 regulation, that has to go back down to that first level  
12 supervisor that made the original decision in order to  
13 determine whether it affects that decision or not.

14 Clearly, if it doesn't, then we do have a dispute  
15 and it can come up the supervisory channels. But any new  
16 information under this particular regulation must go back to  
17 the party that made the original decision.

18 [Slide.]

19 There is a document that is on the web and I have  
20 actually given the web site here. It is called A Suggested  
21 Approach to Resolving Least Burdensome Issues. What I will  
22 say is that, for just simplicity purposes, what I would do  
23 is to call your attention to this particular document if you  
24 are interested in knowing more about how we try to resolve  
25 issues under Part 10.75.

1 [Slide.]

2 You will find that, in that particular guidance  
3 document, there is a flow chart. It is a very, very simple  
4 flow chart. That is why I will call this body's attention  
5 to this particular document.

6 What it says, and I apologize--I realize some of  
7 you can't actually read this but you do have copies of this  
8 in your handouts. What it indicates is that anybody who has  
9 a dispute with any of the review organizations within the  
10 Office of Device Evaluation, they are to take that dispute  
11 back to the actual review organizations making that  
12 decision.

13 In other words, if it is coming out of a  
14 particular branch, they should go back to the division where  
15 that branch is located and work all the way up through the  
16 Division Director to make sure that, in fact, through  
17 informal channels, there isn't some sort of reason to change  
18 the particular decision that is under dispute.

19 If it can't be resolved at that level, what we  
20 suggest is that you come to the Office of Device Evaluation  
21 at the office level, which is the next higher level, and  
22 bring information specifically to the attention of the  
23 Program Operations staff which is a staff organization  
24 within our organization.

25 The Program Operation staff will generally advise

1 a company as to whether they need to go through a more  
2 formal channel actually requesting an appeal under 10.75 to  
3 the office level or whether they feel that, perhaps,  
4 additional information could be brought to the division's  
5 attention that might actually result in a change of the  
6 initial decision.

7           So I guess what I am saying here very  
8 simplistically is that, if you go to the Program Operations  
9 staff, sometimes they will intervene on the company's part  
10 and go back to a review organization and bring additional  
11 information to their attention that could change the  
12 decision without elevating the dispute to a higher level.

13           In certain cases, the Program Operations staff  
14 will believe that that is not the case and they will advise  
15 if someone actually requests a supervisory review at the  
16 office level. In the past, generally, those have come to my  
17 attention.

18           If, of course, they cannot be resolved, then what  
19 we recommend is that they go to Mr. Weinstein as the  
20 ombudsman for the Center. Also, it is important for all  
21 parties to recognize that they can to the ombudsman at any  
22 particular point at time. They don't have to follow this  
23 particular flow through the organization, but this is the  
24 one that I think is very simple and it is one that we  
25 typically use in the Office of Device Evaluation.

1 [Slide.]

2 As far as the least burdensome provisions of the  
3 FD&C Act, and this is really as result of FDAMA, there were  
4 two sections that were actually changed as a result of the  
5 amendment. One is under Section 513(a) which deals with  
6 premarket approval applications. The language that was  
7 included as a result of FDAMA is basically that the  
8 Secretary shall consider with the applicant the least  
9 burdensome appropriate means of evaluating device  
10 effectiveness that would have a reasonable likelihood of  
11 resulting in approval.

12 Again, if you are interested in the least  
13 burdensome provisions, this is the one sentence that applies  
14 to the premarket approval applications.

15 [Slide.]

16 If we look at the 510(k) program, what you will  
17 find is that FDAMA also changed the Act. Specifically, it  
18 changed Section 513(i) to state that in making such a  
19 request, and this is a request for additional information  
20 that we need in order to make a substantial equivalence  
21 determination--in making such a request, the Secretary shall  
22 consider the least burdensome means of demonstrating  
23 substantial equivalence and request information accordingly.

24 What I will do is I will basically characterize, I  
25 think, the least burdensome provisions pretty much as our

1 Center Director has in the past, and that is that least  
2 burdensome is a work in progress. Right now, I will call  
3 your attention to the web site that we have here because  
4 this does include all of the information up to date that we  
5 have actually put out to the world to describe how we are  
6 trying to implement the least burdensome provisions of the  
7 modified law.

8           Basically, what you will find here is that there  
9 are a number of documents where we have come up with, for  
10 example, this very simplified dispute-resolution process.  
11 We put out a guidance on that. There are some changes in  
12 language that we are instituting in some of our boiler-plate  
13 letters where we request additional information from the  
14 regulated industry. That language is included there.

15           There is also a document which we are trying to  
16 finalize at this particular point in time which is called  
17 the least burdensome concepts and principles documents.  
18 Basically what this does is it outlines what we believe the  
19 fundamentals are to achieving the least burdensome  
20 provisions under the law.

21           I think that if you look, from a broader  
22 perspective, at the entire issue of least burdensome, what  
23 you will find is that, if we have concepts and principles  
24 that we all agree with, if we provide ample opportunity for  
25 communication and collaboration with the regulated industry,

1 and if we have a very efficient and effective means of  
2 resolving disputes, and whether that is through 10.75 or  
3 through this particular body, we will probably be very, very  
4 close to implementing, I think, the letter and the spirit of  
5 FDAMA in relation to the least burdensome provisions.

6 That concludes my remarks. If there are any  
7 questions, I would be glad to answer them.

8 DR. SOX: We have an opportunity to ask questions  
9 of Mr. Phillips. Does anybody wish to do so? I would  
10 actually like to ask one question. It focuses on the  
11 meaning of effectiveness. You list the relevant factors and  
12 one of those is probable benefit versus probable harm in  
13 effect.

14 Do you intend to have that framed in the context  
15 of patient outcomes, things that help patients?

16 MR. PHILLIPS: It is an excellent question,  
17 actually. If you go to that particular part of the  
18 regulations that describe what is valid scientific evidence,  
19 you will find that there is actually a regulation that  
20 defines effectiveness, and it does define it saying that  
21 there has to be a significant clinical effect in the target  
22 patient population.

23 So the answer is yes, it is based upon outcomes.  
24 I think, to add a little bit to that definition, of course,  
25 in order to try to streamline the process, quite frequently,

1 we do go to surrogates so we don't actually have to look at  
2 actual outcome measures. But the regulations are clear.  
3 Yes, it is an actual clinically significant effect in the  
4 target population.

5 DR. SOX: Then if I could ask a follow-up  
6 question. In the next slide, you describe some of the forms  
7 of scientific evidence that you consider to be valid  
8 starting with well-controlled and then partially controlled  
9 investigations.

10 Then there were two others, studies and objective  
11 trials without matched controls and reports of significant  
12 human experience, which clearly represent pretty weak forms  
13 of scientific evidence. Do you get many PMA applications  
14 that really turn on the interpretation of those forms of  
15 evidence as opposed to the higher forms of evidence where  
16 there are at least partial controls?

17 MR. PHILLIPS: The answer to that is no. Quite  
18 honestly, the vast majority, and I will say probably  
19 99 percent, of the PMAs come in with prospective clinical  
20 trials that are included. So they are well-controlled  
21 investigations that I believe come in.

22 Some cases are partially controlled studies as  
23 well. But the latter two, I believe, really reflect the  
24 fact that applicants, by regulation, are required to bring  
25 all information that could really affect a decision to our

1 attention. So the PMA is supposed to be a compilation of  
2 virtually everything that is available to an applicant that  
3 is relevant to the decision making.

4 That is where those latter two categories come in  
5 to play more than anything else is just going out, doing a  
6 literature search, finding out any information which is  
7 relevant to the decision making.

8 In some cases, I think that results in some  
9 evidence which does not meet the definition of valid  
10 scientific evidence being submitted as well. That is where  
11 we have to sort of sort things out quite frequently.

12 DR. SOX: Thank you. That is helpful. Dave?

13 DR. FEIGAL: If I could just add, I think that,  
14 particularly the broad categories are used to collect data  
15 about safety so that even when there are single case reports  
16 or other things which normally would not be very helpful in  
17 evaluating effectiveness, if there is a signal there of a  
18 safety problem with the product, we have access to all that  
19 information.

20 DR. SOX: It sounds as though the sponsors come  
21 forward usually with what would be considered valid  
22 scientific evidence with good controls.

23 MR. PHILLIPS: Yes.

24 DR. SOX: Thank you.

25 Other questions for Mr. Phillips? Thank you very

1 much. That is very helpful.

2 Our next FDA speaker is Ms. Lillian Gill who as  
3 Acting Deputy Center Director for Science in CDRH. Ms.  
4 Gill?

5 MS. GILL: Good afternoon. I am the Acting Deputy  
6 Director for Science but my full-time job and permanent  
7 position is Director of Compliance in the Center, so I will  
8 be talking about some enforcement-compliance issues in our  
9 process for dealing with appeals.

10 I think Mr. Pellerite spoke with you this morning  
11 on our types of actions so I am going to follow that up a  
12 little bit with how we handle appeals to some of the  
13 decisions we make in that end.

14 I don't anticipate many disputes in the compliance  
15 and enforcement arena to come before you, but I will talk to  
16 you about the 1 percent--since Phil will claim 98 percent of  
17 those, I will talk to you about the 1 percent that might  
18 come before you.

19 Scientific issues, in my area, would probably  
20 involve the manufacturing process itself, questions about  
21 the process, issues that we raise in our correspondence and  
22 actions that we take involving that process, which we call  
23 the quality system of the company or the good manufacturing  
24 practices.

25 It could also involve the evaluation or a

1 correspondence with the manufacturer. In our look at  
2 evaluating the data-supporting applications, particularly  
3 the integrity issues, how the data was collected to support  
4 any applications and the actions we may take as a result of  
5 finding that the data was not collected, preserved, recorded  
6 in a way that we think could support the application or  
7 might be questionable.

8           So appeals may come to us based on that. And they  
9 can also come on decisions we make on product performance  
10 information particularly that that we might use to determine  
11 whether or not the performance of that device could incur a  
12 public-health risk which might lead to an advisory recall or  
13 anything issued. Larry Kessler may have talked to you this  
14 morning about advisories.

15           We certainly have any of the formal processes that  
16 you have heard before. Citizen petitions come into the  
17 office asking for relief or asking us to take action, not  
18 take action. We have the administrative reconsideration of  
19 actions. We also have requests, formal requests, for  
20 internal agency review of our decisions.

21           For our more formal actions, enforcement actions,  
22 that we take, which are the seizures, the injunctions and  
23 the civil penalty, many of those disputes are put on the  
24 table and discussed by the time we reach that stage. In  
25 fact, most of the injunctions have gone through the

1 negotiations with the attorneys and the scientific personnel  
2 which we get either from the Device Evaluation staff or that  
3 we get from the outside, and we are required, in many cases,  
4 to have scientific expertise as a special government  
5 employee in these kinds of activities we take.

6           So, much of that has been discussed and ironed out  
7 before we reach what we consider a consent decree which  
8 primarily spells out how the problems are going to be  
9 remediated.

10           In the injunctions, we certainly work with the  
11 states attorneys, associate attorneys, in the various  
12 district offices. Again, those scientific issues are placed  
13 on the table. So, any disputes involving the seizures that  
14 we might take on a product are primarily appeals to have the  
15 product given back to the manufacturer for remediation kind  
16 of activity they may take.

17           In the civil-penalties area, all evidence would go  
18 before an administrative-law judge for a hearing before a  
19 decision is made, but, in most cases, those are resolved.  
20 The scientific issues as well as the observation issues are  
21 resolved before it reaches that point.

22           Most of our activities occur in what we call  
23 compliance activities or the warning letters that we issue.  
24 We have a lot of discussion with manufacturers when there is  
25 disagreement over observations made during an inspection,

1 items listed on the form left with manufacturers which we  
2 call the 483, or the letters that we may send to them out of  
3 headquarters involving marketing product with a questionable  
4 510(k).

5 Those are primarily handled either through  
6 correspondence, lots of correspondence, with the firm in  
7 question, or they might also be handled through meetings.  
8 We do grant a lot of meetings, requests for meetings, to  
9 resolve some of the issues. So our informal process gets to  
10 the root of the majority of those.

11 We also have a number of appeals for investigation  
12 observations that come through the chain of the district  
13 office. Our investigations are done in twenty-one-some odd  
14 districts around the country so if there is a question about  
15 observations and the manufacturing practice of some of the  
16 investigation staff, the district, itself, will contact the  
17 center for an independent assessment of the those  
18 observations and, in some cases, the firm will ask us to  
19 intervene at which time we bring together the firm, the  
20 district and iron those out.

21 So that is the way that we handle most of the  
22 disputes coming in through compliance. I am free to answer  
23 any questions you have.

24 DR. SOX: Any questions for Ms. Gill?

25 DR. RAMSEY: One quick question. Could you give

1 some examples of issues under your control that might come  
2 to this panel for discussion?

3 MS. GILL: One question might be the scientific  
4 evidence that we would think would support a recall of a  
5 product, what we might think is a malfunction that would  
6 lead to a significant public-health risk, a scientific  
7 dispute about that information that may come to the panel.

8 DR. RAMSEY: If I may, just a follow-on to that.  
9 We have heard a little bit about levels of evidence for PMA  
10 applications and so on. What levels of evidence would be  
11 part of your request or a dispute that would involve that  
12 type of an issue.

13 MS. GILL: Our level of evidence is reasonable  
14 likelihood that the manufacturer of this product, using  
15 these good manufacturing practices, would produce a product  
16 that might cause harm or injury. So it is the reasonable  
17 likelihood that this practice might produce a poor product.

18 Coming before the panel, the evidence--we  
19 certainly would collect any evidence from our reporting  
20 system that would suggest the product is already  
21 malfunctioned in its current manufacturing state. The  
22 company or the scientific dispute might resolve around how  
23 significant the malfunction might be.

24 So it may end up being an engineering type of  
25 discussion combined with the clinician's interpretation of

1 what the malfunction might cause.

2 DR. SOX: Anybody else on the panel wish to ask a  
3 question? In that case, thank you very much.

4 MS. GILL: Thank you.

5 DR. SOX: We are now going to move ahead to hear  
6 views and comments from the public. In response to the  
7 advanced notice of this meeting, three people notified the  
8 executive secretary in advance that they wanted to address  
9 the panel. They are Mr. James Benson, Dr. Charles Swanson  
10 and Ms. Mary-Lacey Reuther.

11 I would like now to find out if there is anybody  
12 else in the room that would like to address the panel. If  
13 you could so signify by raising your hand, if there is a  
14 large number, we may have to allocate time in an arbitrary  
15 way. Anybody else?

16 It looks like the three of you have got the floor.  
17 Why don't we proceed first with Mr. Benson.

18 **Presentations from the Public**

19 MR. BENSON: Thank you, Mr. Chairman.

20 DR. SOX: Excuse me, Mr. Benson. Before you  
21 start, I would like you to speak very clearly so that the  
22 transcriber can hear everything that you say. If you can  
23 provide a copy of your remarks and any visual aids that you  
24 use, that would also be requested.

25 Finally, could you state your name and your

1 affiliation. Thank you.

2 MR. BENSON: You be the judge of whether I am  
3 speaking clearly enough. I don't know how to do that one.  
4 Les asked me yesterday for comments. I don't have a formal  
5 presentation. I have an outline. I would be glad to get  
6 all the spelling correct and we will give you that later, if  
7 that is acceptable.

8 DR. SOX: Thank you.

9 MR. BENSON: Your third point, I am Executive Vice  
10 President for Technical and Regulatory Affairs at AdvaMed  
11 which is the trade association formerly known as HIMA. I  
12 might add that I am an alumnus of CDRH and FDA and I welcome  
13 the opportunity to come here today because I kind of want to  
14 give you, the folks on the panel, a view of kind of how I  
15 saw things, at least when I was at the agency, and how I  
16 think many folks in the industry see these issues that might  
17 come to the panel. So, if I may.

18 We have boiler-plate language about AdvaMed. I am  
19 not going to bore you with that. We are, I guess, the  
20 largest trade association representing medical devices in  
21 the world.

22 I wanted to start--I guess my hope is that this is  
23 the last time you folks will have to come together. I don't  
24 mean that to sound as a putdown at all, but I think if you  
25 go back over what Dr. Feigal and the other speakers said,

1 there are mechanisms in place and I think it would be  
2 wonderful if disputes could, in fact, be resolved at a level  
3 before it had to call the panel together.

4 So I think at the same time it is critically  
5 important that the panel exist, and I will try to explain  
6 that in a second.

7 I said I wanted to give you perceptions from kind  
8 of both sides of the aisle. I used to say when I was--I  
9 have to compliment Dr. Feigal and say that he is a lot  
10 smarter and a lot quicker than I am at learning things  
11 because I think I was with FDA for twenty-one years and it  
12 took me a long time to really accept the fact that there  
13 were legitimate disputes that arose.

14 I think those legitimate disputes are rare but my  
15 knee-jerk reaction used to be, go back through the  
16 supervisory chain. The folks in the agency are responsible.  
17 They will resolve those issues. Frankly, I think until the  
18 generic-drug scandal came along, that kind of was my  
19 reaction and the way I tended to deal with the issue.

20 After leaving the agency and becoming more  
21 familiar with the infrastructure of the industry and some of  
22 the concerns that the industry had, what I learned was that  
23 often--let me rephrase that. I think the kinds of disputes  
24 we are talking about are rare but once you define that rare  
25 universe, often what happened is a sponsor--and I think the

1 focus that I want to take really is on PMAs, sometimes  
2 510(k)s but especially at the early stages of a PMA process.  
3 That might be at the IDE stage or even now, as FDAMA allows,  
4 meetings that come prior to the IDE stage.

5           Often, in that rare universe that I describe, what  
6 happens is a manufacturer will be asked for additional data  
7 or a study that they don't think is appropriate. The  
8 particular reviewer might. So, hence, you have a dispute.  
9 How does that get resolved?

10           I think often what happens is the manufacturer or  
11 the sponsor will say, "Okay; we will do it your way." That  
12 may not be the best result of that dispute. Maybe there is  
13 a better way. We talked about scientific evidence and I  
14 wanted to mention that I think often where these disputes  
15 occur is when traditional evidence, randomly controlled  
16 studies and so on, may not work for reasons of ethics or for  
17 reasons of just raw numbers.

18           You have a breakthrough product. How do you move  
19 that product along? This is where, I think, some good solid  
20 scientific judgment is critically needed.

21           I had another thought that I wanted to mention. I  
22 think why this panel and why this process is so important is  
23 that, number one, it brings order to what has been sort of a  
24 mix of avenues for resolving disputes. I think, perhaps  
25 even more important, and Dr. Feigal and I have talked about

1 this in the past, it kind of gives permission for there to  
2 be a dispute, for there to be a disagreement.

3 It is not the end of the world. It is not a  
4 winner and loser. It is an honest scientific disagreement  
5 that needs additional heads to resolve, and those heads may  
6 be represented on the panel or, as I kind of teasingly said  
7 earlier, maybe those heads can come together and resolve  
8 issues even before you all have to be called together.

9 I wanted to also give you a reaction and some  
10 thoughts on the process that has gotten us this far. I  
11 think the appointment of Les Weinstein as ombudsman--and Les  
12 has been there, what, six months--

13 MR. WEINSTEIN: Seven.

14 MR. BENSON: Seven months, now, from March. I  
15 think the direction that Les has, whether it comes from Dr.  
16 Feigal or himself or others, I don't know--it doesn't  
17 matter--has been to really get into an outreach mode. He  
18 has come to a number of meetings of the industry to find out  
19 first-hand what some of the issues were.

20 I think Dr. Feigal mentioned to me at one point--I  
21 don't know whether you have implemented this or not but I  
22 think it is a terrific idea. Phil Phillips talked about the  
23 least-burdensome effort. One of the provisions of that in  
24 FDAMA is these early meetings that I spoke of earlier.

25 I think the program calls for you to sit in sort

1 of at random in some of those meetings. So you have first-  
2 hand information of how that process is working. I think  
3 these kinds of things--I am not going to try to give you a  
4 full litany--are terrific in terms of really dealing with  
5 the problem.

6 If we get some of the procedures and everything,  
7 and we are really going to solve the problems of these rare  
8 disputes, I think that is terrific.

9 Dr. Feigal spoke to the draft guidance that is out  
10 there. I think the principal concern that the industry had  
11 with that document--I think, if I understood correctly and  
12 maybe not--has been resolved, and that is the steps that one  
13 has to go through, or the steps that one might have to go  
14 through, that are outlined in that document are--instead of  
15 being a very linear flow chart of steps, rather are a  
16 combination of various approaches to resolving disputes.

17 Under that umbrella, I think it is a good thing  
18 because, again, it brings order to the process. The concern  
19 we had was that, by the time you exhausted all those steps,  
20 you may be--I was thinking, in fact, earlier when you were  
21 speaking, you don't want to wait too long if there is a  
22 critical recall that is needed. You want to make that  
23 happen fast.

24 Likewise, for a breakthrough product, you don't  
25 want to wait forever, going through a lot of steps. You

1 want to be able to resolve those things in a swift way. So  
2 that concern, I think, is gone, if I understood you  
3 correctly.

4 I understand that the final guidance will be  
5 published soon and we look forward to that. I wanted to  
6 mention that. I want to talk a little bit about dispute  
7 resolution and how the least burdensome provisions of FDAMA  
8 and dispute resolution come together. I think Phil Phillips  
9 spoke to that so I am not sure I even need to do that. I  
10 think the points he made are germane and appropriate.

11 I think one thing I did want to mention is that  
12 the opportunity for the public or stakeholders or, in our  
13 case, sponsors and the agency to come together at  
14 appropriate times, at appropriate levels, are very important  
15 to the process. They are mandated by these early meetings.  
16 My experience with the agency, both inside and out, has been  
17 that when a meeting was requested, it is generally granted.

18 I think the opportunity there to really review,  
19 for the sponsor and the reviewer or reviewing group, to come  
20 together to figure out what is appropriate science, what is  
21 appropriate evidence, for that product is a critical step.

22 I think that the least burdensome process is not a  
23 way of sidestepping good science but, rather, to make sure  
24 that the science that is brought to the table is, in fact,  
25 appropriate. Dispute resolution, I think, will only help

1 that process, and that is really the point I wanted to make.

2           The Congressional intent, which also was spoken to  
3 in terms of dispute resolution and why it was part of FDAMA,  
4 I think I have kind of covered in the difference in  
5 perceptions. Often, a sponsor, in frustration, will go to a  
6 member of Congress--that is always an awkward process. The  
7 agency resists that kind of pressure, as it should, and it  
8 is inappropriate, Most folks in Congress don't even like to  
9 do it.

10           But the reality is it happens. I am sure you have  
11 gotten calls to nudge something along. That is not a good  
12 thing. So I think, in part, Congress is saying, "Let's make  
13 sure we have a vehicle in place such that we don't get  
14 called on for that sort of thing."

15           So let me just say, in summary, I think the work  
16 that has been done to date, the existence or the appointment  
17 of Les Weinstein, the activities, the philosophy that Dr.  
18 Feigal has expressed is terrific. I also wanted to mention  
19 one last point that I think has also been very good, and I  
20 am glad that it will still be part of the process.

21           Phil Phillips mentioned the--what is the group  
22 that you referred to? The Program Operations staff. The  
23 Program Operations staff historically has also served a very  
24 critical purpose in the dispute resolution. I think Phil  
25 and the folks that are in that group have acted very

1 responsibly at not increasing the friction but rather  
2 reducing it. So I think that has been an important element  
3 and I congratulate you on that.

4 Mr. Chairman, that is it. Thank you very much.  
5 Be glad to answer questions if anybody has any.

6 DR. SOX: Thank you, Mr. Benson. Panel members?  
7 Questions or comments for Mr. Benson? Actually, I did want  
8 to ask you something. Because if your experience in the  
9 agency as well as your work now in industry, you have got a  
10 broad perspective. I guess I am interested in knowing what  
11 your level of satisfaction is with the process now, taking  
12 the perspective of sponsors and advocates and manufacturers.

13 Has FDA got it about right, or are there some  
14 significant problems, recognizing that it is not in the  
15 interest of members of your organization to put out a  
16 product that is harmful and, perhaps, puts them out of  
17 business or hurts their reputation.

18 MR. BENSON: Just to that latter point, I think no  
19 one, including the industry as a whole, wants to see bad  
20 products out there or problematic products. That just hurts  
21 everybody. You can put it on a public-health plane and a  
22 people plane. You can put it on an economic plane. In any  
23 case, it is bad news across the board.

24 Let me answer you this way. Over the past, let's  
25 see, three or four years, CDRH has been under a great deal

1 of external pressure generated by the enactment of FDAMA. I  
2 think folks that are not knowledgeable about device law and  
3 CDRH processes don't realize how intense that legislation  
4 was, much more so than for the Center for Drugs or other  
5 parts of the agency.

6 They also had a self-initiated process of  
7 reengineering where they really looked, sort of in an  
8 introspective way, at ways of making things more efficient.  
9 I think the combination of those two things, whether it is  
10 the putting together the least-burdensome process, as we are  
11 describing here today, the work on least-burdensome--there  
12 are many others that I could mention--have gone a long ways  
13 at reducing the need for dispute resolution in a formal  
14 sense.

15 So I think if you recognize the drain on resources  
16 that it takes to implement these things and to think them up  
17 to begin with, we keep putting pressure on them saying, you  
18 have got to collaborate, you have got to work with the  
19 industry, you can't go off in a vacuum.

20 I think that is efficient in the long run, but if  
21 you have got a deadline to face, it doesn't feel efficient  
22 at the time. I give them very high grades. I still think  
23 the permission issue that I mentioned, it is okay to  
24 disagree. The order that the guidance and the panel and the  
25 ombudsman practices represent I think will all come together

1 at making it even better in the future.

2 DR. SOX: Thank you very much.

3 MR. BENSON: My pleasure.

4 DR. SOX: Our next speaker is Dr. Charles Swanson.  
5 Dr. Swanson, would you identify who you represent and the  
6 floor is yours.

7 DR. SWANSON: Thank you. My name is Chuck  
8 Swanson. I am the Chief Quality and Regulatory Officer for  
9 Medtronic. We are a medical-device manufacturer that deals  
10 extensively in implantable medical devices and, in  
11 particular, class III medical devices. So we have a strong  
12 interest in the role that dispute resolution plays in the  
13 PMA process, particularly.

14 You have heard from Jim Benson giving you kind of  
15 the industry's view as a whole. What I would like to do is  
16 give you maybe a little more personal view of how we see it  
17 as an individual manufacturer.

18 I don't pretend to be able to speak for all of  
19 industry. The majority of medical-device companies are very  
20 small, and Medtronic is very large with about 25,000  
21 employees. But I think the issues that we face are  
22 fundamentally not different, particularly, from those  
23 manufacturers who make PMA products. So I think I can speak  
24 with some confidence that I reflect that part of the  
25 industry.

1           Now, first of all, let me respond to some of the  
2 questions that you raised there about is the agency  
3 functioning properly. I would like to say they are going in  
4 the right direction. Are they doing everything right? No.  
5 But then, is industry doing everything right? No.

6           I think what we need to have, it seems to me, is a  
7 healthy dissatisfaction with the status quo. One of the  
8 things that we need to do as an industry and as FDA is try  
9 to work together. I think one of the things that I have  
10 been pleased about is the interest that FDA has shown in  
11 collaboration with industry in trying to find better ways to  
12 do things.

13           I think this Dispute Resolution Panel and Les  
14 Weinstein's role as the ombudsman provide additional  
15 mechanisms for the resolution of scientific disputes. I  
16 look forward to that, not so much that I want to use them on  
17 a regular basis. I hope we don't have to, but it is good to  
18 have them there as a safety valve when we need it or when  
19 the agency needs it.

20           Now, my hope is that, Lillian, we never get into  
21 dispute resolution that I have to come here for that kind of  
22 reason. Actually, I hope I don't have to come here at all,  
23 like Jim. But my expectation is that the major role is  
24 going to be in resolving disputes regarding the approval of  
25 new products.

1           From a PMA manufacturer's standpoint, the main  
2 things that we are looking for, and I can say it very  
3 simplistically, is predictability, number one, that we can  
4 understand what the requirements are going to be and have  
5 confidence that, when we start developing a process, knowing  
6 that FDA is not going to see the final results until the  
7 end, that we are doing the right thing.

8           So predictability is very important. Reasonable  
9 requirements; the requirements that reflect the nature of  
10 the device, the conditions of the use and the risks that it  
11 poses. This gets to the issue of least burdensome, and how  
12 to find the least-burdensome means to provide the reasonable  
13 assurance of safety and effectiveness.

14           And then, finally, the timely submission review,  
15 once all of the data have been collected and were put in the  
16 package for FDA to support the market approval.

17           FDAMA dealt with all three of those. In terms of  
18 the predictability, it hit as fostered collaboration between  
19 device sponsors and FDA. Actually, FDA, before that  
20 happened, really tried to increase the collaboration by  
21 informal meetings. FDAMA allows us to go the step further  
22 and get to meetings that allow for binding agreements so  
23 that there is a higher degree of assurance.

24           So I think we are moving in the right direction  
25 there. But predictability, by itself, is not enough because

1 if the requirements are unreasonably burdensome, they may be  
2 very predictable but that is not what we are looking for.  
3 Again, that is what the least-burdensome means is all about.

4           Where predictability and the reasonable  
5 requirements, in my judgement, play the biggest role, is,  
6 number one, in breakthrough products, whether they be  
7 significant new technologies that are being applied or  
8 whether they represent significant new therapies.

9           Now, in my twenty-four years or regulatory  
10 experience, I have had a number of these products that I  
11 consider to be breakthrough. They are tough. They are  
12 tough for FDA and they are tough for industry. They are  
13 tough for FDA and industry because we don't have an  
14 experience base to fall on.

15           It is not unreasonable for FDA to make more  
16 conservative decisions when, in fact, they don't have an  
17 experience base. It doesn't mean it is right, but those are  
18 the facts. Where we have disputes there, we would like to  
19 able to resolve them, whether it is through the chain of  
20 command or whether it is through, now, Les Weinstein's role  
21 as the ombudsman or through this Dispute Resolution Panel.

22           The other area where changes can occur--because  
23 devices tend to evolve. You come up--once a breakthrough  
24 product is there, it is refined and improved through  
25 continuous generations. With time, what you find is that

1 you begin to understand what FDA wants and the process  
2 becomes relatively predictable until there is a significant  
3 change in the environment, whether that be the political  
4 environment or a product problem.

5           The issue that was behind this many years ago was  
6 the Temple Report which really said that devices needed to  
7 be more rigorously clinically evaluated, and some took that  
8 to be randomized double-blinded controls, the drug model.

9           That is appropriate for some, but it is not  
10 appropriate for all. We had to go through some really  
11 significant times trying to figure out what were the  
12 appropriate clinical requirements for devices. So those  
13 kinds of environmental shifts do raise significant issues.  
14 Again, all of these mechanisms are opportunities to resolve.

15           I would just like to close with some comments  
16 about when do we choose to go into dispute resolution. You  
17 have got to look at a number of factors. What does it cost  
18 to do the testing that FDA wants you to do? How much time  
19 is it going to take to do the testing? How much time and  
20 what is the cost of appealing the decision and what is your  
21 likelihood of success.

22           All of those factors play in. The importance of a  
23 timely dispute-resolution process is if it takes longer to  
24 get a decision than it would take you to do the test, then  
25 you are just going to do what FDA wants. I don't think that

1 is in anybody's interest and I am glad to hear Dr. Feigal  
2 speak to that, Phil Phillips speak to that.

3 I think all of us need to understand that we need  
4 to work together to make the process work. Industry has an  
5 obligation. We don't want to produce bad products.  
6 Occasionally, product problems are going to arise and we  
7 have to deal with them, but, in the preapproval process, we  
8 both have to come up with the mechanism that will provide  
9 reasonable assurance that the product is safe and effective.

10 There is where we can have honest differences of  
11 opinion between reasonable people, what that is. So I  
12 really am pleased that this Dispute Resolution Panel is up  
13 and running and I will be interested in how it proceeds and,  
14 again, I also appreciate the activities of Les Weinstein. I  
15 think he is going to be a person who will contribute to CDRH  
16 in helping to bring new products to market.

17 With that, I will be happy to answer any  
18 questions. I don't have any formal notes that I can leave  
19 behind. I have just a few handwritten scribbles. So,  
20 hopefully, I spoke better than I write.

21 DR. SOX: You spoke very clearly and thank you.

22 Panel members, do you have questions for Dr.  
23 Swanson?

24 DR. RAMSEY: I will ask one question. You  
25 mentioned predictability as a key component for this

1 process. This is a new panel and, almost by definition,  
2 now, we are unpredictable. What would you recommend? In  
3 terms of our functioning, what would be more optimal for you  
4 in terms of criteria of predictability?

5 DR. SWANSON: That is a very good question. I  
6 don't know that I have a good answer for that. I think, as  
7 I said, probably the most important thing to us is the  
8 ability to get a timely decision so that we can get on with  
9 the process of bringing the product to market and doing the  
10 evaluation we need.

11 Where we have a difference of opinion, we need to  
12 understand whether the Dispute Resolution Panel is going to  
13 come down on FDA's side, on our side or somewhere in  
14 between. But timeliness, I would say, is probably the most  
15 important attribute I can see now.

16 DR. SOX: Actually, I have a couple of questions  
17 for you. The first has to do with the premarket approval  
18 application and product development protocols. It sounds as  
19 though the latter, the product development protocols, is a  
20 really good way to make sure that the FDA and the  
21 manufacturer are on the same page, right from the get-go,  
22 and to minimize your uncertainty except in so far as the  
23 data, itself, may be unpredictable.

24 So my question is why go the other route? Why not  
25 all of us go the PDP route?

1 DR. SWANSON: The PDP versus the PMA? Actually,  
2 when FDA resurrected the PDP process a few years ago as part  
3 of their reengineering activities, I had the honor of  
4 serving as one of the industry people on that panel. I  
5 think that there are things that that process has to offer.

6 The difficulty is getting agreement on everything  
7 up front, even with the formal meetings under FDAMA, the  
8 scope of the agreement is limited, generally in terms of  
9 what kind of valid scientific evidence or clinical data or  
10 the details of the protocol.

11 With the PDP, it is nailing down every single  
12 item. It is easiest to do when you are dealing with the  
13 tenth generation of a product, like a pacemaker. But those  
14 are the ones that probably need it least. The breakthrough  
15 products are the ones where it is virtually impossible to  
16 come up with those decisions.

17 So it is a great idea. The devil is in the  
18 details.

19 DR. SOX: That is a nice segue into my second  
20 question which has to do with the breakthrough product  
21 category. Both you and Mr. Benson mentioned that and I got  
22 the impression, perhaps wrongly, that perhaps that  
23 evidentiary threshold ought to be lowered for such products.  
24 I wonder if you could either set me straight or confirm that  
25 I read you right and perhaps to give an example of a

1 breakthrough product and how it was handled and how that  
2 process worked out.

3 I am just having a little trouble getting my arms  
4 around this particular category.

5 DR. SWANSON: I will give you an example of a  
6 breakthrough product that Medtronic has--there are several--  
7 that is currently under review right now is a device that  
8 uses deep-brain stimulation for treatment of Parkinson's  
9 disease to provide relief for the major symptoms of  
10 Parkinson's.

11 It is the first of a kind, the first kind of  
12 device alternative to drug therapy. Should the requirements  
13 be lowered? I would say to you they shouldn't be any more  
14 than the least-burdensome requirements would. My point when  
15 I said that FDA, when dealing with the unknown, tends to be  
16 conservative. They want to make sure.

17 That doesn't mean that they intentionally  
18 overspecify. They don't know any more than we know. There  
19 are honest differences of opinion over what that should be.  
20 That is where I think particularly the scientific and  
21 medical members of the Dispute Resolution Panel have good  
22 things to offer, because when you have two sides that have  
23 been discussing these issues and have come to reasonable  
24 disagreements, a third party can sometime help bring light  
25 and bring conciliation.

1 DR. SOX: Any other questions from the panel?

2 Thank you very much, Dr. Swanson.

3 Our last speaker is Ms. Mary-Lacey Reuther. Would  
4 you tell us where you are from and proceed.

5 MS. REUTHER: I would like to say good afternoon  
6 and Happy Halloween to everybody here. I am Mary-Lacey  
7 Reuther, the Deputy Executive Director of the Medical Device  
8 Manufacturers Association. MDMA is a national trade  
9 association based in Washington, D.C. We represent nearly  
10 140 manufacturers of medical-device products, diagnostic  
11 products, and health-care information systems.

12 We are the national voice for the entrepreneurial  
13 sector of the medical-device industry and we seek to improve  
14 the quality of patient care by encouraging advancements in  
15 medical technology.

16 MDMA has and continues to strongly support the FDA  
17 Dispute Resolution Program as an important mechanism to  
18 resolve scientific controversies that may arise between FDA  
19 reviewers and the company whose product is being reviewed.  
20 MDMA helped to shape the vision of this program and worked  
21 hard for its inclusion in the FDA Modernization Act of 1997.

22 We believe that it is vital for medical-device  
23 companies to have a formal avenue for their voices and  
24 concerns to be heard while they are going through the FDA  
25 clearance and approval process. MDMA was created to

1 represent the small businesses and entrepreneurs in the  
2 medical-device industry.

3           These small companies, the source of most of the  
4 innovation and medical technology, have a limited amount of  
5 resources to sustain themselves while progressing through  
6 the regulatory clearance and approval process. A scientific  
7 dispute, if not handled properly, could jeopardize an  
8 important development medical-device technology from  
9 reaching the patient because the company either goes out of  
10 business or drops the product because it becomes too costly.  
11 For this reason, MDMA is very interested in how FDA  
12 implements and how you implement the dispute resolution  
13 provision in FDAMA.

14           MDMA also believes that an efficient and timely  
15 resolution to scientific controversies will help FDA to  
16 fulfill its mission to promote the public health by promptly  
17 and efficiently reviewing clinical research.

18           MDMA is encouraged by FDA's efforts to implement  
19 FDAMA's dispute resolution provision. It is a pleasure for  
20 me to stand here today and deliver these comments at the  
21 first meeting of FDA's Dispute Resolution Panel. Yet, we  
22 are still concerned because the agency has not finalized its  
23 guidance document.

24           I understand that you guys are working on it and  
25 are in the process of doing that, but we wanted to say that

1 we really believe the finalization of this draft guidance  
2 document is important to insure the future of this and that  
3 the leaders of the Device Center approach resolution  
4 predictably.

5           With all due respect, I would like to reiterate  
6 some of our concerns that we did voice about the draft-  
7 guidance document. I understand some of these probably have  
8 been or will be corrected, but I just want to go over them  
9 one more time so that the panel knows.

10           First, the Dispute Resolution Panel should not be  
11 limited to the review of formal agency decisions or actions  
12 but should be open to disputes that arise earlier in the  
13 product-clearance or approval process.

14           Second, there needs to be a swift time line of  
15 review by the Dispute Resolution Panel. A several-month  
16 wait between a sponsor's request for review and a final  
17 decision will dissuade many companies from using what was  
18 intended by Congress to be a responsive and timely process.

19           Third, the final recommendation of the Dispute  
20 Resolution Panel should stand unless the decision  
21 contradicts the law or would pose a significant threat to  
22 the public health. Providing the CDRH Director with  
23 unfettered authority to overturn the panel's recommendation  
24 would compromises the independence and integrity of the  
25 process.

1           Once again, I thank you for granting us the  
2 opportunity to say a few words about this very important  
3 matter to the medical-device industry. We look forward to  
4 working with you and the agency in making this successful.

5           If you have any questions?

6           DR. SOX: Thank you very much, Ms. Reuther.

7           Questions or comments from the panel? Scott?

8           DR. RAMSEY: I have heard "timeliness" twice now.  
9 Could you guys give us a sense of what you would consider a  
10 timely turnaround for a dispute?

11           MS. REUTHER: Oh, gosh. You put me on the spot  
12 here. I couldn't answer that, to be honest with you.  
13 Probably--I don't know. I think it varies based on that,  
14 but--not months. Exactly. Six months would not be. I  
15 think it goes back to what Dr. Swanson said about would you  
16 do FDA recommended or versus is it going to take longer for  
17 you to go back through and do the trials than for FDA.

18           Does it take longer to get an FDA decision than to  
19 do the trials. I think it is very important to consider  
20 that and that a company, especially with a break-through  
21 product is considering that. So timeliness would depend  
22 upon the product, but definitely not months.

23           Any other questions?

24           DR. SOX: If there are no other questions--oh,  
25 yes; Dr. Swanson. Please.

1 DR. SWANSON: I can't help but take the  
2 opportunity to respond to the question about what is a good  
3 time frame. My own recommendation would be 60 days. I  
4 think that is a timely way and it gives the opportunity to  
5 work it up at least some point through the chain of command  
6 before it goes to, whether it is the ombudsman or the  
7 Dispute Resolution Panel. But I think 60 days is a  
8 reasonable time frame.

9 DR. SOX: In their wisdom, CDRH has made our panel  
10 pretty small, which increases the probability of convening  
11 us on relatively short notice. So we will do our best.

12 Any other comments from the panel? David, would  
13 you like to make any concluding remarks? And then I will  
14 call upon you, Les.

15 **Closing Remarks**

16 DR. FEIGAL: I would like to thank the folks from  
17 industry that came to speak to the issues. I don't know if  
18 I should be gratified that it wasn't mentioned because it is  
19 something which is less of a concern or if it is one of  
20 those fears that is difficult to bring up on a day such as  
21 Halloween.

22 But the thing I was gratified not to hear was a  
23 concern that entering into a dispute-resolution process  
24 would create a bias or negative feelings on the part of the  
25 agency. I realize that there often are strong feelings

1 about issues that result in disputes and one of the things  
2 that we have often heard as a concern is whether or not even  
3 getting into a dispute, even challenging someone, would, in  
4 fact, have consequences and at least, if not result in  
5 retaliation, at least sort of sour the field.

6 I think that what we really strive to do in the  
7 Center is to set the tone that these are really science-  
8 based decisions, these are evidence-based decisions, and  
9 that there are a lot of difficult judgments and close calls  
10 and that it is perfectly legitimate to ask a question about  
11 how a decision has been made, why it has been made, and to  
12 argue whether or not there is another way to look at the  
13 same evidence or whether the threshold for a decision has  
14 been set too high.

15 So, if it still is a concern, the reason that I  
16 wanted to bring it up is to point out that I think that the  
17 overall leadership and culture of the center is to really  
18 create the kind of atmosphere where we are asking questions.

19 If you think of what the basic paradigm is of  
20 consumer protection through a regulatory body, the paradigm  
21 is that you identify issues that are relevant to the stage  
22 of the development of the product. They are different for a  
23 product early in development than late.

24 You collect evidence that addresses those issues  
25 and then you analyze that evidence to try and make a

1 decision. The decisions vary. Sometimes, it is to allow  
2 marketing authorization for a product. Other times, it may  
3 be around putting special controls on a product that seems  
4 to be having a problem.

5 But these really are evidence- and science-based  
6 disputes. I hope that our intent to do that will also be  
7 recognized as our usual way of doing business.

8 I don't think I have any other concluding remarks  
9 other than perhaps if anything is going to be unpredictable,  
10 it will probably be the timing of these meetings since they  
11 will be driven by events and we appreciate your willingness  
12 to have us call you and have this be a little less of a  
13 scheduled process than some of our other panels.

14 I think, as we begin to work through some of these  
15 processes, it will have benefits that will go beyond even  
16 the individual cases that we consider. It will also, in  
17 many cases, establish approaches that will have benefits at  
18 other times in the agency and in the development of other  
19 products.

20 Thanks very much.

21 DR. SOX: Thank you.

22 Mr. Weinstein, the last word?

23 MR. WEINSTEIN: I would just like to thank  
24 everybody here at the Center who helped put together today's  
25 panel meeting. Without naming specific names, let me just

1 thank the various offices: the Office of Systems and  
2 Management, in particular; the Office of the Center  
3 Director; the Office of Device Evaluation; and the Office of  
4 Compliance. Thank you very much.

5 DR. SOX: I think this meeting, despite its  
6 brevity, has given us a good opportunity to learn. I value,  
7 very much, the opportunity to hear from representatives of  
8 the industry. Whether we are going to meet often or  
9 frequently, I don't know, but I think we are well prepared  
10 for our task.

11 At this point, I am going to adjourn the meeting.  
12 Thank you very much.

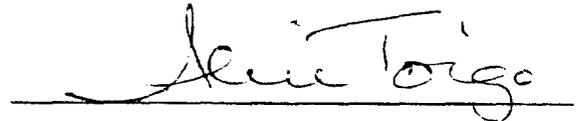
13 [Whereupon, at 2:45 p.m., the meeting was  
14 adjourned.]

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## *C E R T I F I C A T E*

I, **ALICE TOIGO**, the Official Court Reporter for Miller Reporting Company, Inc., hereby certify that I recorded the foregoing proceedings; that the proceedings have been reduced to typewriting by me, or under my direction and that the foregoing transcript is a correct and accurate record of the proceedings to the best of my knowledge, ability and belief.

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