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AT

DEPARTMENT OF HEALTH AND HUMAN SERVICES

FOOD AND DRUG ADMINISTRATION

**DEVICE GOOD MANUFACTURING PRACTICE**

**ADVISORY COMMITTEE MEETING**

Tuesday, April 29, 1997

8:15 a.m.

Parklawn Building  
5600 Fishers Lane  
Rockville, Maryland

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P R O C E E D I N G S

**Call to Order**

DR. ZABRANSKY: I would like to get started. My name is Ron Zabransky. I am the Chairman for today's panel meeting. I wish to thank the FDA for providing this nice facility for our meeting.

Our meeting this morning is to address a particular proposal that the FDA is putting before this panel as well as the industry and this has to do with, of course, the issue of inspections. It is to provide a model for risk-based planning for determining where the FDA headquarters and their field resources should be focused as far as inspections are concerned.

I would like to have the panel introduce themselves and we will start over on the righthand side and move across.

MR. BARTH: My name is Don Barth. I am with the Hewlett-Packard Company.

DR. ZABRANSKY: Could you also state your role on the panel.

MR. BARTH: I am in the regulatory affairs function with Hewlett-Packard and I spent quite a lot of time in Washington with the trade associations and standards

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development organizations, so I get the privilege of meeting a lot of the folks in the room here today.

DR. ZABRANSKY: And you are an industry rep.

MR. BARTH: Yes, I am.

DR. HUGHES: Allen Hughes, Assistant Professor, George Mason University, and I am a consumer rep.

DR. PIERONI: Bob Pieroni, Professor of Internal Medicine and Family Medicine, University of Alabama. I am a health professionals rep.

MS. THIBEAULT: I am Anita Thibeault. I have my own consulting firm, Anita Thibeault & Associates, and I am an industry rep.

DR. ZABRANSKY: I am Ron Zabransky. I am the VA Medical Center in Cleveland. I am a government representative.

MS. ALDRICH: Rita Aldrich. I am with the New York State Department of Labor. I am a government representative.

DR. CORNWELL: Edward Cornwell, Assistant Professor of Surgery, University of Southern California. Health representative.

MS. SMITH: I am Linda Smith. I am nursing faculty at the State University of West Georgia full time. I am also working at my doctorate at the University of

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Alabama with 25 years of nursing experience. I am a consumer rep.

DR. ZABRANSKY: Thank you.

At this time, I would like to ask Sharon Kalokerinos, who is the Executive Secretary or something of that nature for this panel, to provide some basic and background information.

MS. KALOKERINOS: Good morning. First, I would like to say if you need a number for messages, they can call the Conference Control Center, which is located across the hall. That number is 443-2585.

Secondly, agency procedure requires that we go over the conflict of interest requirement specified for Special Government Employees and that a statement regarding conflict of interest be read into the record.

#### **Conflict of Interest Statement**

The following announcement addresses conflict of interest issues associated with this meeting and is made a part of the record to preclude even the appearance of an impropriety.

To determine if any conflict existed, the Agency reviewed the submitted agenda and all financial interests reported by the committee participants. The conflict of interest statutes prohibit Special Government Employees from

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participating in matters that could affect their or their employer's financial interests. However, the Agency has determined that participation of certain members and consultants, the need for whose services outweighs the potential conflict of interest involved is in the best interests of the government.

Full waivers continue in effect for Donald Barth, Dr. Edward Cornwell, and Anita Thibeault, and full waivers with amendments are in effect for Dr. Ronald Zabransky, Dr. Robert Pieroni, and Linda Smith for financial interests in firms at issue that may potentially be affected by the committee's deliberations.

Copies of these waivers may be obtained from the Agency's Freedom of Information Office, Room 12A-15 of the Parklawn Building.

In the event that the discussions involve any other matters not already on the agenda for which an FDA participant has a financial interest, the participants should exclude themselves from such involvement, and their exclusions will be noted for the record.

With respect to all other participants, we ask in the interest of fairness that all persons making statements or presentations disclose any current or previous financial

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involvement with any firms whose products they may wish to comment upon.

Thank you.

Also, for those that wish to make statements from the floor, we ask that you provide us with a business card, so that we can identify correctly in the record.

### **Open Public Hearing**

DR. ZABRANSKY: First of all, this particular meeting was officially announced. It was seen in the Federal Register published April 14th, Volume 62, No. 71. There have been a number of people that have requested to make presentations, and they are on the agenda. Anybody that wishes to make statements from the floor, comments from the floor, will be allowed no more than 10 minutes, and we will proceed with that probably toward the end of the morning and maybe even early this afternoon depending upon how the time schedule goes.

At this time, I think we will start with the general introduction. Dr. Bruce Burlington, who is the Director of the Center for Devices and Radiologic Health, will present the overview of the risk-based planning model that they are proposing.

Dr. Burlington.

### **Overview of CDRH's Risk-Based Planning Approach**

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DR. BURLINGTON: I am not sure how this is going to work as a discussion dynamic because it look at like we have got the podium positioned here behind the pane, but there is no portable microscope -- or microphone, so we will do the best we can -- no portable microscope either.

I wanted to say good morning to the panel. We certainly appreciate your joining us this morning. It looks like from the audience, although we have some interest, it is a little less controversial than when you were here a couple of years ago and we were looking at the quality systems regulation.

In a way I find that surprising because I think the inspection strategy, the risk-based approach in figuring out where the Agency is going to go look to enforce the quality systems requirements is, in fact, something that is terribly important. It is something that should be of interest to industry.

I hope we will get some feedback, not only from the panel member, but also during the public hearing.

I am going to start this morning with a few minutes talking about a risk-based approach and the need for a risk-based approach. Recently, the Center and the Agency have disseminated for public consideration some documents

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which provide background thinking on reengineering our processes using risk-based approaches.

We are doing this for a couple of reasons. Number one, it has become increasingly apparent over the last few years that there simply are not going to be the resources provided in the discretionary domestic budget in the funding that the Agency gets to do everything that is set forth in the statute as our responsibility, and in picking and choosing among what we do we want to maximize the public benefit to be achieved from the resources that are available.

We believe in order to do that, we not only need to undertake an evaluation of where the action is, risk-based approach, we also need to reengineer our processes, so that as we pursue our work, we can do so in an efficient way, minimizing the resource allocated to any given job and maximizing the result accomplished from it.

In order to do so, we have tried very hard to look at the work that the Agency does from the viewpoint of industry, the viewpoint of practitioners who are using products, and the viewpoint of patients who are the recipients of the use of medical devices, and we are going to ask you to help us further that in regard to our quality systems and inspection program.

When you think about process, all the standard management textbooks say you have got to look and for an organizational viewpoint, what are your inputs, what are the outputs, what are the results of the organization working on those inputs and how do they matter to the people that you are doing the work for, the patients, the doctors, and the industry as well.

In thinking about inputs, we receive data in regard to our inspection program from a lot of different sources. We certainly get registration listing to find out where the companies and where the smokestacks are. We have information on quality systems both from publications through standards committees, both technical and scientific publications, and we seek input in public fora, such as this one, as a further source of input.

When we think about outputs, what are the outputs of our inspection process? Hopefully, in the end, they are a higher quality product emerging from the factory door and feeding into the stream of health care products, but the more direct output, particularly from the company's point of view, is when the Agency comes and inspects, they see an inspector shows up, and they get a notice of inspection and at the end of the inspection they get a variety of documents. They may get nothing or actually today, if they

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have had a good, clean inspection they get a post-inspection letter that says we came and inspected these processes, and we found you to be in substantial conformance with the quality systems good manufacturing requirements.

If problems have been found, they may get what in FDA parlance we call a Form 483. It is really a notice of observation. It is a description of what the inspector saw that was areas of concern. They may get a chance to respond to that. And they may, in fact, get a warning letter as an output from the inspection.

Those are intended to be Agency's assessments of where they need to change their quality systems in order to improve the assurance that products flowing from the factory will meet standards for the health care community.

I believe it is helpful to think about those inputs and outputs in a general sense, and we are doing that as we go about reevaluating, reengineering, or doing continuous business process improvement of our inspection program, but we also have to think about where are we going to go to do the inspections.

Now, we know that there are today 8,000 or so sites that are registered as medical device sites. We know -- and Ms. Gill is going to in a few minutes give you more details on this -- that we don't have anywhere near the

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capacity to get to every one of them every year. We can't even meet the statutory directive of being at every site every other year.

Recognizing that some business entities may operate more than one site, and an inspection may cover more than one physical site, and reducing it, we still come down to somewhere around 4,300 different sites we ought to be at. Ms. Gill says it is more like 2,500 inspections we ought to be doing every year, maybe some more, and we are not doing that. We are far short of that.

So, what we are looking at in terms of ability to meet the statutory directive is right now we are staffed and funded to get about halfway there, and we ought to be doing the right half.

How should we set out to do the right half? Ms. Gill and I talked several months ago and said, well, there are a number of factors that we could consider. We could put all the effort into for cause, and not do any surveillance and just, you know, follow tips, follow leads, but that didn't seem to make a lot of sense. There was a clear intent by Congress that we do surveillance inspections, as well as for cause, that we go out and sample the world even when we didn't have any reason to think there was a problem.

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We could only go to the big companies on the theory that they put out a higher volume of products, and so that that is where the risk may be, and that might be a reasonable way to consider it.

We could follow the adverse event reports and just way wherever we are getting a lot of adverse events, there seems to be likelihood that there is going to be problems. We could follow recalls and say wherever there have been a lot of recalls, we could think that that is potentially a fertile area to go out and do surveillance inspections, or we could come up with a model that says let's have a structured surveillance component to our inspection program and let's try and focus our surveillance efforts to be where the most important or where the greatest chance of finding problems might be, where the greatest protection is afforded to the American public.

We do intend, not only to have a more focused surveillance inspection program, but we also intend to put a larger proportion of our inspection efforts into for cause, but it is exactly this model that Ms. Gill is going to be discussing with you in a few minutes and for which we are going to seek your advice in helping us weigh the factors that direct our efforts in helping us weigh the impact of if we have an industry sector that had a lot of problems a few

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years ago, we went out and inspected intensely, we may have taken some actions, yet, they continue to show up as a foci of adverse advents, as a focus of recalls.

Is that someplace we should go back to right away or should we say that is an inherent part of the business they are in and therefore we should put our energy somewhere else for the next few years?

Those are hard questions. Those are questions that we believe we will have a better answer for with your input.

One of the underlying themes that applies, not only to the inspection and quality systems program, but applies to everything that we do at the Center, is that when we look back at the way we have done our work over the last few years, we recognize that we have been driven by volume, that in premarket, focusing on getting 6,000 510(k)'s processed in 90 days has caused us to put disproportionate energy there as opposed to putting the energy in PMAs or IDEs, and as a consequence, we have done a better job meeting timeliness goal in the last couple of years on 6,000 510(k)'s than we have on 50 PMAs a year.

In adverse event reporting, in terms of processing 100,000 applications a year, the sheer volume of processing, figuring out what is there, getting it coded, has driven us

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to put a disproportionate amount of energy into dealing with the volume rather than focusing on the hazard analysis and adverse event warning.

Similarly, in compliance and quality systems, we believe that the sheer number of sites doing business has driven us to try and cover the waterfront rather than to focus on what is most important. Reiterating, helping to change that model helping to make it a risk-based approach that will result in better payoff for the consumer in assurance that there is a quality product rolling out the factory door is the purpose of our discussion here today, and we appreciate your help in making those decisions.

Thank you.

DR. ZABRANSKY: Thank you, Dr. Burlington.

At this time, I would like to proceed to have Ms. Lillian Gill discuss the actual model itself. After that point, then, we will have some open discussion as to what this will mean, at least from the panel.

Lillian.

#### **A Risk-Based Planning Approach**

MS. GILL: Good morning. Thank you, panel, for your time and attention that you are giving us today toward the advice that the Office of Compliance needs in the development of our priorities for the future.

[Slide.]

As Dr. Burlington has discussed with you, CDRH has chartered a course toward reengineering our work efforts, and these will be based primarily on the identification and the focus of what we see as our dwindling resources on high-risk and high-impact products or work areas.

[Slide.]

Like other Center offices in CDRH, compliance is faced with determining how best to utilize our resources and those resources in the field where our inspections are conducted.

Should we set these priorities on legal obligations, such as our biennial requirement or are there effective alternatives? The Food, Drug, and Cosmetic Act requires that all Class III and Class II manufacturers be inspected every two years to determine compliance with good manufacturing practices.

It has become more difficult to meet that obligation as our resources directed toward all FDA inspections has declined from around 1,100 to 800 over the period of about four years.

[Slide.]

This chart is an illustration of what Dr. Burlington mentioned earlier today. It illustrates our

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capacity, our capability, or, as you can see, our incapability, over the past three years of carrying out those biennial obligations. Although we made a little progress in '96 toward meeting the goal, as you can see, we are still quite a long way from inspecting those firms that we are required by law to inspect.

Forty-eight percent of those eligible forms or subject firms were inspected in '94. What you have is the total number of firms here, 49 for '96, 4,747 Class II and III manufacturers for biennial inspection for inspection, the number subject to inspection for any given year, for '96, for last year, would have been 2,374.

What we actually inspected was about 53 percent of that, so we are falling short about 1,100 inspections that should be conducted in any given year, and these are routine surveillance inspections.

I might add also that the numbers you see here in the surveillance coverage is not distinguishable in terms of risk. These are manufacturers that a district has in the inventory and are subject to inspection. It is not based on product classification. It is not based on nature and problem with the device. It is sheerly based on having to get out and do the biennial inspection and cover their inventory every two years as required.

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The priorities in the past compliance program were focused on inspecting firms that had not been inspected every two years or not received their biennial inspection, or those who had never received a GMP inspection, so it was not risk-based in terms of looking at the classification of device again.

Even with this focus, as the chart indicates, in '96, there were 515 manufacturers that were registered two years or longer that never received a GMP inspection.

[Slide.]

To address some of these areas of concern, the Office of Compliance is proposing this risk-based approach to direct where those 1,200 routine GMP inspections will be conducted. The objectives for this plan, therefore, are to identify and prioritize our concerns, to put resources towards addressing these concerns in the appropriate place, and to accomplish these tasks in a manner consistent with the Government Performance Results Act, or GPRA in our terminology.

This requires us not only to identify problems, but also to focus on the resolution of these problems, and that includes communicating with the manufacturers what we have found, and it includes working with them to develop

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strategies to minimize the reoccurrence of the problems found.

[Slide.]

Since there is little indication that additional resources will be available over the next few years to increase our coverage in our high-priority areas, Compliance plans to refocus the FTEs from the routine GMP conformance or surveillance area that you see on the left to what we are calling the targeted surveillance area.

I want to clarify at this point that targeted does not mean that the Office of Compliance and the Office of Regulatory Operations will be targeting any specific manufacturers or developing any enforcement plan of actions against specific manufacturers.

Targeted in this chart means that we will be looking at the high priority areas, we will be devoting those resources toward working on the highest priority devices that are either experiencing problems or through which we have some great concern or need for additional investigation.

[Slide.]

What it means is that we are dedicating these redirected resources in the four specific areas you see here - pre-approvals, so that safe products can get to market

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sooner. It means we will be increasing our coverage on for cause inspections, these follow-up on emergency situations or issues that require prompter investigation.

It means that we will be making return trips for follow-up inspections to those firms that we have done an initial inspection and found some violations. It also means that we will be focusing time and attention in the high-priority areas that we are determining or identifying through this model.

The focus of this presentation and the effort that you have before you is the development of those devices in that last category, the risk-based surveillance.

[Slide.]

Using this plan, our anticipated benefits, as you see, will be the dedication of greater energy to improving the quality of products manufactured. We will have, we think, a more effective coverage of the device industry. Hopefully, this will lead to a decreased incidence of device-related complaints, reportable events, and recalls, and it will be a device-based compliant activity versus manufacturer-based actions that might be taken. I want to emphasize in this particular one that when we look at the devices, when we identify problems in these areas, hopefully, it will be across a particular device industry,

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it will not be singled out on a manufacturer unless we see some indication that there is not a pattern of problem, that the GMP problems are specific to that particular manufacturer, but our goal is really to resolve the problem with the device.

[Slide.]

So, what are we using to develop our priority list and how are we going to determine what rises to our highest level of attention?

We have developed what you see and what you have in your hand, a risk-based model. It is a simple model. In this effort, we are talking about risk, and we are considering risk, not specifically that a device is risky, but that we are calling risk in this case determining what that is through a number of data sources, such as the mandatory and voluntary data provided to the Agency through MDR, the deaths, serious injuries, and malfunctions, the recall data, numbers of recalls, units recalled were used. The recall data is important because it has received an additional level of scrutiny in that they are classified in the Agency. Class I's receive a health hazard evaluation through a group of technical, scientific, and medical personnel within the Center, and we are using the classification of the device, as well as any current

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technical or scientific knowledge of the product in our decision of what is on our list of high-risk or high-priority risk devices.

The process we use, however, to prioritize this large number of devices must have a starting point, because it is such a large number of devices, and therefore, we have used in this model primarily the MDR and the recall data.

[Slide.]

While we realize the limitations in some of the data in those databases, such as particularly with the MDR data, the uncertainty in distinguishing between user error and device failure, we do feel that these systems are useful in providing direction for our planning.

We have also tried to compensate for some of these limitations in the data by making some adjustments to it, such as weighting the data, to make the model a little more scientific, if you will.

For example, we use data over five years, and we weighted the data in the more recent years heavier than we rated that in the earlier years. We also gave the recall data a heavier weight, a higher rate, because it does receive that extra level of scrutiny as I described earlier, through the health hazard evaluation committee.

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Our final product was a listing of devices, product codes of devices. It will say on your chart -- that is product codes -- with a priority score from 1 to 100, based on that weighted MDR and recall data.

[Slide.]

Based on that priority model which ranks all of the devices that are listed in our database, and the device classification scheme, the Class I, Class II, and Class III, that the Center uses, we developed how we will approach the work planning for this year, the latter half of this year and next year.

We will use these pieces of information to identify top priority devices for more in-depth evaluation, and we will use this information to determine the parameters for our routine quality systems inspections.

[Slide.]

For that set of devices identified for further study, for further in-depth study, we will begin with those listed, those priority devices that are ranked 90 and above. These devices will undergo further scrutiny by a CDRH team of lab scientists, reviewers, epidemiologists, compliance, consumer safety officers, whatever the makeup of the team is most appropriate to determine which two or three will be further investigated for any given year.

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We don't anticipate being able to accommodate more than two or three, because we are looking at a rather in-depth evaluation of the problems with these devices and we do feel that it -- we do anticipate that it will take quite a lot of resource to do thorough investigation, thorough information gathering on those few. We have looked at, I think are considering as a first candidate, implantable pacemakers.

In the selection of these two or three, the teams will, as I say, evaluate the MDR and recall data. They will incorporate current knowledge of the device, and they will develop what we are calling an assessment tool for generating information about those devices across the entire industry.

[Slide.]

The goal is to get a snapshot of the device's successes and failures, and again I am talking about those for more focused, more in-depth study, to gain knowledge of any new and emerging technologies in this product area, to gain information on actual and potential problems associated with the device usage, and to identify any areas needed for further research, further development, and on monitoring.

This information will be shared with industry, as will potential solutions and a call for strategies for resolving some of the problems found.

Again, I want to emphasize where noncompliance situations are found in the data gathering in the inspection that we feel present a particular risk to the patient. Those will receive the appropriate enforcement followup. However, the goal is not to take an "I got you" approach when we go out on our evaluation of these devices. Rather, it is to identify what the problems are and to seek adequate solution of those.

This latter path may involve voluntary industry corrections or FDA industry task groups, such as what is currently being done with external defibrillators and CDRH staff.

[Slide.]

The other aspect of this planning model uses the priority ranking and the classification for routine surveillance inspections, that reduced area that I showed you in the figure earlier identified as routine GMP conformance.

In addition to offering an alternative to the biennial inspection requirement, one that as you saw we have not met in I think well over five years, this approach

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broadens the coverage on Class III and Class II/Tier 3 devices. It does meet or suggest meeting the biennial requirement for those Class III and Class II/Tier 3, but it also decreases the frequency for those lower priority devices.

[Slide.]

Specifically, this plan calls for 15 percent of the firms in Class I, the Class I device firms with priority scores between 100 and 70 to be inspected in any given year, and it goes up to 50 percent of the firms in the Class III and Class II/Tier 3 categories to be inspected in a year, those with the priority score of 100 to 70.

This priority group with the ranking of 100 to 70, these Class III, Class II/Tier 3, Class II, and Class I devices represent 101 of the 1,957 pro-codes that are in our data system, and the 104 total for these four sets of devices, a pro-code can represent any number of devices in that same category, so while it is only 104 pro-codes, that could be many, many devices and a large number of manufacturers.

This plan for routine surveillance coverage also means a different approach in the scope of the inspection. The current compliance policy guide guides the field to conduct limited or directed inspections on a first visit.

Comprehensive inspections are required and they are asked to conduct those if they found problems and are going back to verify that the problems have been corrected, and the philosophy behind that is we will go in, and I will show you what is involved and limited in some of the elements of the comprehensive inspection in a few slides, but the philosophy is that we go in, look at a couple of key areas, and if we find no problems on those specific devices we have inspected, we make some assumptions that what we have looked at, the quality systems are okay.

If we do find problems, the compliance program directs us to discontinue the inspections if the problems are significant enough to raise flags in our mind that the system is not under control.

[Slide.]

For that group of devices with 100 to 70 ranking, in terms of FTEs, if the comprehensive inspections are conducted as we are suggesting here, for the Class III and the Class II/Tier 3 products, we are looking at 21 FTEs or 32 percent of the resources devoted to these higher classified devices.

As you can see, that total 65 FTEs for simply looking at the devices that have a ranking score of 100 to 70, there are 57.4 FTEs available for this work, so we have

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just in this group alone exceeded what we have available for conducting these inspections, and I raise this because a later question that I put to the committee is should we change and conduct the comprehensive inspection for those Class III and Class II/Tier 3 products with the thinking being we give it a little more scrutiny because of the problem and because of the classification of the device.

If you say yes, we will have to find the resources from another program, but we will be guided by what your advice is.

I don't have any comparative data for '95 or for '96 on the FTEs spent on devices classified in this way, but I do believe that this will mean a significant increase over what is currently being done because Class III and Class II/Tier 3 devices are not receiving priority attention in the work planning scheme.

Also, if the Center puts more emphasis on device evaluation, as Dr. Burlington suggested earlier, applies more attention and resource on the Class III or the PMA devices, certainly the time that the field will need to spend in inspecting those facilities will increase as well.

Added to that will be design control, and that is new with the new quality system reg, and that will also

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increase the amount of time spent during an inspection for both the limited and for the comprehensive inspection.

[Slide.]

This chart shows you what the coverage is for those lower priority, lower ranked devices with a priority score of 69 to 40. Considering the amount of resources required just for those in the 100 to 70 category, we have looked at conducting the limited inspection, making the scope of the inspection for these products limited for all classifications, however, we will increase the frequency for the Class II and the Class II/Tier 3 and the Class III products.

This category of rankings from 69 to 40 represents 239 or about 12 percent of the 1,957 device types in the system, and as I said before, all of these inspections would be limited in scope.

[Slide.]

As I mentioned earlier, I wanted to give you some idea of what is covered in a limited or directed inspection, and by following these particular key areas, investigators are able to focus on what we consider are actual and potential problem areas during the inspection.

The average limited inspection is planned to take approximately 24 hours or three days.

[Slide.]

The comprehensive inspection, according to Compliance Program 7382.830, includes the elements of the limited inspection plus all of the other requirements under the GMP, and I might add that that compliance program that I sent to the committee is being updated to incorporate the new quality systems reg, as well as a number of other changes that have occurred.

Comprehensive inspections take approximately 70 hours to conduct and as I said before, with the design control requirements, with the new design control requirements, CDRH is considering adding about 20 hours to the inspection module to cover design controls. Some of that we will have a better handle on after our year of becoming more familiar with how to inspect these.

[Slide.]

In summary, for the routine surveillance inspections, Class III and Class II/Tier 3 firms would be inspected every two years. Class III and Class II/Tier 3 would receive comprehensive inspectional coverage particularly those with the priority score of 100 to 70, those with the lesser score would receive a limited inspection.

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Class II and Class I firms would be inspected anywhere from every 2 1/2 years to every 6 1/2 years, and firms that manufacture products with pro-codes lower than 40 would get an inspection 7 years to 10 years and out.

On the next three slides I have listed five major issues for discussion by the committee and for which I would like your input on by the end of today.

Four of these deal with the strategy, the planning process and the strategy developed here, and the fifth really does deal with an outcome or a consequence of this process. I am asking for your advice on all, however, I realize that the last issue may yield only some very fruitful discussion given our time limitations, but I will be appreciative of any feedback given on any and all of those issues.

[Slide.]

The first question: Is this a reasonable approach to prioritizing resources for the Center and for ORA's planning efforts?

The second deals with the model itself. Is this a reasonable model in terms of the data sources used and their weighting or the attention that we have placed on the elements of this model? And as I have said, are the recall and the MDR weight appropriate?

[Slide.]

The third question deals with the scope of the inspection. Should all inspections be limited? Should we focus on the key areas on the initial inspection and follow up with a comprehensive inspection as the current program calls for, or given the high priority ranking as determined by problems we have seen with these devices, should we be conducting more in-depth inspections for some of those devices?

Is there any addition benefit to doing that?

Should the frequency and scope of inspections increase for Class II and I? Certainly, we have seen that the resources may not allow us to conduct comprehensive inspections, but should we be in those facilities more frequently given their priority score?

[Slide.]

The final question for discussion is how should CDRH approach some serious problems with GMPs that we might find which may affect the safety and effectiveness of a device when the solution could very well be a recall or other action which might limit the availability of the device.

Although our goal is to find out what the problems are, the reality is when we go in and give increased focus

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to some of these higher classified, high-priority devices, we may find some problems that actually impact on the public health.

We have in the past received quite a bit of feedback that our removal from the market of certain key devices has an adverse effect on public health. I would certainly like to hear discussion from the panel on this particular issue at the end of the day.

Thank you.

DR. ZABRANSKY: Thank you , Lillian.

I am sure that we have -- at least I do -- I have a page full of questions already. Maybe you had better stay up instead of running away. I would like, if you could, to just briefly define for us again Class III and Class II/3, so we really are on the same page as what we are talking about. Just briefly. I am sure we are all familiar with it, but just to make sure that we are all speaking the same language.

MS. GILL: Devices are classified from a highest risk to lowest risk, and if I butcher this, Dr. Burlington, jump in because I am not quite sure I know all about the Tier 3's.

The Class III devices are the devices which are most critical to public health. It is life-supporting, life-sustaining devices.

Class II devices are those devices for which there are standards developed for, less risky supposedly standards for evaluating them, and the Class I devices are really your lowest risk, your lowest classification of devices.

The tiering for Class III -- and Dr. Burlington will answer that --

DR. BURLINGTON: A few years ago we put in place a tier system for premarket review in which we said if we know a lot about a device, we have seen a great many of them before, and we largely rely on standards, we will basically do a labeling review and that will be Tier 1. We look at the device application when it comes in, we take a quick ministerial look at it, we check the labeling for conformance to claims, and we process those very quickly.

Tier 2 products are those products where we have seen similar products before, we know a fair amount about them, and we believe that they need an engineering analysis or typically an engineering analysis, and they are assigned to a lead scientist for review, who may or may not consult somebody in another discipline, but typically, it is handled by one person.

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A Tier 3 review is a product where we need a multidisciplinary team assembled, typically representing a clinician, a statistician, an engineer, a materials science toxicologist, a variety of different disciplines that bring to bear on that specific product and do the multidisciplinary review.

So, they are a combination of the most scientifically and technically complex products and the least understood products. It is important to understand that the law says that if you have never seen a product before, if it's brand-new, then by default, even though it may appear on its face simple, it is a Class III product and the absence of familiarity with it creates a risk which the Agency has to handle for the public by taking a comprehensive look at the product.

DR. ZABRANSKY: Thank you. Let's start with some questions from the panel. I will reserve mine until later because maybe some of those will be picked up.

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DR. CORNWELL: I have a number of questions. Maybe I should get the answers to the questions as I go along, because I think the answers are going to direct my subsequent question.

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The priority score, if I understand it correctly, is based on weighted five-year data, and it also includes weight based on adverse events, as well as recall data.

MS. GILL: Yes. For MDRs, we consider death, serious injuries, and malfunctions, weighted the deaths at 50 percent, and weighted the other two lower. We reconsidered for recalls, both the number of recalls as well as the number of products recalled.

DR. CORNWELL: And so the score is applied to the device rather than the manufacturer?

MS. GILL: Yes, it's a device score.

DR. CORNWELL: So all manufacturers making a single device, regardless of their individual performance history, receives the same score?

MS. GILL: The devices in the system receive the same score.

DR. CORNWELL: Manufacturer A and Manufacturer B both make the same device. The device over a period of five years has had X number of adverse events, and regardless of their individual history, even if Manufacturer A has had no adverse events, they, as a manufacturer of that device, they fall within the same priority score, their device is in the same priority score as Manufacturer B?

MS. GILL: Yes.

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DR. CORNWELL: And then Manufacturer A and B both have the same chance, 50 percent chance of undergoing a comprehensive inspection based on that device's priority score, is that correct?

MS. GILL: Yes.

DR. CORNWELL: What is the effect of this proposal on any -- this will all guide their surveillance inspections. What, if any, effect would there be on inspections that would be driven by a disproportionate pattern of adverse events over a period of time, would there still be inspections guided by that?

MS. GILL: I am not quite sure I understand.

DR. CORNWELL: If you saw a pattern of adverse events occurring with the use of a device an alarming number of times, would it require a new five-year waiting period process for computing a new priority score for any changes in the inspection frequency to take place?

MS. GILL: You are talking about any particular device, because you could look at it in two ways. If it were a device with a problem that came to our attention at any time during the year, we could consider that a for-cause, and this does not drive the for-cause.

There is a separate module for conducting those, and that is the emergency type of inspections that would be covered. Also, this --

DR. CORNWELL: And those for-cause inspections would still continue?

MS. GILL: Yes, they would still continue. Also, the data used to determine where we would go for routine surveillance in any planning cycle would be reevaluated and updated as we begin a new planning cycle, so they would not have to wait if there was some indication that across the board these types of products were causing problems.

DR. CORNWELL: Okay. And then what would be the procedure for determining which firms are inspected? There is a 50 percent likelihood for Class III, manufacturers of Class III or Class II/Tier 3 firms to be inspected, 35 percent for Class II.

Within that chance, is it totally random chance or would an individual manufacturer be more likely to be inspected among those 50 percent that are inspected based on their own history?

MS. GILL: A couple of variables there. If, in a particular district office, where that manufacturer resides or where any number of manufacturers reside, if they had received an inspection the year before, they certainly

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wouldn't be a candidate for inspection this year, and we are talking every two years for those higher class devices.

So, it would be random. It might be whether or not they had received an inspection, it might be number of products they manufacture. It could be a number of factors that a district would use to determine which manufacturers they visited.

DR. CORNWELL: Thank you.

DR. ZABRANSKY: Anybody else?

DR. HUGHES: Allen Hughes, George Mason University, consumer rep.

I guess what has me a little bit concerned is just how much emphasis you put on the medical device reporting program in terms of determining risk and priority, and so I am just wondering if there is going to be any kind of update given to us as to that program, how it is coming along, how confident are you really that you get the appropriate kind of information from this particular program is my general question on that.

MS. GILL: Updates, and I think that is one of the areas that is undergoing some reengineering in the Center, and we are looking at making sure that the system and the reporting that we get is as solid as we can possibly get it.

When we use the data from MDR to evaluate particularly devices for further study and in-depth study, we will be taking a look at those individual reports, not just using the score based on numbers of MDRs in, but we will be looking at those actual reports, making some determinations on how valid the information that we have is and how to follow up on identifying the problems and getting some corrections for those.

Changes in the program, there are some MDR people in the audience who might be able to give you an update on where we are with some changes on that. What types of changes would you like updated?

DR. HUGHES: That is what I am not really sure of. I need a better understanding overall of the medical device reporting, how it has I guess evolved over the years and just how well it is indeed doing these days or how well you perceive it to be doing, and what measures you have for how well you perceive it to be doing.

DR. ZABRANSKY: It is my understanding that was changed, what, just a couple of years ago. The issue is whether or not it has improved since it has been changed.

DR. BURLINGTON: There are two principal elements to adverse event reporting. One of them is the voluntary system, and then there is the required reporting for

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manufacturers, which comes not only from the information manufacturers receive from their distribution chain, but also from required user facility reports, so that when a hospital, nursing home, other user facility has an adverse event reasonable attributable to a device, they have an obligation to report it back to the manufacturer and/or the FDA.

That system produces about 100,000 reports a year or a little over that. The voluntary reporting system from practitioners produces a very small fraction of those. Most of them come through the required reporting.

We know that it does not represent a comprehensive analysis view of what is going on and devices used. I don't have the exact figures with me, but I believe it is about a third of the devices get reports and about two-thirds of the devices out on the market basically never get reports, that the reports tend to be heavily loaded into devices that are used in critical care situations.

Certain types of devices, because they have various other external factors going on, have large numbers of reports, for instance, breast implants continue to receive a very large number of reports and dominate the statistics. So, it is not a perfect sample.

However, when we look and say what are the data we have of experience in the world that tells us which devices are problematic, this is one of the few sources we can look to. There is very, very little in the literature that would help us figure it out.

DR. ZABRANSKY: Linda.

MS. SMITH: Linda Smith, consumer rep.

I certainly share Dr. Hughes' concern, and I did before coming here, I did a certainly nonscientific, but a brief and informal survey of colleagues of mine, high-level nurses who have worked with medical devices daily, and I asked them what do you know about the requirements or the procedures for reporting of malfunctioned medical devices or devices that should cause harm either to patients or to user, whatever, and I have to tell you honestly not one single person that I asked knew anything about it.

It took some research on my part to even find a form that I, as a nurse, might use to report these devices or failures, and so I would just urge the FDA and these statisticians to look upon the data with some question that it is certainly not a population data, it is only sample data, and in that it is very, very important that we have voluntary procedures for reporting malfunctions, those procedures are just unknown really to the vast majority of

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folks who are using these devices with patients, and particularly nurses that I have contacted.

So, I would say that if we are looking only at the MDR data, and we are not just looking at that, but that that be in question, and that there be some way to improve that system somehow.

DR. ZABRANSKY: Related to that is the issue of the actual scoring. This is not in place at this time, is that correct? So, you are devising a new scoring system, as well?

I am addressing the scoring system. We are looking at things that are above 70 or above 90. The scoring system, this is part of the proposal, as well?

MS. GILL: Yes.

DR. ZABRANSKY: So this is not in place. I guess that one of my concerns is how -- and this relates to this, whether using the MDR or the voluntary reporting -- you know, how are you going to use that scoring system, what is the basis for it? We haven't seen -- are you going to say that MDR is going to be 80 percent of the report or of the score? I think we would like to see some details on how that score is going to be developed.

MS. GILL: I thought I had provided it in the package. MDR was 40 percent of the scoring, and the recalls

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was 60 percent of the scoring. It is not on a chart. It is with the package of information.

MS. ALDRICH: How much has the experience base that you have from the way you are doing inspections now been used an input into this whole discussion? For example, there are statements in the package about the current system shows that two-thirds of personnel resources are used in routine surveillance inspections, that these have the lowest impact on public health, but I was just wondering if you had looked at either your statistical data base or anecdotal information from the inspections that you have done over the years to see how well that correlates with the plan that you have now.

You know, have the inspections in the past actually worked out that way, that inspections of low-priority facilities haven't yielded much data, that the system of doing routine surveillance inspections for high hazard devices hasn't been adequate and therefore you need to extend the inspections? I mean has that been looked at?

MS. GILL: Yes, and in the past, as I said, the program focused mainly on visiting those places in the routine surveillance program, in visiting those establishments that hadn't been either inspected by FDA in over two years, or an initial inspection by FDA.

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Some of the lower classified device inspections, we simply have not been able to get to. I think the decisions are being made that for Class I products, we probably won't get to those, but some of the lower tier Class II inspections are being conducted, some of that driven by what is actually the inventory of the particular district.

They are still following the biennial mandate and in some cases, they are looking at what device manufacturers are in their particular area. If they manufacture Class II or Class I products, they are making some attempt to get to those. So, it has not been a risk-based program in the past, it has been driven by what your inventory is, how frequently you have been there, and in some aspects, is this a higher classification device and has received a less frequent FDA inspection.

DR. PIERONI: As a physician, I receive forms to report adverse events voluntarily, but I don't see in the medical literature, and I suspect in the nursing literature and other literature for medical personnel, outcomes, follow-up needs.

How much advertising goes on among paramedicals to tell us the need to report and the fruition, the final outcome of reporting adverse events?

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MS. GILL: That is a program that I believe is some of the effort we have undertaken this year, and I know there is a plan for that office, that particular responsibility falls under the Office of Surveillance and Biometrics, but there is a plan to get more training for users and user facilities on how to fill out MDR forms, the 3500A, and when to report and what kinds of things to report.

We have just finished a large training effort where around the country we have trained a number of people -- "we," that office, has trained a number of people to go out and do just that, let institutions, let user facilities, let users of products know how and when and what to report into that system.

DR. ZABRANSKY: I think you are referring to something a little deeper than that. You can read consumer reports about the number of recalls on cars, and that is something that, as a consumer, I can pick up, but where am I as a user of laboratory devices do I see a summary of all the recalls of various laboratory devices?

DR. PIERONI: Not only that, that is true, and also the individual who reports, does he get a form informing him of the outcome of his reporting?

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DR. BURLINGTON: I know exactly what you are talking about. I file reports, too, and I don't get any response back to the reports I file even though I write on the bottom of them my job is Center Director.

It is a weakness in the system, and it revolves around the confidentiality of the reports and the need to evaluate them, that we use them as a source of input. We need to develop better systems for getting feedback, and even if that feedback is summary, you know, at the least we should be offering you a thanks for having reported, and then there ought to be summary feedback and saying here is the profile of what we have seen.

The recalls are, in fact, available. They are published. They are in both FDA documents, as well as in the trade press, but I suspect that is very sparsely looked at by the medical professionals. It is really something that only the device industry themselves focus on.

DR. PIERONI: Thank you.

MR. BARTH: Good morning, Mr. Chairman, thank you. Good morning, Ms. Gill. I believe that industry is in favor of this approach because it focuses on areas that are higher risk and possibly areas where there are problems. To use a favorite term of Dr. Burlington, this is sort of a triage of the entire situation.

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However, in reviewing the list, the actual list that you provided us, 50 pages of 50 items per page, for a total of 2,500 items. In the first 20, I noticed that products that my company makes are there, and I always thought that we made very low-risk devices, that we have been at it for over 40 years.

For instance, an ECG electrode was in that list. Now, I am not sure why an ECG electrode is there. I am sure there is probably a very good reason, it fit the profile, the criteria of whatever was applied.

I do know that in the past, electrodes had a plug problem where they might have been plugged into an AC outlet, and pardon me just for -- I am expanding on this, I am using it as an example, really, I am not complaining about that one issue.

But that was an example of a one-time problem. You know that was an incompatible -- a plug that was compatible with an AC outlet. A standard was written to correct that problem. A lot of folks wrote MDRs over a period of a couple of years, and so that database probably got inflated, but that problem then was solved. This is an example perhaps of where data in the database indicated, not a systemic or a chronic problem, but a one-time problem, that the people who make those devices -- and it is very

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broad class, you can imagine ECG electrodes, it just glues to your chest -- you know, will then be subject to inspections, and the inspections won't do a thing, because the standard is already in place.

Another example of worrying about the data that is being used -- and, of course, you do have to start somewhere, so it is logical that MDRs and recalls be looked at -- it is my understanding that a large percentage of failures that are reported in the MDR database are user error.

DR. ZABRANSKY: Excuse me. Are what?

MR. BARTH: User error. Now, imagine what that may mean. Perhaps the manuals weren't explicit enough. Perhaps there is such turnover in hospitals, that people aren't routinely trained properly, whatever, you can come up with 10 more reasons, but the point is all the inspecting in the world will do nothing to solve that problem.

You can go in and inspect, inspect, inspect, and you are not going to solve the problem of user training.

Just as an example, another area that could generate errors, inspections would nothing for, is the role of third-party servicers. Not to raise that whole issue again, Dr. Zabransky I think is indicating I should leave that topic, and I will, but again, this is an example of a

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problem perhaps caused by people that were not as well trained as the original manufacturer in servicing techniques.

Just imagine that that may happen. Whether you debate it or not, that is fine, but if that did happen, inspections would do nothing to solve that problem.

MS. GILL: I think you are right on those points, Don, and certainly we do recognize that a high number of reports to the MDR system could be a one-time event, could be an increased enforcement focus on a particular product.

Some of that, we tried to address with the weighting, some of those other things we will attempt to address as we look at the data more carefully to see exactly what the problem may have been and is it resolved.

The issue of the user error gets at one of the things that I have mentioned here and have been saying often. We continue to get these reports, albeit they may be user errors. Our job is addressing the issues that come before us, and if we continue to see this kind of thing, I think that we need to investigate what the actual problem is because some could be a user error problem, and it could be a human factors problem with the product itself, and part of this suggests that we look at what the problem is, get some resolution be it training, be it a design issue that the

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manufacturer might be able to address, and deal with the problem as best we can, and get it out of our system.

I think you are right, and this attempts to get at some of those.

MR. BARTH: I couldn't agree more.

Following up on what Dr. Cornwell raised, I think a very, very important issue, is the inspection history. You know, a device could be a risky device because of its application or classification of the device, but if the manufacturer indeed has a good history of compliance, and taking into account the inspection history, I think would be very important. I think that would lower your need to do comprehensive versus limited, and also the frequency inspection could be dropped, and obviously, i think that both of those should be done, so as to address the issue of the shrinking resources.

MS. GILL: And that, Don, is regardless of the classification of device?

MR. BARTH: That is right, because if someone is making a defibrillator, let's say, okay -- and it just happens that my company does make a defibrillator, so my comments may not be unbiased -- I don't know, I am not a health care professional, I am an engineer, but I would imagine that you don't use a defibrillator unless you think

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someone is about to die, so it is likely that 100 percent of the people would die if you didn't use a defibrillator, but maybe 30 or 40 percent don't die because you do use a defibrillator, however, that still means that maybe 60 percent yet did die.

Does that mean that the device failed because it didn't save the other 60 percent? Taking into account the etiology of the disease state in that case, you know, and you can imagine that from any other devices, would be equally important.

MS. GILL: Yes, but --

MR. BARTH: Because all of them might have had the device applied, but only 30 or 40 percent lived.

MS. GILL: And that is where the review of the actual report, because of death associated, and there are other factors, how was the device performing, we would need to make sure that it was not the device and the performance of the device.

MR. BARTH: I have many other comments, and I am not going to make them all now, because I would be hogging the phone, but I will make one more comment about the MDR reporting system, and that is, that it is comprised of three major parts: the reports of deaths, reports of serious injuries, and malfunctions, and death and serious injuries

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are actualities, someone saw a death, someone saw a serious injury, and then make a connection with that device in some way. It is an alleged report at that time, but it does get followed up, and that's good.

Malfunctions, on the other hand, are failures that should they recur, might have caused a death or serious injury, so someone is making a connection, and sometimes an engineering connection, and perhaps that is a little less direct than the actuality occurring. So, just so that the panel realizes that 60 percent of MDRs are malfunctions, 5 or 10 percent are deaths, and the rest are serious injuries, so you have to realize that the actualities that are being reported are in the minority, and the assessments that make an engineering judgment, perhaps improperly, are in the majority.

Is that contentious? Is that true in your opinion?

MS. GILL: I think it is, I think you are right.

MR. BARTH: I just wanted to make sure that they understand that. Thank you.

MS. THIBEAULT: I would also like to echo obviously what my colleague has been saying, Don Barth, and I might add a little bit of a twist also. In my experience in the industry, looking at recall data, oftentimes if you

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take recall data as a lump, it looks ominous, it looks like it is pretty heavy, however, if you dissect it into its specific causes, many times a lot of the recalls are due to statutory regulation problems, which is there is a statute, it hasn't been met, and therefore the product is being recalled. It could be a labeling issue, it could be any kind of statutory issue. And then the rest are generally some problems, physical problems, with the performance of the device whether it is safety related or effectiveness related.

So, using 60 percent of the recall data as the weight, part of that should be considered in terms of we are really talking about problems with devices that affect either the consumer or the patient itself, and so we need to be concerned that we are using real good hard factual data concerning device problems, real things that, you know, really are a problem.

The other side of the issue is from the manufacturer's standpoint, what are the top issues with respect to directed inspections, what are we finding in terms of the causes of those problems, and will that reduce the number of high priority classifications, in other words, if the types of problems happen to be two or three major concerns, and then there is only a small portion of

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manufacturers who are having those concerns, then, maybe the number would also decrease.

So, I think the diversity or the breaking down of the data may need to be looked at one more time to try to focus in on things that really are problems with products and their use and their potential for damage rather than lumping them all together with some of the other things that may not be in with the focus of what you are trying to do.

DR. ZABRANSKY: I have a question here. If a particular company -- and I am going to use a different company that we talked about before -- Company X has a problem with a specific Product A, but not with Product B, but they are both products are Class III, would that company's products be both subjected to the inspection process?

MS. GILL: No. We would try to kill, I think the field would look at that as one inspection, trying to -- depending upon the processes for manufacturing those two devices -- they may either conduct an inspection for both products while they are there or they may conduct one if they are very similar products manufactured on the same line, and allow that inspection to cover both, but they would not be subjected to two inspections.

DR. ZABRANSKY: But more than that, I am concerned about a particular product that one company may have that has a continual, repetitive problem, as Ms. Thibeault was indicating, and the rest of the industry that manufactures the same thing, which may be only two or three other companies, does not have a problem, because whatever their internal QC is, it is picking up the problems.

Are the other companies that manufacture, that don't have problems, they are going to be subject to the same type of frequency of inspections?

MS. GILL: I think over -- I mean in this pilot, we would consider those kinds of things, but if we are talking about routine surveillance inspections after we have looked at that particular device category and we find the majority of the industry is in compliance and no problems with the product, we would not continue to go there. We would deal with that one manufacturer, and it would certainly, in all likelihood find itself at the bottom of products inspected in subsequent years.

DR. ZABRANSKY: I would like to go back to the overview or the premise for doing this in the first place. It is primarily because you the FDA is not able to meet the statutory requirements of inspections on a biannual basis,

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so you are doing about a quarter of them instead of 50 percent of them.

Is this because of lack of staffing of is it because the number of nonroutine inspections is excessive and therefore is taking away from the routine purposes?

MS. GILL: I think it is a resource question. We certainly have seen a decrease in field investigative resources that would cover the routine inspections, and we have seen, because priorities shift and for-causes increase, there is some increase in other areas, which are taking resources away from the routine inspections. As crises hit, we must address those, so there has been some bleeding away of that resource to address some higher priority areas, but I think in general, the resource has decreased considerably.

DR. ZABRANSKY: If you reduce the number of inspections on less than Class II lowered tiered products and Class I, would you now be in compliance -- and that is the term that comes on us -- would you not be in compliance with the statutory requirements? In other words, you wouldn't be meeting the biannual inspection on the Class I's and the Class I/Tier 1, Tier 2?

MS. GILL: Yes, you are absolute ly correct, but we are not meeting it now. Yes, we would not be.

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DR. HUGHES: I guess a follow-on on that is just simply, you know, should there be some sort of proposal to change that regulation, then, is that an ultimate goal of this or what?

MS. GILL: I think there are some proposals in the works to change that obligation.

DR. ZABRANSKY: Now, this is statutory, so we have got to go to Congress.

MS. GILL: Yes, to Congress to change that, yes.

DR. HUGHES: While I have the mike, I would like to make one point, one bit of confusion that I would like for someone to walk me through with regards to your model, and that is, I have been -- in scouring through this and looking at some of the high-priority items, especially from this additional sheet that you gave, and I have been looking for heart valves here.

In addition, I went through the compliance program manual -- or not that -- but I guess the other, I guess 50-page item that Don mentioned. I finally found it on page 36 with the priority of 1.8, and that just seems -- that seems to imply that heart valve manufacturers are only going to be reviewed once every seven to 10 years or so. Am I right?

MS. GILL: As the model would suggest, unless there have been problems reported with that device or unless

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the Agency receives some information in that indicates we do a for-cause inspection, they will be low on the priority list.

DR. ZABRANSKY: Linda, go ahead.

MS. SMITH: I have several questions. I am Linda Smith.

I noticed, as Dr. Hughes has noticed, that we are talking about being able to evaluate a model, and although I really want to say on record that I think that there is validity in what you are trying to do, and certainly in this era of limited resources there is no such thing as a bottomless pit, and we need to, as you said, to do some triaging and that is appropriate.

My concern is I am looking for why these particular variables were used, what sort of model fitting you have used with your multivariate statistical techniques, what were those statistical techniques.

I am really hungry to see some clear evidence that these variables, you know, factored out in some very important way, and why the cut scores, why did you use the greater than 90 or the weights that you have used.

I am sure you have -- well, I am assuming you have some statistical evidence -- but I would be very, very interested in getting ahold of how those cut scores were

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developed. Although I think that there is validity in looking at risk-based model, we have to make sure that the statistics that are used are going to be valid and that when we look at what is going on from years now that we will have used as much of the data that we have in as good a way as we can.

And then that is my -- truly, my central concern is that right now we don't have good data, and I understand the MDR is what we have, but is there a way to create a central database to streamline reporting, to streamline recording and then also that would allow for better dissemination of the information, develop an instrument.

Now, the instrument that I have are the voluntary reporting form that I found, I found was inadequate, and I don't know if that has been really heavily looked at as how do we develop an instrument that will be valid and reliable in terms of what we want it to do. We want to have good, clean data that we can use as sample data, and I don't think this form is going to do it.

So, those are my questions, and one last real important question is if we are looking at resources, I think there are ways to streamline it, especially for the I and II risk areas, that there might be better ways to routinely inspect or do on-site inspection in a limited way

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or more resourceful, more efficient way using some technology.

We have got a lot of technology we can use, some advance technology perhaps, using things that are available that could provide the on-site inspector with better resources to make those inspections less cumbersome in some way, I don't know. I think if you have already done that, please let me know.

MS. GILL: No, we have not come up with a different inspectional approach that would -- what I think I understand you are saying -- limit the time that is spent there, hit the key areas. We have made an attempt in the old program to do that. We are certainly looking in the Center and in the field at some other ways that we could get the information in a shorter time period to make the inspection more effective, but I don't have any of those that I can share with you today. I won't mention what Don had on the table, a third party, but there are a number of things being considered.

DR. ZABRANSKY: I have a question concerning the efficiency of the inspection process. You cited about 70 hours and perhaps as high as 90 hours per inspection. I just was doing some crazy math here. I looked at 55

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inspectors. Is that what I saw looking at the number of FTEs?

MS. GILL: Fifty-seven FTEs.

DR. ZABRANSKY: And I was multiplying out the number of hours available to an inspector and dividing it by the number of hours that is going to be required for inspection, and I am finding that I cannot find 20 percent of each individual's time.

Now, are these inspectors solely doing routine inspections or are they also doing the special on-demand or problem inspections, as well, and that accounts for the other parts of their time?

MS. GILL: They are doing all types of inspections. They are doing all of the areas you saw listed under the targeted area, the premarket approval inspections, the for-cause, the followup. They are doing routine surveillance. Some of them are doing foreign inspections. They are doing all types of things, and then the report writing that also accompanies that, and then some of that could be a significant amount of travel depending upon where the manufacturer is located and where the inspector's home base is.

DR. ZABRANSKY: When you were saying 70 to 90 hours per inspection, I was thinking that the travel time

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and the submission or the preparation of the report would be included in that.

MS. GILL: Yes.

DR. ZABRANSKY: But it is not necessarily.

MS. GILL: Not necessarily, and also that 70 hours was for the comprehensive inspection. There is less for the limited inspection. As I have indicated, the current program directs investigators to conduct the limited inspection unless they are going back for a followup.

DR. ZABRANSKY: Thank you.

DR. CORNWELL: Along those lines, Mr. Chairman, could I also ask, in the face of diminishing resources, going from Fiscal Years '94 through '96, you at the same time showed -- actually from '95 to '96 -- a 10 percent increase in the numbers of manufacturers that were actually inspected, 1,269 in Fiscal Year '96, which got you up to 53 percent of manufacturers, up from the 48 percent figure I think you had cited previously.

MS. GILL: Yes.

DR. CORNWELL: How was that accomplished, were a smaller percentage of these comprehensive inspections or were they just more efficient in '96, or how did you actually manage to increase the number of manufacturers that were inspected?

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MS. GILL: It could be a number of factors, and certainly the limited inspection, as we have been trying to encourage, and I think the vast majority now have been limited, could be fewer follow-up inspections, which are comprehensive, therefore giving us more time to cover more firms, as well.

DR. ZABRANSKY: Don.

MR. BARTH: I really wasn't going to broach the topic, Ms. Gill, but since you did mention third parties --

MS. GILL: Don, third parties are not on the table for discussion today.

MR. BARTH: That's right, they are really not on the table, but just to continue your statement for the end of this one, other regions have faced shrinking resource problems, as well, in Europe particularly, and what they have now is a robust free market, third-party system, scientific organizations that are very well qualified in medical devices, that perform inspections, and in fact, that is how the inspections are done in the European union, which is I believe up to 18 nations now.

The reason I mention that is that is directly addressing the resource issue at the governmental level, and FDA of course is looking at this, and we are encouraging them to strike mutual recognition agreements, such that at

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the very least, FDA inspectors will not have to travel to foreign lands to do inspections, which to me is the height of absurdity when you have people in those countries already doing inspections.

And, by the way, the criteria that is used by the third-party system that most of us were international shippers engaged in Europe is just about virtually identical to the new quality system regulation GMP, so the focus is just about a 99 percent overlap.

But despite all that, ending that statement, I did actually have a question, and the question I had was, Ms. Gill, you had said that if a problem were found in the directed inspection or limited inspection, let's say, not directed, a limited inspection, that then that might kick off a comprehensive inspection if a problem were found.

MS. GILL: The current program, Don, calls for -- and I have been using limited and directed the same -- but the current program calls for the investigator, if he finds that there are significant problems during that limited inspection, to close out the inspection, cite those.

We then say that, you know, the problems we found aren't indicative of everything that could be going on, it is the manufacturer's responsibility to have a good quality system auditing process in effect, and the comprehensive

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inspection would be upon followup. It would not trigger in the plant a comprehensive inspection at that point.

MR. BARTH: Okay. I was going to suggest that perhaps a limited inspection that uncovered a problem area could then yield to a directed inspection on the problem area rather than a comprehensive inspection, and perhaps some other criteria would kick off because the difference is between three days and two weeks. You know, maybe there is an in-between step that should be taken and considered rather than, you know, something fairly limited to two or three days to two weeks, maybe something five days, you know, could be still more contained and yet address the problem area.

The other thing I wanted to mention, too, is since necessarily, in a risk classification approach to inspecting, some people will be inspected more, because now you are differentiating, it is not across the board.

Perhaps one needs to think about the remedies, because naturally, when you are inspected as manufacturer, you are exposed to substantially more risk yourself as a business. You have a regulator coming in. As a regulatee, of course, you are obligated to comply, and thus you are exposed to more legal and statutory risk by undergoing this

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new criteria that will again expose some people necessarily more than others because of the risk criteria.

Perhaps we ought to be thinking in terms of remedies to be going back to an earlier day when there were two steps of Notice of Adverse Findings leading up to regulatory letter, and what happened as of the Safe Medical Devices Act was that those two steps of Notice of Adverse Findings were dropped, and the warning letter was instituted, which brings you to the maximum remedy, okay, of civil and administrative penalties, and it just seems to me if more people are going to be exposed, then perhaps there ought to be a more stepwise approach to remedies, as well.

MS. GILL: I just want to comment that one of the reasons why some of those changes were made in moving to the warning letter is that in the Agency's view, in some ways put us in a continuous loop of writing and writing, and really not reaching some resolution of issues.

I agree that we can communicate what the problems are, but if we are going to burn a lot of resources in doing some writing and consulting and letter exchanges back and forth, then, I am not sure we are going to have the resources to go in and do some of the audits.

You are talking about going back to what was a system of a lot of explanation of problems.

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MR. BARTH: There was a lot of overhead there for sure.

MS. GILL: Yes.

MR. BARTH: What I am thinking of is just if you got 10 people who are inspected all equally, fine, then, they all have the same criteria. Now you are going to single out three for more inspections, and other seven will get a lot less.

But it seems to me that in return for more inspections for the three, that they should not then be exposed to the maximum step that can then take -- you go from the -- you know the 483 is really just observations, it is not any kind of notification, but then the first remedy is really the warning letter, and there is nothing in between. It is a rather big step.

MS. GILL: Yes, but keep in mind also I think you are talking about the more focused device area that I talked about, those two to three that we would look at. If we do find problems across the board, then, the remedy may not be the warning letter and the enforcement action depending upon what it is we do find. That could be an issue that manufacturers themselves would need to address. It could be a technical conference really to get at what some of the

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problems are, and not necessarily a warning letter to resolve the issue, so we have considered that.

MR. BARTH: Is that a commitment?

MS. SMITH: Don, could I just ask for clarification? You said that you felt that great investigation would yield greater risk. I am not sure I understand, and does that transfer to consumer risk? I didn't catch what you were saying.

MR. BARTH: No, I am sorry, the risk I meant there was the legal risk that one entails whenever one is before a legal -- for instance, you have a lot of taxes, and you send it in, you are fine. Okay. But if you get audited, now you are greater risk. You may be perfectly fine, but you are still at greater risk. Okay?

MS. SMITH: Thank you.

DR. ZABRANSKY: I don't want to cut off the discussion, but we do need to take a break. Let's take 15 minutes and return by 25 of, please.

[Recess.]

DR. ZABRANSKY: A number of questions have come up during the break, a couple from the audience and also from the panel members concerning Attachment C, which some of you folks may have picked up as you came in. It is this

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fantastic list of devices and how this was actually compiled, and what some of the information means.

I do not want to get into specifics because there are just so many here, and this is really why the issue has come up, because I looked at one that was brought to my attention, and I thought it was ludicrous, and then I saw another one that looks very peculiar, but I do not want to go into specifics on how each item was discussed or prepared because we would be here for the next three weeks.

But it is my understanding that Mr. Steve Sykes, from the FDA, would be willing to at least provide some general information on how this chart or groups of charts was compiled.

Steve.

MR. SYKES: My name is Steve Sykes and I am with the Office of Science and Technology in the Center. As I got up this morning and I looked in my closet, and I said, well, I have nothing really important to do today, so this is why I look like I do. If it is any help, I have been in Florida for a week, so I am not really from here.

Let me describe to you off the top of my head and from my best recollection how we pieced this model together. I am speaking to you as the leader or member of a team of people that sought to do this.

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Recall the goal, if you can, for just a moment. We are looking for a numerical approach to be able to sort devices from top to bottom based on risk. A numerical approach requires that we are going to have to have some kind of numerical input. That input can be derived from two primary sources. It comes from the MDR database, and it comes from the recall database.

The MDR database has three kinds of information in it. It has information on deaths, serious injuries, and malfunctions over about the last dozen years. The recall database has two kinds of information in it. It has the number of recalls that have occurred, as well as the number of units that have been recalled.

Those are effectively the sum total of all the numeric data sources that are available for us to use in the construction of this model. The data are imperfect. We accepted that from the beginning. All data sources used in all models of any type are imperfect. You attempt to deal with those limitations as best you can.

We attempted to deal with it in this case by assigning various weights to that data based on its importance in the construction of the overall model, and secondly, and to be lost here, is our confidence in the quality of that data.

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We chose to assign 40 percent of the overall model to the MDR data, based in part on the fact that we have what might be best considered limited confidence in the overall quality of that database.

I did an exercise earlier this year where I simply looked at the overall MDR database for each of the 1,900 and some-odd devices in that database, and looked at their performance over the last five years, and I personally was impressed at the extent to which that database reflected the kind of reality that at least I hold in my head for how devices perform in general.

Yes, there are dramatic exceptions. Some devices appear way at the top of the MDR database, that you would immediately recognize should not be there, and they are there for a variety of reasons - they got a lot of public press, and there are a number of other reasons that you can arrive at.

There are also devices at the bottom that would cause you to turn your head a little bit and say why is this the case, but in aggregate -- in aggregate I was impressed at the extent to which the MDR database represented more or less the kind of reality that we think is going out there.

On the recall side, we have far greater confidence in that data. It is data that we collect ourselves, and it

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is a high degree of accuracy. So, we are stuck with an enormous database with a dozen year history that is perhaps not ideal, a smaller database for which we have a great deal of confidence that is much better. So, we have to put those two together.

The first task here was literally to put them together. This is the first time that you are seeing this list available anywhere, because it is the first time it was ever put together in this way. They are two separate databases that exist in Agency files, and it took some degree of effort to put them together into one.

That, in and of itself, was a substantial undertaking, so what you see here is unprecedented. Next, came the act of putting this together. The first thing we did was to sort, using nothing more aggressive than a spreadsheet or using the spreadsheet as a database, sort for each category.

That is, for example, the death information was simply sorted from top to bottom, so that the devices with the most deaths are on the top, and the number with the least deaths are on the bottom. Those are then percentile-ranked, so that the top device is percentile 100, the bottom device is percentile zero, and everything else is percentile in between.

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That exercise was conducted separately for each of the data sources, so separately for death, serious injuries, malfunctions and so on. Those are the individual columns that you see before you.

As you scan across, I think you can be impressed that on the first few pages, the devices that you see on the first few pages have a high percentile rank in each one of those categories. There are cases where it has a high percentile rank in three or four of the categories, but most are very high in all five. It is hard to deny the rankings for the top devices.

Similarly, on the bottom, you tend to see the same thing in inverse, and there are some surprises. Heart valves, as you pointed out earlier on, is a surprise, and you would not normally think that is the case. Somewhat closer inspection of that particular device might reveal that the number of problems have been relatively low, they have been concentrated in a small number of manufacturers, and they are a PMA device, so that it tends to get high premarket review.

The rankings then for each one of these categories -- I am sorry -- the weighting factors for each one of these categories was decided in a small committee, a committee of which I was a member, and we looked, as I said, at our

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confidence in that data and the extent to which we felt it was appropriate to weight it in that model.

In aggregate, 60 percent of the weighting of the model comes from the MDR data, 40 percent comes from the recall data.

DR. ZABRANSKY: The reverse.

MR. SYKES: Thank you, the other way around, 60 percent comes from the recall data, 40 percent from the MDR data, but I said it authoritatively, didn't I?

[Laughter.]

MR. SYKES: Within the MDR data, you have three kinds: deaths, injuries, and malfunctions. Deaths were top-rated at 50 percent, malfunctions and injuries were less a percentage. I think it is 30 and 20. Thank you.

Within the recall data, the actual number of recalls was at 80 percent, and the number of units recalled is at 20 percent. So, the model is, by and large -- now in composite here -- is, by and large, driven by the recall data, to a lesser extent by MDR deaths, to an even lesser extent by MDR injuries, way down the list at less than 10 percent total would be the number of malfunctions.

If I haven't sufficiently muddied the waters, I can answer whatever questions you have.

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DR. ZABRANSKY: Please do not pick on specific items. We would be here all day, because I have already been marking up a whole sheet, and I hate it, so please, not specific items.

MR. BARTH: Steve, your attire is very appropriate. I vote that we never wear ties again. So, thank you.

MR. SYKES: Thank you.

MR. BARTH: Regarding the recall data, maybe you could just clarify a little bit more, when you say the number of recalls and the number of units.

For instance, if a company had a recall that involved, say, 10 companies, let's say five do a recall of the same device and maybe one company has, you know, 10,000 devices. Is five the number of recalls and the number of units, say, if that is all there were for all five, 10,000?

MR. SYKES: That is correct.

MR. BARTH: So it is the number of individual recalls regardless of the number of units that were recalled?

MR. SYKES: That is my understanding.

MR. BARTH: Thank you.

MR. SYKES: Wes Morganstern can fill us in on some details.

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DR. ZABRANSKY: Would you please use the microphone and give your name, please. Thank you.

MR. MORGANSTERN: Wes Morganstern from the Office of Compliance.

Just to address Anita's concern about the recalls, Class I recalls were not included -- pardon me, the lowest risk, Class I -- Class III recalls were not included in the data at all, so that has eliminated most of those that were strictly violations of the Act, and that was all definitely health related.

DR. ZABRANSKY: You have a question?

DR. PIERONI: My question?

DR. ZABRANSKY: Did you have one?

DR. PIERONI: Well, it was a specific question, and I was just wondering of the utility. I know a lot of work went into it, but I am wondering about its utility. I mean, for example, you mention condoms with a 40 percent failure rate and spermicidal condoms with a zero percent, and I don't think that purports to the latest findings.

You mention -- and I know I am getting into specifics -- but just to give an overall example, you mention the prostate specific antigen for males -- I don't know too many females with prostates -- but for males, as far as the morbidity rates, are considered, quite frankly,

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much higher, because in the first place, it has never been proven to work, it has never been proven to save a life, and in the second place, it leads to a slippery slope where there are numerous operations that are unnecessary. I just have difficulty seeing the utility of some of these rankings.

MR. SYKES: Let me respond to that in two ways. First of all, you are taking -- I think to compare two items -- how do I want to say this -- too close together is probably a mistake. Recall the total accuracy that you have in the numbers to begin with.

I think there is something different between the numbers on page 1 and the numbers on page 50. There is something different between the numbers on page 1 and the numbers on page 20, but there may not be that much difference between the numbers on page 1 and page 2.

We have to draw the line someplace based on our confidence in that data set. We are effectively drawing three bins. Those bins are numbers above 90 -- Lillian, do I have this right -- and bins between 70 and 40?

MS. GILL: Seventy to 100, 69 to 40, and then everything else.

DR. ZABRANSKY: Would you repeat that, please, would you repeat what she said?

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MR. SYKES: Seventy to 100, 40 to 69, and then zero to 39. So, out of this entire 50-page database that you have, all that you are really doing is coming up with three bins, low, medium, and high.

So if you would look at it in that kind of term rather than this device has a priority score of 60, and this one has a priority score of 61, and that doesn't feel right, think of it in the larger context.

DR. ZABRANSKY: If we, as a panel, or any individual, is this list available to all the manufacturers to say, well, I don't think that this right? Again, I am not looking at specific numbers, I am looking at, as you said, the grouping of high, low, or intermediate, and say that I don't even think this product belongs on this list? I am wondering why even some of these things are even listed here even though they are classified as devices, but I wonder why they would even consider giving them a ranking.

So, you know, how can we or how can other users question the validity of this, and to go back Dr. Pieroni's comment, how is it going to be used?

MR. SYKES: Let me ask Lillian to respond to that.

MS. GILL: I guess I would ask you to keep in mind that we have -- all of these are products that are registered with CDRH -- and all of these are products in the

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database. We have an obligation certainly for the II's and III's to visit them.

Why they are on the list, why they shouldn't be on the list is an issue that Device Evaluation is now wrestling with, you know, should they even be in the database I think was one of your questions. That is something that they are wrestling with in terms of whether or not they are required to have some type of FDA premarket or preclearance review.

Whether or not they are to receive an inspection is an issue that Compliance has to wrestle with. Certainly the Class II's that are on there, that look like products that you would say why in the world is it on the list, it is there because they have registered with us, and certainly if it is a low priority, few problems, low classification, as I said, it certainly won't get that level of attention.

DR. ZABRANSKY: Rita.

MS. ALDRICH: I am going to try to reask a question I asked before that I don't think I made clear, but I understand that what this list amounts to is the only way you could come to a numerical ranking, but what I am wondering about is, for example, if you have done 3,600 inspections roughly in the last three years, how are the results of those past inspections being used as input into this kind of ranking.

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In other words, you have a lot of data from those inspections that show you whether or not a manufacturer of a particular product that might be on this list was worth inspecting. What was the efficacy of those inspections, how has that, your history of inspection, been factored into the proposed plan?

MS. GILL: The history of the firm has not been factored into this plan. Where that information would be useful, since the history of the device firm is kept in a particular district office where that firm is located, the district would use that information to determine whether or not -- say, it's a Class III product -- the district would use the result of any knowledge of that firm to determine whether or not they were on the list of firms to be inspected in '97 or whether they might be on the '98 list or the '99 list, depending upon the classification.

So, the information, the past history of the firm, and whether or not we visit that firm would be used by the district office in determining where to go first.

MS. ALDRICH: But I didn't mean individual firms. I mean, you know, what kind of generic information can be pulled out of those 3,600 inspections to assist in ranking the devices and how and in what order of priority they

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should be inspected. I mean that is data on the efficacy of inspections. That is the sort of thing I meant.

MS. GILL: If you are talking about for the focused list of devices, that information would be folded into whether or not we selected any of those to do an in-depth study. If we knew, say, defibrillators, external pacers, or something on the list, had a clean inspectional history, no problems with that device -- well, I will go back to clean inspectional history because it would be on the top priority list based on the MDR and the recall problems that the database showed.

But if there were some indication that we knew enough about the industry, that we knew enough about what we thought were some of the problems, if it is a state-of-the-art problem, and this is as best as we are going to get folks for this particular device, we may say there is little to be gained in looking at this device across the board and the manufacturing process of it.

Does that answer it any better?

MS. ALDRICH: But in any words, it doesn't get factored into the priority ranking?

MS. GILL: No, it isn't factored into the -- the history of any particular device is not factored into the model.

DR. ZABRANSKY: Don.

MR. BARTH: This is not on any particular device. But the nature of the medical device industry is a continuum of engineering. Devices are not blockbuster devices, you know, like a drug company might have literally a market of hundreds of millions of dollars, and they would think of nothing of putting tens of millions into the development production.

Generally, devices, the vast bulk of devices are continually updated and approved over time. Lots of changes take place, so there is a creep over time, frankly, of technology and instructions to users, and you learn and you feed that back, and I think that really is part of the intent of what FDA wants us to do, is to continually update and continually to have this continuum go on.

The problem is, is that as FDA has become over the past few years a bit more stern about calling any change at all whatsoever a recall, and some people feel this way, is that it has put a real -- it has put the manufacturer in kind of a difficult position because you want to upgrade products, you want to have the creep, it's good because the creep actually incorporates all your learning, your experience, your knowledge, okay, into ongoing small improvements, but the problem is, is that more and more

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manufacturers, in responding to the sterner environment, are reporting even these product updates as recalls, Class II recalls. Lillian, you said you must visit II and III, and I think you meant I and II, I being the most serious.

MS. GILL: Yes, I and II.

MR. BARTH: So, I, there is not problem, those are very serious recall, and you need to take immediate action, but again we need to be concerned, I think, about the database that comprises the Class II recalls, and III are just safety notices, because more and more, people are on that edge of product update versus since it is a medical device, anything I do to it potentially will impact safety and health, if you just want to take a very expansive viewpoint, so that gray areas introduce problems, and perhaps that has been reflected in the database, too.

MS. GILL: I guess I would take a little exception to that, Don, in that changes to the device might be handled through a different process in the Center, and it may go through review, and not necessarily the recall information, so you may have a little of that there, but I think that the Class II recalls are -- since they do receive some Agency oversight, aren't necessarily changes or technology creep.

DR. ZABRANSKY: Thank you. I would like to move on. Hopefully, perhaps if individual panel members or

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anybody has any comments on this, I am sure the Office would be willing to receive them. I know that I am going to share this list with some of my colleagues and see what happens.

We would like to move on to comments from those individuals or organizations who have requested specifically to address the panel and the FDA in regard to this proposal, and we do have scheduled somebody from the industry to address these, and first, we would like to hear from the Medical Device Manufacturers Association.

### **Industry Viewpoints**

#### **Medical Device Manufacturers Association**

MS. ONEL: Hi. My name is Suzan Onel. I have copies of our statement up front if you haven't seen it already. I am appearing as counsel for the Medical Device Manufacturers Association, the MDMA. The MDMA is a national trade association representing 130 independent manufacturers of medical devices, diagnostic products, and health care information systems.

The MDMA seeks to improve the quality of patient care by encouraging the development of new medical technology and fostering the availability of beneficial innovative products to the marketplace.

To achieve these goals, the MDMA represents its members' interests with regard to the laws and regulations

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administered by the Food and Drug Administration and the U.S. Congress, and any application of those laws and regulations. Members of the MDMA have had a variety of different experiences with the FDA relating to the inspections of their facilities. These experiences range from positive to negative.

The MDMA is pleased that the FDA is reconsidering its use and application of field resources and that it has invited the Good Manufacturing Practice Advisory Committee to hear testimony and consider various approaches.

Because the document on Prioritization of Device Surveillance: A Risk-Phased Approach to Work Planning is relatively new, there has not been much opportunity for MDMA members to review and comment on this document. Therefore, our comments are preliminary and MDMA members request the opportunity to submit additional comments and to have this topic reviewed more carefully after additional data is produced by the FDA.

Some progress has been made during the last two years through the efforts of the FDA regional offices and the Office of Regulatory Affairs. Through interactive communications, constructive changes have been made which have produced benefits for both the FDA and device manufacturers.

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It is our belief that device manufacturers are conscientious about their efforts to comply with a reasonable interpretation of the Federal Food, Drug, and Cosmetic Act and its implementing regulations, in particular those relating to the GMPs.

The requirement for internal audits functions as a method to increase the likelihood of compliance, and the ever present possibility of product liability complaints represents a powerful inducement for device manufacturers to do the right thing.

The FDA inspection represents the process whereby the public has the opportunity to receive assurance of manufacturer compliance. However, it is the experience of many manufacturers that the FDA inspection is unnecessarily time consuming and results in the presentation of specious observations for which there is no explicit foundation in the Act or any regulation.

it is the desire of the MDMA to support a revision of the FDA inspection process that will result in the efficient use of field resources and maximize the possibility that those who do not comply are quickly detected and subject to appropriate sanctions.

It is MDMA's belief that those who do not comply are rare and that their failures can be readily detected.

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Generally, the violative manufacturer, if inspected by a competent inspector, can be detected during an inspection lasting no more than two days. Likewise, confirmation of compliance can also be made within the same period, irrespective of the size or the device type. The historical performance of the device industry since the implementation of the 1978 GMP regulation provides adequate testimony to support this statement.

The FDA indicates that there are approximately 800 inspectors in the field. Although this number has been reduced from 1,100 four years ago, this should be an adequate number to inspect existing manufacturers in order to provide reasonable assurance of compliance with the applicable provisions of the Act and regulations.

It would be helpful for the GMP committee to know more about how inspection resources have been used over the last four years. For example, what is the average duration of an inspection, how much time is devoted to questionable document review, what percentage of inspections are completed within a two-day period and what percentage exceeds two days, how many inspections involve more than one inspector, what differences exist between the 21 districts, and how are these inspections related to compliance and improvement of compliance.

It would also be helpful to survey those who have been inspected to evaluate whether device manufacturers believe there is a benefit commensurate with the effort invested by the FDA inspector and whether the FDA Form 483 and/or the EIR represent a fair characterization of the manufacturer's performance.

The MDMA appreciates the efforts of the FDA to analyze information generated by experience with recalls and the MDR regulation. However, it questions the usefulness of this information as it applies to the inspection resources. There are a number of reasons for this uncertainty, and a number of these comments have been already discussed.

The initiation of a recall that becomes known to FDA is generally voluntary. Many of the activities that are labeled as a "recall," are not the product of a violation of the law. Many times the reason for the initiation of a field action could not have been foreseen, but instead are the product of unusual variables that develop only through experience in the marketplace.

Although the FDA has evaluated experience with recalls in the context of requirements under the GMP regulation, these efforts have been subjective and not subject to an objective evaluation process.

Likewise, reliance on MDR submissions is suspect for a variety of reasons. For example, the 1984 MDR regulation was subject to increasingly more expansive interpretations by representatives of the FDA. As a result, the annual reported number of events rose from an average of 5,000 to 10,000 to more than 100,000.

Many manufacturers reported events, not because there was a reportable death, serious injury, or malfunction, but because they wanted to avoid conflict with the FDA. The effectiveness and preventative benefit of the MDR regulation from 1984 to 1996 has never been established.

Therefore, the value of using reports from this period is questionable. The current MDR regulation applies a completely different set of criteria for reporting, and it is further questionable as to whether this reported data can usefully be coupled with the data generated by a different regulation.

The MDMA believes it is more useful for the FDA to focus inspectional efforts on devices in Class II and Class III as directed by Congress. Clearly, all Class III device manufacturers should be inspected once every two years. The depth and the length of the inspection should be directly related to the historical performance of the manufacturer. Again, a survey of past FDA performance coupled with the

observation of those Class III manufacturers who have been inspected would be most instructive to an evaluation of how experience of the past can be applied to resource allocation in the future. A similar approach could be applied to selected manufacturers of Class II devices.

MDMA notes that the FDA risk-based approach to resource allocation of inspectional duties only focuses on the determination of which parts of the medical device industry require inspectional priority. MDMA believes that the FDA should also focus on how it inspects.

The FDA should carefully scrutinize present inspection procedures in order to concentrate on ways to make inspections more effective and efficient. Many of the present inspection procedures are unnecessary and time-consuming.

By addressing new approaches to inspectional efficiency, FDA could find that it has more resources to inspect more manufacturers. MDMA hopes that the FDA will meet with members of the industry to assist it in coming up with more effective ways to carry out the inspection process.

In order to further maximize resources, MDMA strongly suggests that the FDA adopt a third party audit system. MDMA is aware that the FDA has been exploring this

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possibility as a means to assess medical device manufacturer compliance with the provisions of the Act and the regulations. By making this possibility a reality, the FDA may find that it can focus more of its attention on inspectional priorities.

In conclusion, it is the expectation of the MDMA that the GMP Advisory Committee will encourage the FDA to develop and release to the public more detailed and objective information about how FDA has applied resources to required GMP inspection of facilities.

The MDMA believes such public review will benefit the FDA, industry, and the public. In this regard, the MDMA offers its resources to assist the FDA and the GMP Advisory Committee.

Thank you for the opportunity to present these views.

DR. ZABRANSKY: Thank you, Ms. Onel.

Are there some questions from the panel? Dr. Pieroni.

DR. PIERONI: When you speak about third party audit, could you be more specific, is that another layer of bureaucracy?

MS. ONEL: It meets with the types of ideas that are already being thrown out, third party reviews, third

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party audits. It would take away from the bureaucracy of FDA, and it would -- level of objective interest.

DR. PIERONI: By whom?

MS. ONEL: By the groups that develop the system. I don't have any specifics here right now, but the MDMA is addressing this, and they are coming up with proposals.

DR. PIERONI: Thank you.

DR. CORNWELL: Your statement mentions the MDMA's belief that those manufacturers who don't, as you put it, comply are rare and their failures can be readily detected.

The system that is being considered here really has, at least from the national standpoint, has nothing in it that will make it more less likely to pick up those who have in the past not complied.

Is it the position of MDMA that the system should have this randomness approach that is being considered here, that is, every manufacturer within a given priority score is equally likely to be inspected as every other manufacturer without regard to their own personal history?

MS. ONEL: No. Actually, it is MDMA's position that historical performance of the manufacturer should be taking a precedent over a more generalized approach, which is what the FDA's current proposal seems to be going towards. Rather than looking at device categories, it

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should look at maybe an overlay of what the manufacturer's past historical performance has been.

DR. ZABRANSKY: I assume you have not had the time or an opportunity to receive comments from your individual members concerning this because although the FDA has been thinking about this for some time, I am aware of that, but you are speaking for the organization, but I am concerned about the companies that you are representing, how do they feel, because we have already heard from Don Barth that he thought that this approach has some validity to it that is being proposed, and I am hearing the opposite from you.

MS. ONEL: What I am suggesting -- and as I said in the beginning, the MDMA hasn't had a full opportunity to review it in detail and discuss it completely with the membership, so I don't have the individual positions of the different companies, which is a direct answer to your question -- but from the preliminary review, the position of the MDMA is that historical performance should be looked at. That may be in conjunction with the what the FDA proposes or it could be instead of.

Clearly, what the MDMA wants to say is what is on the table right now, it doesn't seem to be complete enough.

DR. ZABRANSKY: Don.

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MR. BARTH: Dr. Zabransky, of course, I would never disagree with MDMA. They are our colleagues, and I represent them, as well. What I meant to say was that I do believe that the risk approach, in that it differentiates on some criteria that points to risky devices or bad players, is a good idea. I don't think anyone would disagree with that.

However, I think Suzan also brought up the inspection history issue, which is a valid point. Dr. Cornwell brought that up, and I agree that that is an important component, not just the absolute device itself, and taking into account everything else that we have said today about the uncertainties of the MDR database and recall database, perhaps there is going to be an opportunity for industry to have some kind of a dialogue, so that we can rationalize the criteria even further.

It is a good start, it is the right direction, and we just now need to roll our sleeves up and get to work.

MS. ONEL: Thank you.

DR. ZABRANSKY: I would like to hear from a representative from Medtronic, Inc., Mr. Robert Klepinski.

**Medtronic, Inc.**

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MR. KLEPINSKI: Hello. I am Bob Klepinski from Medtronic, and I am here to disagree with some of the premises and talk about what this is and what it is not.

Firstoff, the whole system, based on the FDA assumptions and the FDA history and the FDA goals, this is a fine system. Lillian Gill knows her job, she knows how to do it, she knows how to go after the goals and accomplish them, and basically assume everything in the FDA history, this does it.

I want to talk about what this is not. This is not reengineering. Once again, not, not, not, not reengineering. This proposal is listed in the Federal Register as one of the different reengineering steps, and this is the furthest thing from reengineering we can possibly have.

What we have here is a refinement, an attempt by Ms. Gill's organization, which you can quibble with some little details, but real good attempt to solidify what they are currently doing, to write down what they are currently doing, and get an organized plan at what they are currently doing, but it is not reengineering.

Now, I come from a PMA-oriented company, heavily into Class III devices, and we are already living under

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this. We have been living in this world for about three years.

I did a random sample of a couple plants from one of our businesses, and I looked at a satellite manufacturing facility that, during the 1980s and early '90s, was inspected about every other year. They were running about an average of 1.2 per year. The last three years we have been running at 2 per year, and that is counting actually 1997 as a full year.

I looked at the main design plant for that, and they are running at about 3.6 inspections per year. We are already in a risk-based world. This has been going on for a long time, and it is de-facto existing. This is merely a formalization of it. This is not yet to say whether it is good or bad, this is merely formalization of what is currently going on.

What I think is happening is that Mr. Zabransky's question was directly on point, is there are factors within the Agency which are using resources and driving decisions that underlie Ms. Gill's assumptions and what she has to work with to accomplish this. The environment in which we are working drives us to this, and you are correct about the use of resources.

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There are many things that have moved Medtronic to this 3.6 per year. First of all, pre-PMA inspections, then post-PMA inspections. Then, there is amount of resources used for clinical site inspections for PMAs. Then, there are nonclinical laboratory site inspections.

If you look at the situation, right now Medtronic is in an unusual position that in five pending PMAs before the Agency from various diverse businesses, if one does a pre-PMA inspection, a post-PMA inspection, and as what I am told -- this number may be wrong -- but I am told the goal is to do about five clinical inspections for a PMA now, and the last time we had two nonclinicals, that would be a total of nine inspections for a PMA. That would mean 45 inspections to cover the current pending PMAs, which is about a full-time equivalent, which means a full-time equivalent just on these PMAs, which is not all of our business, and we are heavily into risk-based system where all of this is driving the system and increasing inspection loads, so it has taken over.

I have had district offices tell me that it is hard, with the current target inspections, to get anywhere to a follow-up inspection. So, I contend the system has existed. We can live with it. I mean we have lived with it for years, but I want you to know that what you are seeing

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today is nothing new as far as the effect on Class III device companies. It is a formalization, it is an attempt to make it more organized and rigorous.

I guess the point is whether that is good or not, and I contend that the FDA right now, today, has an opportunity, and you all know what an opportunity is today. That is when your boss tells you that you have a sticky, horrible job to do, and it is an opportunity for you.

But the FDA truly has an opportunity today. Kim Trautman has worked hard and long trying to get all these systems organized to revise the GMP. It is a dramatic new step to include design into the former GMP. It is an attempt to at least harmonize the words with the ISO standards and with the EN norms for quality systems. So we have a sort of harmonization in the words.

As I always say, the FDA is harmonizing its words, but not in its heart. We still have an inspection system based in the traditional U.S. way, working from complaints up. We have an opportunity at this point to actually talk about quality systems and inspection quality systems, and we have it looks like firmly rejected that.

Now, when we talked about reengineering, one of the things that has to be reengineered is a way that Ms. Smith, I believe it was, talked about the way inspections

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are done. Currently, in the United States -- well, first of all, as a backup -- some of the representatives who are not in industry may not understand that when we talk about these field inspectors, they do not work for Ms. Gill.

They are in an entirely separate organization, and nowhere related with the Device Center. They are in Operations, there is no reporting responsibility, and they live in two different worlds, and there is different standards, and they do things differently, and they are not always in concert, and I contend actively work against each other in that there is different groups within FDA causing more work for Ms. Gill, therefore, she has to go to a strategy like this to limit resources and the two are not always in concert.

We have got people in ODE who want more PMAs instead of PMA supplements, which generates more pre-PMA inspections, which means you have more to handle, and the two are not in concert. So, please do not think there is any organized, unified group looking at the engineering as to how these things fit together, that is, how many to do and when to do them and how to get them done can be two different things.

Inspections work from the bottom up in the United States. You go to the complaint file. Everybody is

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trained, has been trained for years to go to the complaint file. I had a recent inspection where it was supposed to be five days, and I called down the first day and said, "How did it go?" "Well, they are looking through the complaint file."

Called at the end of the second day. "How did it go?" "Well, they are looking through the complaint file."

And you know what this means? They are looking through paper and reading. Three days they read through that paper. You have the impression of going out for an inspection and look at quality systems like in Europe. No. You think they are going to go in the quality manual and go down the procedures? No. Three days they are instructed to look through the complaints to find a "gotcha."

Now, Ms. Gill said they don't do "gotcha" inspections, and everybody in Washington says we don't do "gotcha" inspections. Everybody in the field has been trained to go to the complaint file and look for one, and once they gotcha, then, you concentrate on that. So, three days -- three days, then a day and a half -- one day they looked at some systems, they had a half-day close-up, and they were gone.

Now, those inspections are not teaching quality systems. They are taking a lot of resources away that you

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could spend on it. So, I contend we have this opportunity moment where we should be working on quality.

Dr. Burlington said our goal today was "to have quality product rolling out the door." Now, the system we have lined up today says that we are going to ignore quality systems entirely for about 70 percent of the industry, that there may be people who will have design history requirements, design controls put upon them, will have nobody from the United States Government look at them for seven and a half years.

So, this tells me that the only people in the United States that are actually working on quality systems on the inspection level are the notified body folks from Europe. If there is any improvement in our day-to-day processes, this is because notified bodies are driving it. We are not in the U.S., and the current strategy may be a reactive one for Ms. Gill to survive at this point, but it is not taking the opportunity to go forward and teach quality systems.

Now, I personally do not believe the resources argument. I am a sarcastic person, and I don't believe the resources argument because I have tried to use it, and I was wrong when I tried to use it.

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I am in the corporate law department, and I would bet -- this is a gross generalization, but I guess I like them -- I would bet that every corporate lawyer in every law department in the United States in history has said I don't have enough time to do proactive work, we don't have enough resources, I have to be reactive and put out fires.

I have learned over the years that the only way to get out of that mode is reengineering, is to take a deep breath, stop, just drop everything, look at your systems, and go back and say how can I teach from the beginning, and occasionally, you get a little victory and you work from that, but resources is almost never the cure.

I think in this situation, the compliance may be have been driven into a corner based on all the FDA assumptions where they have to go to this plan, but this is not solving the situation.

So, I guess in brief my message is I can't quibble with the details of the plan based on all the assumptions. What has to be done is to challenge the way we are doing things and try to move to a quality systems world, and this is not only not a step towards it, but it may be a step away from it for those manufacturers who will never see an inspection.

Thanks.

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DR. ZABRANSKY: Questions from the panel?

MR. KLEPINSKI: Any questions?

MS. SMITH: I have a question. You were talking about the complaint file, and I am just curious how valid and reliable are those files, how accurate. Do you have a sense, are they really right now or can they be trusted?

MR. KLEPINSKI: Well, that is a major part of the inspections. I mean training them, how to do quality followup on complaints is a major part of the quality systems regs. In fact, Ms. Trautman had made some changes to the complaint handling to make it quite more detailed this year.

Getting company procedures in place to make sure that all complaints go into a system and get followed through the system and treated is a very important educational part of quality systems training. It always was in the GMP, and it is getting more emphasis now.

The actual complaints, however, are reflective of the quality of the system of how they did them. I contend that we should do what notify bodies do, is start by looking at how you get your complaints into your system, whether you have a net out that gets everything that was salesmen comments, get them all in there, then, have somebody assigned to march through them, analyzing every one, and

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analyzing those systems is something that should happen with every company.

It is a critical part of knowing whether you answer your customer needs and whether you have defects in the products. That is where you get early warnings. So, a company has to have a rigorous system for analyzing them, going through them, looking for one that you can disagree with is not very productive.

Going through and say, aha, I gotcha here, here is a problem, we are going to say that you had no system because I disagree with your conclusion, that is not productive, and a lot of that goes on today.

So going through them serially, looking for a place to second-guess you, I contend is a very inefficient and ineffective way to do that, but the teaching of the system and building into it is critical, extremely important.

DR. ZABRANSKY: Any other comments from the panel?

DR. CORNWELL: Yes, a question. Mr. Klepinski, you speak bluntly and, as a surgeon, that appeals to my style, so let's just get down to the nitty-gritty.

The tenor of your comments seemed to suggest that the inspection process is rigorous, will be more rigorous, and is maybe even onerous as it relates to your particular

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company. The information that was given to us looking generally at the inspection process as subjected to all manufacturers is that roughly only half of manufacturers who were subject to inspection get inspected in a given fiscal year.

You seem to be challenging the concept of redirecting the focus, I mean because basically there is noncompliance, and so this is redirecting the focus of noncompliance. You seem to be challenging the concept of directing the focus of inspections perhaps more frequently to those in the higher risk categories as compared to the lower risk categories. Is that what you are doing?

MR. KLEPINSKI: I may even be more sarcastic than that. I contend this has already happened and that because of the PMA process and because -- well, first of all, I have to agree with Mr. Barth that you would be a fool to think that the FDA cannot take into account the seriousness of certain devices when it makes its decision.

I mean every district has to do that. You are not going to say I am not going to go inspect the pacemaker because I haven't hit the tongue depressor company this year. I mean you have to make some basic calls. You would be foolish not to consider risk in this.

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My statement is that this is merely a formalization of what has gone on before, and that we already have the factorial risk-based system. This is merely a detailed implementation of how to do it. But I am contending that by formalizing it and making it more rigid, it means we are sort of giving up on the important message, and I do absolutely disagree with the idea that direct inspections, targeted inspections, should take over.

I think that the inspection of quality systems on a system basis, something that is hardly done at all today, is one of the most critical things to the United States to quality, and that's you are starting from the ground up and building your systems is how quality products come out the other end.

I don't think the inspectors with the current complaint-based system are getting time to do that. I don't think they are trained to do that. Too often people make a conclusion saying I disagree with your choice on analyzing Complaint A, therefore, you have a bad system. We aren't working through and building quality in.

So, I contend to the extent we are formalizing this, to the extent we are making a more organized system to accomplish this, we are going in the wrong direction, yes, wrong direction for quality.

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DR. ZABRANSKY: Any other comments?

Thank you very much, Mr. Klepinski.

Are there any other individuals from the audience that have not indicated that they wished to address the panel?

Five minutes, and please indicate your name and your organization.

MR. LIEBLER: I am going to try to do this facing the panel. Bernie Liebler from HIMA. I don't have any prepared text, so under five minutes should be no problem.

I really want to ask a question. I don't want to sort of state an opinion, but I was puzzled by the interchange just before the break between Ms. Gill and Mr. Barth.

My understanding is that FDA GMP inspections are to verify compliance with FDA's regulation, which applies to quality systems or good manufacturing practices depending on how you want to call it, and the risk-based approach is based on the apparent risk presented to the public, I guess, based on the statistical model or semi-statistical model that they put together.

But Ms. Gill's comment was that because a company is making an apparently high-risk product, they get an equal opportunity to be inspected regardless of their compliance

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history with the GMP regulation, although the reason for inspection again is to verify compliance with FDA's regulations unless I don't understand, and that is certainly within the realm of possibility.

And then she responded that the response to inspections may not be specific response to the companies, but could be response to the industry, which says that FDA is thinking about using compliance inspections to solve systemic problems which may be intrinsic to the use of the device, to the design of a device, which may be limitations of the current state-of-the-art.

And if they are really talking about that, I flat out don't understand how they think they can do that, either legally, logically, scientifically, or any other way. Compliance inspections are for that purpose, to make sure that manufacturers comply with the regulations.

It would be good if , as the previous speaker said, they were also used as a means of encouraging quality systems and moving us to more quality systems approach, but they are not a means to solve systemic difficulties with particular devices.

I don't know if somebody can clarify that.

DR. ZABRANSKY: Thank you.

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Are there any other representatives here in the audience that wish to speak to this issue? I see a hand up there.

The gentleman from HIMA, would you please make sure that a card goes to the recorders. Thank you.

MS. CHAN: First of all, I would like to applaud Bob Klepinski's talk.

DR. ZABRANSKY: Would you please introduce yourself.

MS. CHAN: Dawn Chan of Digene Corporation.

DR. ZABRANSKY: Thank you.

MS. CHAN: If I wasn't in an FDA forum, I probably would have stood up and clapped loudly, but since you have my business card anyway, I will say it loudly.

I wanted to mention a couple of things with regard to inspections and complaint handling. Digene is involved in the FDA pilot program, and we have a history of three inspections every two years with almost our first inspection several years ago was three citations, and the last two inspections have been zero citations.

We are very happy to be part of this program. However, we understand that we have other industry members out there who are not inspected as regularly as we do, and

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we are in the PMA and the Class III/Tier 2 device, new product, new technologies arena.

I just wanted to make sure that -- we understand that our complaint system and our complaint procedures as part of our quality system is very important, and I wanted to address some of Linda Smith's concerns that if we don't, in our health care systems, have appropriate forms for reporting, our users, our clinicians, and our health care providers can always call up the manufacturer and lodge a complaint, and under our complaint system we are obligated to report these as medical device recalls or reports if they fall into that category. That is one thing we need to remember.

I would also like to be bold enough to make a recommendation to FDA when reviewing complaints as part of the inspection program, and this is part of Bob Klepinski's goal to have FDA look at our quality system, and if FDA doesn't want to change its position from coming in and looking at our complaints because obviously, that is a very quick place to find out how our products are doing in the field. We understand that as the manufacturer, however, perhaps we can look at that instead of we gotcha, instead of taking that attitude, we can look at that as let's see how many complaints you have your products, and let's then look

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at the quality system you are putting into your company to resolve or to track or to fix these problems.

Thank you.

DR. ZABRANSKY: Thank you.

Any response?

MS. GILL: I can't address the type of inspection done now, and I hear the message, I have heard that a couple of times now in other industry meetings that I have had, and I think that is an issue both that CDRH and ORA are going to address.

I didn't want to let this opportunity pass. I have heard comments from two industry representatives at this point, Mr. Klepinski and the last one I heard, and they seem to imply that this process is something that isn't new. They imply that they are receiving a large number of inspections, and that I hope the implication isn't that this is repetitive inspections.

I just want to clarify that FDA could be in any given facility for any number of times based on what the issue is. I think for Mr. Klepinski's company, for Medtronic, if you are heavy in the PMA business, you will get inspections as you roll products out.

The manufacture a lot of products, and it is FDA's responsibility to make sure that these products are being

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manufactured in a way that produces a safe product, but FDA can also be in the plant based on some of what we have talked about today, some of the for-cause reasons, some of the reports that we receive, some of the followup on violative inspections.

So, I didn't want to leave the committee with the impression that we are doing three and four and five repetitive type inspections a year. That could be for any number of reasons that we are in the plant.

DR. ZABRANSKY: Thank you.

At this point, I would like to suspend for lunch. We are scheduled for an hour. Please do not take more than that. Be back here promptly at 20 of.

I would also like to have from the panel members, if you have any early departures that says that we have to adjourn or that you have to leave before 4 o'clock or 4:30, because we should be able to complete our business by that time.

After lunch, we are going to address the five questions that Ms. Gill has put to us. These are on the last two pages of one of the handouts that she gave us, and these are the five issues that we are going to discuss and respond to ourselves.

Let's resume in one hour. Thank you.

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[Whereupon, at 11:40 a.m., the proceedings were recessed, to be resumed at 12:40 p.m.]

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AFTERNOON PROCEEDINGS

[12:40 p.m.]

DR. ZABRANSKY: I would like to resume our discussions. Thank you for being prompt.

As a result of your deliberations over lunch, I wonder if the panel has any other last-minute comments they would like to make before we start addressing the specific questions.

Dr. Pieroni.

DR. PIERONI: I just had a comment. I wonder if we could address GAO's criticisms, minor criticisms after FDA as far as the handling of medical devices. This is in the GAO report of 97-21.

Is it germane to what we are discussing today? I don't want to put you on the spot either.

MS. GILL: You did by asking me a question. I said as soon as I put something in my mouth, someone would ask me something. I think if you are referring to -- you may be referring to the GAO report on MDR data, and I don't know a lot of the specifics about that.

I do know that they had some concerns about the reporting, the followup, how many manufacturers are complying with the requirement to report to the Agency. Other than that, I can't give you a lot of specifics on it,

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and I don't think -- I guess I would say I am not sure that it has a direct bearing on what we are talking about in this model today other than it is a report on the Agency's -- it is an assessment of the Agency's ability to implement the MDR mandate.

DR. PIERONI: Thank you.

DR. ZABRANSKY: One of the speakers toward the very end this morning mentioned that we should be looking at, during the inspection process, at the quality systems or the quality assurance program that is set up within the company.

Again, these themes elves are documents and processes that are in place, and by looking at the specific document or the system, they may not be able to discern what is really wrong, and it is only by the corrective action taken to a specific recall or a complaint that you will find out this is where the changes to the quality systems would be made.

If there is something wrong with the quality system, and it is brought out by a recall or by a failure of a product, then, there would be a change in the quality system. I know of one specific instance -- again, talking about microbiologic media -- if the wrong QC organism is

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used, the inspector may not know that, but it would only be discernible by a failure in a recall.

Any other comments?

#### **Open Committee Discussion**

DR. ZABRANSKY: I would like to start addressing the specific questions. One of the things that we may wind up with looking at these things, hopefully, these questions will be freestanding, but they probably will not be, in other words, an answer or a response yes or no or that we may come to here, you know, might be dependent upon a later question that we may be discussing, and we may have to go back and address some of these, but let's try to keep them as freestanding as possible, and if we can give a short yes or no answer, let's do that, if we have to qualify it, we will do that.

I am sure that the more qualifiers that are added to it would be helpful to FDA in how they are going to set up the program.

First of all, regarding the work plan, is this a reasonable approach -- and we are talking about the plan that we heard this morning as presented by Lillian -- is this a reasonable approach of prioritizing the resources for the Center and ORA in their planning.

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First, let's hear some discussion and then we will start with kind of a -- just to get a consensus vote, and I am not looking for majorities or otherwise, just a consensus. Any general comment?

DR. CORNWELL: I think, in general, the concept of -- you know, that there is pie here that is shrinking -- and the concept of applying diminishing resources in a focused way to products that are at highest risk for potential damage is a sound one, and so then the issue becomes some of the specifics.

Relative to the industry viewpoints that were expressed this morning, I think it was an important clarification that we are talking about routine surveillance, and we make the distinction between PMA type inspection, follow-up inspection, and the routine surveillance.

We are talking about the application of FTEs towards this routine inspection, so I think the concept is sound, but there is a qualifier that I can only pose in the way of a question, which is since we are talking about the prioritization, here we sit in 1997 and we have a priority score based on -- in part -- based on the performance experience during the previous five years, '92 to '96, would the score be calculated each year, so that in 1998, would

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that be based on '93 to '97, or would this be in five-year blocks?

Each year, do we move up a year in terms of the block, and then at each given year, the percentages or the percentage of manufacturers inspected, of those available to be inspected, that 50 percent number would be each year, 50 percent that year of those?

MS. GILL: Yes.

DR. CORNWELL: So, I will mention concerns about details on later questions, but overall, I think it is a sound concept to try to address the issue of diminishing resources and still try to meet the mandate to protect the public interests.

DR. ZABRANSKY: Don.

MR. BARTH: FDA has got a problem, shrinking resources and shrinking budgets, like the rest of government, and so they have to focus on what matters, and I think this plan is reasonable in that regard.

I would just encourage that as much energy go into other initiatives that can yield as much, if not more, in addressing the shrinking resources and shrinking budget, and we have heard this morning several speakers talk about the use of third parties, that is, independent scientific organizations who can supplant the FDA in doing inspections,

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at least that much, and that would then obviously shrink the need for FDA resources in that area.

So, I think the plan is reasonable, but it is probably one prong of a multi-prong plan.

DR. ZABRANSKY: Any other comments? Rita.

MS. ALDRICH: I agree with the comments already made, but I would also say I would not like to see no resources given to the other manufacturers who don't wind up in this on top of the pyramid, and I would recommend that perhaps other approaches be evaluated for maintaining regular contact with those other manufacturers, a mail-in type of survey, for example.

If they have to do periodic audits of their own programs anyway, perhaps a questionnaire modeled on some kind of an audit form that could come in, in an electronic media even, and be scanned to look for outlying data, so that those people don't fall completely outside of your information gathering, because one of the things I haven't gotten a sense of is what FDA feels the purpose of the inspection is, you know, exactly how much is it that you want from this inspection process.

I would assume that some of it is early warning signs and information gathering, and I wouldn't like to see

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a substantial portion of the manufacturers kind of fall out of that information collecting loop.

I also agree that the concept of the third party inspectors, especially for the lower priority ones, might be a very good option to explore.

DR. ZABRANSKY: Anita, we might as well consider this as a vote as we are going around, so if you don't mind.

MS. THIBEAULT: I think again I agree with my panel members that the concept is a good approach. I am not convinced that the model is correct as it is. I think there are some limitations to that model and some other things that need to be considered from the industry perspective would be again the history of the compliance of the companies involved and also another element which wasn't mentioned this morning, which is the consequences of failure of a device, a particular device, in other words, what is its intended use and what are the consequences of its failure.

Some failures, the consequence is minimal to none, others, the consequences are severe, and so that part is not represented in the model. The other point that I would like to bring up is I had some questions after looking at the slides concerning what kinds of things are being looked at from a comprehensive inspection versus a directed inspection

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versus some other issues, and I am not convinced in my mind that there is a strong correlation with the things that we are looking at during inspections and the goal that we are trying to meet. I will go by saying that I agree that we need to, I think, refocus on quality systems and maybe those things that are being looked at are not necessarily the things that would give us the greatest amount of feedback for the limited amount of work that we are allowed to do.

DR. ZABRANSKY: Bob.

DR. PIERONI: I also agree with the general spirit of the plan itself in view of decreased resources. I am concerned also about this concept, which to me is still nebulous, of third party inspectors. I am just a little afraid that we might have the foxes guarding the chicken coop. I would like to know a little more about who would comprise this so-called third party.

DR. ZABRANSKY: Allen, do you have any comment?

DR. HUGHES: Well, I also applaud the FDA for their efforts on this, and I guess to stick very closely with the question, the work plan, is it reasonable, a reasonable approach, I believe wholeheartedly yes, that it is.

Of course, I do have concerns about the actual model itself that is being used, and we can worry about that

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as we get to the other questions, but certainly it is reasonable, a reasonable approach, and I applaud for them for it, and I hope that we can pull together a reasonable model from this.

DR. ZABRANSKY: Linda, it is up to you now.

MS. SMITH: Well, I agree with my colleagues. I certainly agree that it is a reasonable approach. It is a process that if we look at it as process, this is certainly one way to protect the consumer if, in fact, right now we aren't probably protecting because there just isn't a mechanism to do everything that we are mandated to do.

So, I look at it as a protection to the consumer given our limited resources, that it is a process, and I do have concerns about the model.

DR. ZABRANSKY: I, too, also think that this is the direction that FDA, as all of us, have to be going, the concept now of working smart. I really hate that terminology, I would think that we have been trying to do that for years, but that is the new management jargon.

But at the same time, I think that -- either to address it here or to look at maybe one of the other questions -- is that perhaps we have to define what we expect to gain by this, what are the expected outcomes to

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be, and how that will be done or how successful that will be, will be how those outcomes are measured.

In other words, are we going to go back and take a look at the number of recalls that have decreased or are we going to go back and look at the number of failures, the number of gigs that have decreased during the inspection process, or would there be a decreased number of complaints that might show up through the MDR process.

On the other hand, we are probably going to see increased reporting. We have already heard that they have to do a better job of making sure everybody that are the users of these things are aware that there is a proper process for reporting problems.

If the problems go up because of that, is that going to be false information as far as reporting as opposed to what is really going down.

I think there is kind of a mandate there that we would support the FDA in their approach to doing this, despite the fact that as I indicated earlier, perhaps that now there will be less inspections of the Class I's.

Regarding the model itself -- and I think this is probably where there is going to be a fair amount of discussion -- there are two parts to this. Is the model

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reasonable, and are the recall and the MDR weights appropriate?

I don't see how we can separate those two, so we will just have an open discussion on that and see where that goes.

Comments on the model that has been proposed? Who wants to jump in? Don.

MR. BARTH: Thank you, Dr. Zabransky.

I think the model is not reasonable, to begin with. It's a start, and there is a difference. In other words, I think it needs work, it needs refinement. I think a lot has been said about how it could be refined.

We talked about taking into account inspection history rather than just the risk of the device. We talked about eliminating from the database that is used one-time events, and sometimes one-time events can swamp the database for a given year, in the case of breast implants or when there are other devices that may have caused problems. I don't want to pick on anyone, so I won't cite them, but they have happened.

Third-party servicing is perhaps a source of some of that data, I don't know to what degree, but again, inspections would not address that issue, and the issue of user error and taking into account, a Lillian said earlier,

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that some of that may be human factors problems which probably are fair game for inspection especially with the new QSR. But I would say apart from that, the user errors may reflect more training issues in the environment in which the devices are used rather than inspections of factories where the devices are manufactured.

There is also, as Anita mentioned, consequences. Perhaps that is the same as what I was talking about before, understanding how a device is used in its intended use, the etiology of the disease, if you have got a defibrillator, it is used on people who are facing imminent death, are you going to penalize people because some do die, and not take into account that perhaps all of them would have died, so I think consequences is an important issue, as well.

We heard about process of inspection. If people are going to receive more frequent inspections, then, I think some energy should be put into addressing the issue of how fair are the inspections, especially as the speaker from Medtronic said, there were multiple inspections, and they felt that they were getting inspected to death. That is one thing that I got out of that.

Finally, I would just say that industry, this list that came out, I have no doubt that Steve crunched it properly and it's reflective of whatever data that his team

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was given, but I do think that we need to rationalize that database. We need to have probably industry and FDA sitting down, shoulder to shoulder, and going through the database and accounting for what we consider anomalies, and we have pointed out many already.

DR. ZABRANSKY: Thank you. Let's just move right across.

DR. HUGHES: I agree with a number of things that Don has said with regards to the risk model. Again, it is a very good start, very good effort or a beginning point.

I concur with his remarks that it should incorporate more emphasis on the history of the device manufacturer. I want to emphasize that. I have the impression from this model that it may be too specific with regards to device type as opposed to the manufacturer of a particular device, so somehow that needs to be taken into account in the model.

Also, it does bother me just how long certain manufacturers, those of what would be considered by the model as either the least risky or the least historically the least risky or however it is supposed to be phrased, because in doing these inspections, if a manufacturer has some sense that the entity is not going to be reviewed for a long period of time, say, you know, five years or whatever,

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that that removes some bit of incentive, I think, to keep everything above board, that there really needs to be some sort of a catalyst to keep the manufacturer adhering to good manufacturing practices, and I think that there needs to be some way to have this sort of element of surprise, if you will, you know, there.

So, I think that also, you know, we have looked at a number of limited case studies here where intuitively, certain device areas or certain manufacturers that might kind of slip through the crack according to this model, it just doesn't fit right with an intuitive feel, you know, such as heart valves and various other device types.

So, I think that maybe there are some other factors that need to be incorporated into this besides the MDRs and the recalls, something else that, you know, whether or not you can place a numerical score on it or not, I am not really sure. Possibly you can, and if you can't, then there should be some leeway within the model to take into account these more qualitative factors or these more, you know, feel for what the results are and for the FDA to make that kind of adjustment, and not stick too close with whatever numbers are coming out.

So, those are my general comments on it. I guess, yes, as far as the weights of the MDR and the recall, you

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know, who knows if they are appropriate. I don't think anybody can really answer that. I do feel that MDR should be given less weight than, say, the recall data as personally, I don't feel very comfortable with the MDR, with the MDR -- well, with statistics of the MDR. We know that they are not really appropriate, they are not meant to be used for statistical kind of analysis, so given that, certainly less weight I can see being placed on it, but whether it should be 40 percent, whether it should be 30 percent, I think that is just something that the FDA should be given some discretion and leeway as far as playing around with it, as well as taking into account other factors.

DR. PIERONI: The first part is a tight question. The second part I agree wholeheartedly, the 70 percent for example, we have to put some trust in the FDA, and I do put some trust in their determination even though I do have difficulties with their listing of compliance priority, their compliance priority model.

As far as a starting point, I also agree that the risk-based model can determine priorities reasonably -- let me just put quotes around "reasonably." I do agree with the statements made by Don to some extent. I do feel, though, without attempting to be insulting, that there was some hyperbole. For example, when somebody uses a defibrillator

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on one of my patients, and the patient doesn't survive, we are not going to blame the company unless, of course, there is an intrinsic defect in that defibrillator, and I don't know of any instance where companies are getting sued, for example, if there is user problems, and the device itself is fully functioning. So, I do think that is a bit hyperbolic.

MR. BARTH: That's good input to me. Thanks.

DR. PIERONI: I do agree again you have to look at the user, and certainly FDA has to look at how your device is used.

DR. ZABRANSKY: Anita.

MS. THIBEAULT: In listening to my colleagues, some thoughts are starting to coalesce as to what it was when I was reading this material prior to the meeting that bothered me, and I think it is starting to come together a little bit.

The first part of that question, is the risk-based model used to determine priorities reasonable, the first thing that jumps up at me is what priorities, is it the priorities of which products are having the most problems in the industry, or is it which firms should we be inspecting with the limited resources.

So, I am thinking there are actually two questions going on here, and taking maybe just the information

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concerning what is going wrong with products and trying to take that and applying it to which firms should we be inspecting and how often and to what extent, I think there is a disconnect, and I think that is the problem that I am having with this.

If you go to the second part of the question, are the weights used to determine the importance of MDRs versus recalls, well, the one thing that hasn't come up yet is how many MDRs led to recalls. They are connected in some way, in what way, in what percentage, and so are the weights appropriate? Don't know. There is not enough information to make that decision, because I don't know what the relationship is between those two databases, what their interaction is.

So, I think there needs to be some more thought put into whether or not, first of all, this particular model fills all priorities, and aside from that, whether or not the weights are appropriate based on the relationship of the information.

DR. ZABRANSKY: We are going to skip down to Linda.

MS. SMITH: Oh, I am not last this time.

DR. ZABRANSKY: No. I will be last.

MS. SMITH: I appreciate that. Thank you.

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I have three concerns. First of all, I do not agree, as my colleagues have already said, that the model is reasonable, I cannot given the data that I have in front of me from today and from our materials, I cannot agree there.

I think that it is moving in a direction that is possible and plausible, and the process is ongoing, and I would applaud those efforts certainly, absolutely, but right now that model to me would not be reasonable as it is.

First of all, I would say there are variables that haven't been considered in that model, and I would like to look at those variables, and if, in fact, the two variables that were used so predominantly in that model, if those are the variables -- and they are important variables -- then, what happened to the other variables, and do that, I think, in a way that that would be definable.

For example, the variables like the history of the device, the inspection data, the servicing data, the design data, those are data that could be utilized, and I am not sure I have seen any of it in the model.

The other point would be to improve the MDR, and the data -- and we have said this, I think, all day -- is that the data in the MDR are in question. In terms of the person doing the reporting, the voluntary reporting forms, and my own colleagues who have used medical devices, in

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their careers, the dissemination of that information is not there, it is not readily available, and yes, I certainly agree that all of us would intuitively know to contact a firm or a company, but that is difficult and sometimes what it is, it is just not happening.

So, the MDR needs to be improved, create an instrument that is reliable and valid, and doing that by working with focus groups, working with expert reviewers, doing some piloting, in other words, this form and this mechanism needs to be improved, and then I think that we would have better data, at least more reliable data.

The third thing is that we need to improve, I think, the effectiveness and efficiency of inspections. If our inspectors are looking at only one area, that is to me inappropriate if that is the case, but to improve the effectiveness and efficiency of inspections could be done.

For example, as I have mentioned, using technology, I think there are ways to use technology that would assist in that whole process. We have things that are available. Also, the inspectors, is their inter-rater reliability, and I say that really not facetiously, but thinking that if there is a lot of subjectivity in these inspections, I would think that there would be great variances of inter-rater reliability and that that should be

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reduced absolutely as much as possible and that inspections should be as objective as possible in reducing the subjectivity.

Those would be the three things I would say.

DR. CORNWELL: Again, I would like to start my comments with a question. It is my understanding that the device classification is independent of the priority rank. Is that correct?

MS. GILL: Yes.

DR. CORNWELL: How often are devices reclassified, if at all? Are they ever reclassified, does a Class III stay Class III forever?

MS. GILL: Yes. There is an effort to reclassify devices currently.

DR. CORNWELL: Ongoing.

MS. GILL: Yes. It has been two years I think we started it.

DR. ZABRANSKY: Excuse me. Lillian just affirmed that the device reclassification is going on continually, and it is ongoing. My knowledge, I know it does occur, but maybe not as fast as some companies would like to see it occur.

MS. GILL: Absolutely.

DR. ZABRANSKY: The problem is, in some of these things, writing the so-called standard for a device, so that you can change the classification.

DR. CORNWELL: Thank you. That is an important part of my comments because I am unwilling to call the model unreasonable. I think the approach is correct as I have previously said, but I think it falls short, it stops short and that new, additional weighting I think could improve the model for a couple of reasons.

First of all, I would call the panel members' and the audience's attention to the two slides this morning that went through specifically the priority rank, device classification, the specific scores and how that affects the inspection frequency and the scope of the inspection.

It becomes clear that after all of the work that is done to assign a priority score, the only thing it really affects is the scope of the inspection for Class III and Class II/Tier 3. If you are Class I, you are going to get a limited, 15 percent of those firms are going to get a limited inspection in a given year no matter what your score is.

Your Class II, 35 percent of those firms are going to get a limited inspection no matter what your score is on a given year. If you are Class III or Class II/Tier 3, you

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will get 50 percent of those firms will be inspected. The only difference is whether or not the scope of the inspection is limited or comprehensive, so after all this work, the only thing that it affects is the scope of the inspection for Class III and Class II/Tier 3.

Then, what happens with that inspection. In my area, let's say with the explosion of laparoscopic surgery, if there is 10 firms that make plastic laparoscopes, and one of those firms makes a product that 15 times in the last two years has broken off, the plastic has broken off, and we have to make an open incision to retrieve it, the patient has suffered some injury, some morbidity because of that device malfunction, that experience goes into calculating the priority score, and that score is enjoyed or suffered by all manufacturers of that product, and then based on that score, the scope of the inspection will be affected presumably if it is a Class III or a Class II/Tier 3 device, but any given manufacturer has no more or no less chance of being inspected than any other regardless of the fact that all of those manufacturers are affected by the malfunction of a single manufacturer's device.

So, that is what I mean when I say that after all the work that has been done, and the direction of it I think is very well intentioned and is reasonable to me, the

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direction, it falls short if there is not some similar weighting, as I have been implying all morning, if there is not similar weighting that goes on, taking into account the experience of individual manufacturers, and not just the products across the board.

Regarding the second part of the question, are the recall and MDR weights appropriate, my honest answer is I don't know. I mean it is intuitive, and my intuition is certainly no better than that of members of FDA here.

I would agree with earlier comments that the way to evaluate that is to look at the experience with the inspections and see if there is, in fact, some correlation, so that the weights could be reevaluated. Currently, the MDR weight is lower, it is 40 percent versus 60 percent for the recall data, and maybe that should be changed, but I think that would only be with looking retrospectively at the experiences obtained by the original plan.

DR. ZABRANSKY: Thank you. Rita.

MS. ALDRICH: I think the model is reasonable. It seems to be a work in progress. I don't think we are looking at a finished product by any means. It seems to be based on, as far as the recall and the MDR, weights on broad data rather than on data that has been properly evaluated for the appropriateness of its use in this context, which I

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guess is really what all of us have been saying, that it needs refinement and that the idea of the inherent risk or safety, as Anita said, seems to be very important.

Even if there haven't been a lot of recalls or there haven't been a lot of failures, if the impact of the failure is serious injury or death, necessarily, with some devices, that would be the impact, that that ought to count fairly heavily also, and there should be a way to factor that into the rankings.

DR. ZABRANSKY: I was intrigued by this table here, which I guess shows the distribution, I believe is showing the distribution of the massive charts that are in here, and yet we heard this morning that perhaps only we are going to be looking at those that are in the high category and differentiating those.

I would like to have seen a more modal distribution based upon the numbers, in other words, that there would be a natural break in the chart, and the problem is if we are going to add more variables to what we are doing, more than what we have here now, you will never get a modal distribution of categories, and then it is going to be an arbitrary decision as to where that cutoff should be in the number of inspections, is it going to be at the 70 point or the 90 point, and so forth.

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Based upon that, the model is far from being complete. It needs a lot of carving. It is not even ready for sanding yet. The inspector's inspection history of the company has to come into play here, there is no doubt about that.

The other concern I would have, the other part of that is, is in a company that has an excellent history, and now all of a sudden either is taken over by another company and starts making a poorer or lesser quality product, or for some reason has a problem with a new product, the history is not going to be helpful there, it is going to be misleading.

The inspection process must be definitely standardized. I don't know how true it was, one of the commenters from the audience mentioned this morning that the inspectors do not necessarily know what is going on here within the inner belt, they don't take to each other. I don't know if that is true or not, but if it is true, then, the inspection process has to be definitely standardized.

I know for a fact with some of the devices that are associated with microbiology manufacturers or microbiology device manufacturers, that is, companies in the Midwest do not get the same inspection that a company does here in the East Coast, it's a different category of inspectors.

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Most of the industries associated with pharmaceuticals and some of these are on the East Coast, and therefore, the inspectors in the middle of the country do not get the same equal treatment or less than equal treatment.

We definitely somehow have to focus on more variables, but again, by doing that, the caveat is going to be it is going to just muddy the waters as to where a break point is going to be established for the inspectors to decide when they should go in.

If I had to base my decision about whether this model is reasonable based upon this list that is in front of me -- and I am not being critical of the efforts that were put into it -- I would have to say no, it is not reasonable. I think that there is a lot of things on this list that I am very surprised to even seeing near the top, and I see things at the bottom that I feel should be inspected more frequently only based upon my own personal experience.

That is my basic comment, so again, to reiterate, I think we are going in the right direction, but somehow it needs a lot more refinement before it is put into place, and I don't know how much longer that is going to take and how many more discussions and committee meetings or advice that

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is going to be required from the panel for that particular process.

Does anybody else want to comment on the model at this point before we move on to the next question? Dr. Pieroni.

DR. PIERONI: I just want to follow up on the inspections. The difference, maybe we know why there is a discrepancy between inspections. I know, for example, the IRS audits -- we get back to the IRS -- it audits different cities, different rates, and this seems it is better to move to the city with the low rate obviously, but why is this occurring as far as FDA inspections, and what is the magnitude of the divergence?

MS. GILL: Of why there are different inspections in different --

DR. PIERONI: Localities.

DR. ZABRANSKY: Excuse me. This actually even is coming into the next question here, the scope of the inspections, so we are moving into the next question.

MS. GILL: Someone made -- I think it was Mr. Klepinski -- made this morning the comment that I don't run the field, that they are not under me, and part of the answer to that question is how the management of each district office, once they are given priorities, and if they

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are not, how they determine priorities, where they send people and how in depth the inspection is, which should be dictated by the program, but sometimes, you know, people are different, and they not with the inspectors, but your question was why there is such a variability in numbers and types of inspections conducted across the country.

DR. PIERONI: Yes.

MS. GILL: It probably is different as the investigators we have. We try out best to standardize some of that. We had a tremendous training effort a couple of years ago, and we do have another one ongoing for the quality systems reg and the inspections on that, but try as we can, some of that is driven by workload in the districts, competing priorities for device time and device inspection work and drug work, as well, so a couple of different factors drive that.

DR. PIERONI: I can understand why manufacturers could be unhappy with the disparity.

DR. ZABRANSKY: I would like to move on to the next question relating to the inspection process itself and the scope of the inspection. To me, maybe there aren't even enough questions here.

Are inspections -- should all inspections -- I assume this means should all inspections be limited or

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directed inspections, in other words, directed at a specific complaint to recall problem?

Now, if I read that question correctly -- and again, Lillian, I am going to have to ask you to get up -- why don't you maybe just take chair at the end of the table just in case -- by this, is it implying or inferring that there will be no longer routine inspections? I don't think that is what is meant by that question. Could you clarify that question first?

MS. GILL: The question asks about the scope, and should all inspections be limited or directed inspections. I think I had a slide up earlier that showed there would be a shortfall in resources if we carried through with the plan that says Class III and Class II/Tier 3 are comprehensive. So the question goes to should all inspections be limited inspections, and not the comprehensive.

DR. ZABRANSKY: I see. All right.

Comment? We are going to start with Linda, Ms. Smith, at the other end this time. All right?

MS. SMITH: The first red flag with that sentence is the word "all." I hesitate to do anything in the all or nothing mode, and there may even be some relevance to spot inspections or unannounced, I am not sure. I don't know

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about that process enough, but I would say all inspections limited or directed.

I think that given the model that is being presented right now, if that question is based on the model, I would say no, that would be just my sense that all inspections based on that, no, that there is some work that needs to be done first before I could recommend that.

DR. CORNWELL: I would agree. Actually, if you accept the premise of the model, which is that priority rank from 100 to 70 for Class III and Class II/Tier 3 would direct that a comprehensive inspection be done for half of those firms, then, it answers itself, that the inspections that would be limited as far as Class III and Class II/Tier 3 goes, would be only those manufacturers of devices that have a priority rank that is 69 or less.

Again, this model as proposed does not affect the frequency of inspection; it only affects the scope of the inspection as it relates to Class III and Class II/Tier 3. So, I actually would support, with all the caveats made in the preceding question, and if we accept that with its caveats, my answer would be that, no, the limited scope should be as you suggest on your two tables, only for those with the lower priority ranks.

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MS. ALDRICH: Do I understand correctly that limited means like a routine inspection, what is normally considered just a routine inspection?

MS. GILL: Yes, as described in the program, because they are directed to conduct limited inspections first.

MS. ALDRICH: I think in terms of cost effectiveness, it would seem that a limited inspection plus apparently there is going to be a 20-hour add-on anyway for the design control, which takes us up to 44 hours for what looks like a limited inspection, seems to be a generous amount of time for evaluating program.

Then, if serious problems are found, as was said before, the inspection could be terminated and a more comprehensive one scheduled later, but in keeping with the thrust of all of this, which seems to be how to maximize limited resources, I would think that all inspections should be routine, and the 20 hours for design control on top of that may be hard enough to manage.

DR. ZABRANSKY: Ms. Thibeault, can we jump to you?

MS. THIBEAULT: In thinking about this question, the thing that came to mind is this question that says, for instance, should Class III devices be inspected on a comprehensive basis regardless of the past history.

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The problem that I have with that question is that not all Class III devices are what you might think are significant intended use, they are placed in Class III simply because they have never been seen before or they are a new technology, they are not substantially equivalent to anything on the market.

Well, that means that some of those are not going to be as important as others, and so to say that just because you are a Class III device manufacturer, you get a comprehensive inspection no matter what isn't really a fair approach to that element of the industry.

And then to go on the other side and say, well, Class I and Class II's should always have limited surveillance, well, that isn't a correct assumption either because some Class II's, which were pre-amendment, or maybe are significant and may be a new device that is substantially equivalent, but different, might have more serious consequences than not, so neither one is an all situation, neither one fits correctly.

So, I think again there is some limitations to the model, there are some things that need to be considered, and it needs to be considered in a light of being correct and fair to all considerations, not to penalize one side or the other, and to correctly devise a model that has the right

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level of probability of errors, so that both sides are protected as much as possible.

DR. PIERONI: Again we get back to the priority model and its being updated, how often is it updated, and this needs to be updated continuously because a lot of what we are speaking about depends upon the accuracy of this.

As far as the statement made by Anita, as far as Class I and II being problematic, I would like to know the statistics of this, how often do we have major problems, for example, with Class I and II devices. Could you answer that?

MS. GILL: Off the top of my head, I don't have any statistics on the failure rates for devices --

DR. PIERONI: It is very difficult for me to judge how to evaluate something when I really don't have the data, I don't have the statistics, and I do think it is incumbent upon the FDA to produce this data for us to make intelligent decisions, and at this stage, I believe this is low morbidity and low reports of incidents, but I don't know, and it seems that you don't know, so I would hold this abeyance until I get the data.

DR. ZABRANSKY: Dr. Hughes.

DR. HUGHES: I will try to be very, very brief on this. As far as the scope of the inspection, it seems like

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you are talking about having two tiers of inspection and that being limited or comprehensive, and I think it very well just depends on the circumstances of each device type and manufacture as to whether it should be limited or comprehensive regardless of the class, you know, Class I, II, you know, II/Tier 3, Class III. I leave it to the FDA's discretion to determine just how extensive it should be.

DR. ZABRANSKY: Don.

MR. BARTH: It seems to me that all inspections should start as limited, okay, because the resources and the time, two weeks versus three days I think we said earlier, are just so dramatically different.

I can't see a justification for routinely doing comprehensive investigations of a manufacturer who may be fully in control and doing a great job by everybody's estimation. It just seems to me it is a waste, even though the category of the device may be risky, they are in control by all the requirements, so why are they mandated to go through a comprehensive every time. That just doesn't add up to me.

I would prefer limited, and the limited looks at the complaint handling system, medical device reporting, tracking, failure investigations, internal audits, the fact that they are being done, you know, fairly extensive, and

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the meaty things are part of the limited investigation, and the good investigator can sniff out things that are wrong. They are very experienced, they go around, they do this.

If there is a problem, I guess my preference would be -- I am kind of maybe providing unwanted coaching now, so this all can be disregarded entirely by you -- but it seems to me that to leap into -- to say, okay, we are leaving and tomorrow we are coming back, you know, to kill you basically, because we found serious problems, it would seem to me the right thing to do would be to say to the manufacturer, look, we found inconsistencies or things that are a problem, and we are going to stop the limited investigation and now we require an explanation from you on the spot, what is going on here, because they may have that explanation, rather than just to go into a kill mode.

Then, it seems to me if the explanation is not sufficient, then, perhaps you kick into something different, more expansive, perhaps comprehensive at that time.

So, I would prefer limited for everyone to begin with, and I would say even the frequency of the inspections, if you take into account inspection history, should go down. Some algorithm should drive the frequency down if there is a good record of compliance.

So those are my comments.

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DR. ZABRANSKY: Thank you. Your comments earlier there, Don, I agree with. I think that as much as possible, the inspection should be limited. I think that based upon the track record of the company, that they have not had particular repeated problems, or with any of the devices, should retain that inspection rate or inspection frequency on a limited basis.

Should the company have problems overall with a variety of devices, then, I think that they should be stepped up to a high level, comprehensive if you will, and similarly, if a particular device keeps coming back on the complaint schedule, then, the company should be put on the spot, you know, asked what is going on and maybe a comprehensive inspection at that point.

There is no doubt about it that the issue of a Class III device, perhaps being low risk, is a definite possibility, and I have a real problem, I don't know how you draw the line on that, and this is what Anita was referring to. I think there are a lot of devices out there like that for which, in the case again with laboratory devices, those for which there have been no standards written, and they are going to retain that status until a standard is written.

Well, the FDA is not writing the standard. They are asking the third party consultants, so to speak, to

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write those standards, and they are not doing it either. Consequently, some of these devices stay as Class III, and those should not be. Somehow we have to come into an examination of these types of devices, and perhaps lower that frequency of inspection.

Bob, did you have a further comment?

DR. PIERONI: I just had a comment to your comment, if you don't mind. You mentioned some import of the track record of the device manufacturer, and what about the all too frequent changes in merges, changes in management, and changes in the bottom line, and how that can affect the quality control of a particular company.

DR. ZABRANSKY: I don't think it is the FDA's role to get into the economics of the company.

DR. PIERONI: But I mean in looking at any one company, it is not immutable, things are going to change, and that is why it is why it is very difficult to say because one company has a decent track record, we have seen great companies go downhill because of catastrophic events.

DR. ZABRANSKY: Let's look at the second part of that scope. Is there additional benefit to conducting in-depth inspections of Class III and Class II/Tier 3 if, I guess, only a few problems are found initially? So, in other words, if you only find a few problems with the Class

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II/Tier 3 or a Class III device during the limited inspections, should we back off? Is that what we are saying?

We are going to start with Anita this time and go that way.

MS. THIBEAULT: Having done a lot of what is now called assessments myself, usually, if you are going to find problems that are systematic with the quality system, you find them fairly early by looking at some key, what I call signals of the system feedbacks, things that the system provides you information that lets you know how it is working.

So, I really think that if a group of investigators or one investigator was doing an investigation, and wasn't finding any problems by doing a limited inspection, then, it is probably like that they are not going to find some serious problems, what they would find if they continued looking would be some minor problems, some human error problems, but probably not some systemic problems if the limited inspection was done very aggressively in terms of looking for those system problems.

So, I don't think there is any additional benefit, if you don't find it initially, you probably are going to be

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just digging and digging to try to find the little things that, you know, sometimes go wrong that we all have.

DR. PIERONI: There are problems and there are problems, and as I see it, death is a major problem even though we are all going to face that some day. There are also injuries of various types, minor injuries and severe injuries, and then there are complaints which might be meritorious.

So, to me, using the term if a few problems are found initially, again, what type of problems are we talking about, are we talking about people dying, are we talking about one death, are we talking about scores of deaths? So, really, I would like to have that qualified, and if I do find that people are dying and that there are severe physical consequences, I certainly would want a more rigorous inspection.

On the other hand, if I find frivolous complaints, and something that cannot be substantiated, my feeling would be just the opposite.

MS. GILL: If I could just add for a moment to clarify that question, it was really getting at what Anita just addressed, and if looking at those key items in the limited inspection, you don't find problems which we consider would give it a situation, one, or are serious

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enough for the Agency to consider some type of action, is it worthwhile to continue.

If there are problems and there are deaths associated with the device, then, we are on a different track for the inspection of that firm.

DR. ZABRANSKY: Dr. Hughes.

DR. HUGHES: Let's see. Well, certainly we want to preserve FDA's limited resources as best possible, so given that, it doesn't seem that there should be additional inspection if it appears that there aren't any problems, but I think what bothers me about the statement is if few problems are found initially, what concerns me about this is that slacking off on inspections, that is, not being as comprehensive as possible, for that to become, you know, say habitual, you know, because of the history, because a manufacturer is indeed a good performer, I can't quite go all the way there on this particular statement.

I do believe that a good manufacturer of a good product should be rewarded without having -- that it should be rewarded by not having to be ratcheted, but at the same time, I think that there should be some teeth there that the FDA has to go and do a full-fledged, comprehensive every once in a while.

Again, it is this issue of keeping the manufacturer on his toes, her toes, and assuring that good manufacturing practices are indeed adhered to, and just the idea that the FDA could come in and do a much more thorough review at any time, I think is something that needs to be maintained as part of the FDA's repertoire.

MR. BARTH: One thing I wanted to mention while we are on the topic of the scope of inspection is many manufacturers make Class II and III devices, it is pretty routine actually, and one thing you would want to consider seriously is in doing an inspection by whatever frequency and scope we decide or you decide is appropriate, that at least it be confined to the area of the concern, in other words, to subject Class II production lines to repeated inspections just because the same factory in another area happens to make a Class III device, I think would be to me overkill.

That is kind of a point that wasn't made in any other area of discussion. I just want to raise that again. In other words, the focus ought to be on the problem specifically, and not have too wide of a sweeping net.

But getting back to this question in terms of the few problems, I think, Lillian, from your statement, it is very clear -- and I know that you guys know when you have a

serious problem and when there are just simply a few problems -- and if there is a pattern of problems, say, from a previous inspection and also this one, that kicks you into a new ballgame. If they are serious problems resulting in deaths or serious injuries, that kicks you into a new ballgame. Everyone knows that, no secret.

But if there are just a few problems that can be corrected on the spot, or with a little follow-on, I would say it shouldn't kick in and go into a higher gear.

DR. ZABRANSKY: Rita, I am going to pick on you.

MS. ALDRICH: I am just trying to make sure we are all awake. I really see this question as being the same as the previous question, so my answer is the same as to the previous question, that all inspections it would appear should be routine at the outset, and if -- that is what this is saying -- few problems are found initially, you just make it a routine inspection and go away.

So, my answer is the same as it was, that I would conduct all of the inspections as limited, routine inspections, and sort of the inverse of the way this is stated, if you find serious problems, then you progress to an in-depth inspection.

DR. CORNWELL: I think we should very carefully weigh the answer to this question, because if we do that, if

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all initial inspections are limited, then, we can toss the whole model, because that means your Class III or Class II/Tier 3, you get a limited inspection initially, with 50 percent frequency or half of those firms will get it in a given year, if you are Class II, 35 percent; Class I, 15 percent.

So, all the discussion about MDR versus recall data, you don't have to worry about that model because the priority score doesn't matter. No matter what your priority score is, you will get a frequency of inspection based on your class, which may or may not change this year, and the scope of the inspection is going to be limited, and if it only becomes comprehensive based on the history of that firm -- which is what I suggested before should be part of it -- but it is not part of this model as it currently exists, so if we conclude that the initial inspection should only, and always only, be limited unless there is some other compelling reason based on that individual manufacturer's history, then, we go back to this model being kind of tossed out.

Not knowing enough about the scope of comprehensive versus limited examinations, I am a little uncomfortable with that on the face of it, but I can't claim

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expertise enough, because my knowledge of the scope of inspection is based on what is being testified here.

So, I am a little uneasy with throwing out comprehensive exams on a routine surveillance basis.

MS. SMITH: I agree with Dr. Cornwell, and I would like to just say on that point that there would need to be, I think, some mechanism for FDA -- and this has been said before, so I won't belabor the point -- but that there would be some mechanism for FDA to make some spotchecks or random checks, and I would just like to tell a little story, and that is the State of Florida in terms of nursing licensure for registered professional nurses.

Originally, they decided when they moved to mandatory continuing education for all R.N.'s, they decided that they were going to collect data on every R.N. in the state. It got to be so incredibly cumbersome and also impossible that they could track of all these data, that they went to a 20 percent ruling, and that they would every two years spotcheck 20 percent of all folks to see who -- just checking, in terms of just checking for compliance to the rule that says you must maintain continuing education, you have to have a certain number of continuing ed. units, and that has been effective. It is effective for Florida,

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for the State, it is also effective in terms of the idea that that is what they are trying to do.

So, that was just one point I wanted to make, and the other, when I see few problems, and my colleagues have already brought up the point what are problems, define that, I think that there are ways to make levels out of problems and to prioritize problems if you have statistically sound data that can put your cut points, is it low, medium, high or whatever, that can be demonstrated statistically.

I think there is a way to do that when you are looking at what is the level of problem, and when I am looking at level of problem, if I am an inspector, I am looking through this file and I am trying to think, well, what would be a red flag for me as I am looking through a complaint file.

I have every intention this afternoon to write a letter to Double-Tree Hotel and tell them that this morning, at 0500 hours, I was awakened by the alarm clock which was erroneously set, which I didn't really care for. I have every intention to write that complaint letter, however, is that alarm with my alarm clock at the same caliber as a fire lock, no, absolutely not, and it would never, never be treated that way, so I would say yes, there are ways to put levels on those problems.

DR. ZABRANSKY: The problem with this premise, and I think Dr. Cornwell hit at it, is that the issue of having limited inspections for all of these devices particularly could be a problem. If there is a brand-new Class III device, and it was the first time made by this company, first time out there, I think that whole approach of dealing with that device should be almost a comprehensive review.

Then, at that point, should that look okay, then, perhaps the more limited inspections with the little more limited surveys could go into place.

The concept of limited inspections requires that there be certain key, very specific questions, that can really get to the root of a matter very easily. I have inspected laboratories, and that is the only thing I have ever inspected other than my own.

I know what to look for. I have a list that is provided to me by the College of American Pathologists, and that list is a quarter inch thick of questions, but there are certain questions that they provide that I know what to look for, I know what kind of documents to look at if I want to find out what is going on. It is the old adage, you know, if it looks dirty, it is dirty. I think that is what you were referring to before.

So, that sort of a list, if you will, of key questions should somehow be uniform for all inspectors, and all inspectors should somehow -- and I know you may not have full control over this, Lillian -- but somehow, as inspectors, hopefully, they have inspector colleges that they put their two cents in, and are able to upgrade the inspection process, so that all the inspectors are on the same page when they walk into a facility.

MR. BARTH: Thank you, Dr. Zabransky. I would like to just for a moment shed a little light, I hope, for Dr. Cornwell, on my perception of comprehensive and limited.

The limited inspection is very effective for uncovering evidence of problems because it looks at complaint files, it looks at mandated reports, it looks at mandated audit activities, in those cases, not necessarily the results of the activities, but the fact that they have a process, they are consistent.

Comprehensive is very wide-sweeping and really is not looking so much at evidence of problems as it is exhaustively looking at all the processes in the factory.

For instance, we have several thousand devices that are used in measurements around the factory. All of them are required to be calibrated if they are used for inspection and testing activities, and they are, but if an

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inspector wanted to check the calibrations, the inspector could spend two weeks just doing that.

If the inspector wanted to ensure the training records for all the operators who are involved along all the lines and making all the devices, you could take two weeks doing that. If you wanted to look at all of the processes having to do with clean rooms and check that all the sign-offs and the dates were done, and that they are using updated records, you could take two weeks doing that.

Comprehensive examinations are very, very less focused on a problem or the evidence of problems as they are on just the running of the daily operation of a factory. If you don't have problems, if there is no smoke and no fire, then, I guess, you know, then, you could probably stop looking, but if you do the comprehensive thing, basically, you are looking at the foundations exhaustively.

I am not sure, as a routine thing, that is a good use of resources.

DR. CORNWELL: Don, let me just ask you a follow-up question, because I appreciate that clarification. Maybe the term should be focused or directed instead of limited, because it doesn't sound like it is so limited as you describe it.

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But then do we need this model for prioritization? I mean why do we even need it? If you are a Class III, you will get a limited inspection half the time roughly?

MR. BARTH: I would say that it is a starting point. You know, my vote to begin with was that it was not a reasonable model, okay, because just for the difficulties we are having with it right now.

I think you do have to take into account the existing data, and MDR is a regulation, and recall activity is regulated, as well, so data does exist. To the degree that we have qualified it, it has got to be looked at and rationalized, but I would say that it is much more complex than what has been shown here.

DR. CORNWELL: But what you are saying doesn't take into account the data. If we look at the proposal as it is here, and we take into account your proposal that it start as just a limited exam, and it becomes more comprehensive -- just to use the terminology that has been given -- it becomes more comprehensive only based on problems as previously described, then, we really don't need the model, the prioritization model, because the frequency of the examination is driven by your class, not by the priority score, so we really don't need this.

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MR. BARTH: You are absolutely right, this thing could change in a heartbeat if we took everything into account that was said today, you are absolutely right. The model may really almost be a discussion starting point, and not even an actual operational model, which is fine, because we need to start the dialogue somewhere, if we want to solve the basic problem of shrinking resources and shrinking budgets, and yet you still need to protect the public health to have some assurance of that.

MS. SMITH: Could I just ask a clarification? Don, would you just tell me if I understand this correctly, you are saying that even with comprehensive evaluations from inspectors, that it really probably doesn't -- it could miss major collections of data?

MR. BARTH: Oh, easily.

MS. SMITH: You obviously have to self-report. Is this self-reporting mechanism more valid?

MR. BARTH: Now, when you say "self-report," you mean MDRs?

MS. SMITH: Self-report as --

MR. BARTH: Voluntary reporting?

MS. SMITH: In terms of design and compliance, you fill out some self-report forms?

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MR. BARTH: We have a certain amount of reporting that is required. Under the MDR rule, we have to supply a report on death, serious injuries, and malfunctions, the manufacturer does, and that is where the bulk of it comes from.

We also have to report -- recalls under certain circumstances can be voluntary, so you can report them or not. Most of them are reported just because you don't want the FDA to find out about them two years later and second-guess you, and then you have to go out and do them all over again, so usually, they are reported voluntarily, so there is that.

But GMP data generally is held in the factory for inspectors to view at the factory.

MS. SMITH: Do you think that submission of self-report data could be expanded and become more reliable for the FDA, is that an option?

MR. BARTH: Well, actually, I would go the other way. I think my opinion is that the new GMP, the QSR, now opens up areas of design inspection and validation of design, and those records with the experts are in the factories, and because they are available for inspection at the source, where you have the experts able to comment on

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them, that less data should be sent to FDA. That is my opinion.

MS. SMITH: Thank you.

MS. ALDRICH: Just a clarification. We seem to be talking about prioritization system as only determining the scope of the inspection, but one of the slides that was put up this morning was that it is an alternative approach to the biennial inspection, and changes the -- it is a new tiered approach to routine surveillance. Maybe we are overlooking that, that is one of the big changes, and that broadening the inspection coverage was only one out of the four points.

DR. CORNWELL: We will let Ms. Gill answer that, but I mean the information I heard is that the compliance with the directive towards frequency of examination is not there because of lack of resources. Roughly, only half of manufacturers that are supposed to be inspected are being inspected, and that the premise here is that given these limited resources, maybe that inspection could be directed at areas that hopefully will more beneficially yield whatever problems there are.

So, what we are talking about is directing these resources towards places that are problems, so it is an

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alternative to the theoretic that is not occurring right now.

DR. ZABRANSKY: Don, I want to come back to something you just said. You said that with the new QSR type of inspections, that a lot of the data is on hand, so we don't have to send it to the FDA, and it is therefore available for inspection when they show up.

Well, if we are going to cut back on the inspections, how is the FDA going to find out about it? I mean we have got a dichotomy here.

MR. BARTH: Because a focused inspection or a limited inspection, whatever you want to call it, will look at the evidence of problems. They will look in those mandates repositories, complaint files, MDR files, recalls, which are the evidence of problems occurring in the field under actual operation, and that will then give FDA a pointer as to where they want to look at that time.

In the absence of problems, you are absolutely right. I would say don't look. If no smoke is coming, there is no fire there, so don't look. Okay. But where there are problems, and where there is evidence or a pattern of not complying more than a problem, then, I would say that an investigator will find that and be to follow up.

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DR. ZABRANSKY: Any other comments on this particular issue?

MR. BARTH: One final comment. I know I am ringing an old, old bell here, and it has been heard again time and time again during this meeting, but for those of us that are international shippers -- and many of the large companies are who probably account for a lot of the devices -- in order to ship to the European environment, we must meet the inspection requirements, and they do fairly rigorous, comprehensive inspections in addition, and so it is not as if it is just an FDA failsafe, you know, there are other nations, there are other systems, there are other people looking, as well.

That doesn't let FDA off the hook at all, you have got your mandated responsibility, but the movement towards quality systems, as described by the speaker from Medtronic this morning, is really in place and being used as a regulatory system in Europe today.

DR. ZABRANSKY: Let's take a break for 15 minutes. We have two more issues to discuss. The last one is much more philosophical. Let's resume at 20 after, please.

[Recess.]

DR. ZABRANSKY: We would like to move on to the next issue, which has to do with the frequency and scope for

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Class II and Class I devices, and Ms. Gill would like to read or give a clarification of the question.

MS. GILL: This question primarily asks the question do you agree that we would be providing adequate coverage for Class II and Class I devices, and it says if the infrequency remains unchanged, in other words, if we don't go any more often than what you see indicated here, should we do a more comprehensive look at the entire process. And that's it. We won't be in there as often, and should we do a more thorough look at what is going on in the firm.

MS. ALDRICH: I guess since we have already been asked this question a couple of times in terms of should all inspections be limited, which I guess is sort of the same question again, but in a different context, you can take various pathways to save resources or maximize your use of resources, and I have been saying to members here that we faced this problem in our own program in New York, and we have come to a different decision.

Our decision was to abbreviate the inspections, exempt some firms from inspections if they had an excellent inspection history, but to get there on a regular basis, and not to change the interval, the frequency of inspection.

I can see that FDA is going in a different direction, looking at a change in the frequency. I think either way is acceptable, but I don't think that they can manage to get the benefit that they want if they start to increase the length of the inspections.

So, it seems to me that all of the inspections should remain limited or I would prefer the word "routine," unless there are indications in the inspection that there are severe problems and that those need to be addressed by a comprehensive inspection.

DR. CORNWELL: I frankly don't think that you have the resources to increase the frequency or, for that matter, the scope of your inspection for Class I and Class II devices. It looks like the scope of a comprehensive or the time it takes for a comprehensive exam is roughly three times what it takes for a limited exam, so I would say probably not, but then it raises the stakes for more scrutiny as to what the class of a product is.

By way of example, something we were just talking about, in America in the '50s, you could make the argument that a condom might be a Class I or a Class II, but in America in the '90s, with HIV and other sexually transmitted disease, and babies having babies is probably our biggest social problem, you can make the case that a condom should

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be a Class III item, so that the classification, if you don't increase the frequency or the scope of the inspection, then, the accurate classification becomes critical.

MS. SMITH: I have a real concern with the word "exempt" just because I don't think that should ever happen. I do think that there must be a way to look at regulation as being the minimum to maintain compliance, and that is our goal, is just to make sure that the public or the consumer is going to be protected without overburdening any industry and certainly without working against creativity and working against things that will ultimately benefit all of us in the future.

So, that is the dilemma I think the FDA is in, and certainly the dilemma that I am in, but I do have a problem with the word "exempt" there. There could be a way, as I mentioned before, some mechanism to assure the compliance.

I would, though, look at something that has been troubling me for some weeks, and that is that if we change frequency -- "we" meaning FDA -- if we change somehow the frequency or scope of inspection, looking at it across the board, whatever way we are doing that, if we change it from what it used to be, in other words, less than something that formerly existed, what sort of incredible liability is the FDA going to be facing.

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I am thinking of Value Jet and I am thinking of the FAA, and the work now that is being done against the FAA because of their changes or their practices, and I am not sure I know all of those details, I do know that they are carrying a tremendous burden because of the change, and I wonder if we could please just keep that liability issue in mind as we look at all of this.

DR. ZABRANSKY: Don.

MR. BARTH: I think what you have got shown there is fine for Class I and Class II, because as Dr. Cornwell points out, regardless of the priority rank, their frequency and scope is the same.

I wouldn't be too concerned either about like in the Class I, it looks like it is working out to be about once every six years or even less than that, because many, many Class I devices are accessories or they are used in conjunction with other Class II or III devices, and if there are problems with them, they emerge in that setting usually, not as a stand-alone device by themselves, and as a classified device, Class I is subject just to general controls, it has been deemed to be low risk.

So, it seems to me that you hit the money on that one.

DR. HUGHES: I think as I have stated before, I am concerned about the industry getting into a mode of complacency in terms of how inspections come about. So, in looking at this particular question, this issue of the frequency, I am really not that comfortable with the Class II's in particular, and Class I's somewhat, with the limited frequency on the order of, say, 7 to 10 years or whatever, because I think that is what you said for those that come out low on the priority scale, it would be on the order of 7 to 10 years between inspections, something like that.

I think from a general public perspective, as well as from an industry perspective, you know, the manufacturer should be prepared for more frequent inspections than that even for the simplest of devices, that these simple devices, I tend to think a number of them would have some sort of mass distribution, and if there is some problem, it has the potential to affect a large, large number of people, and this can occur in unforeseen ways.

So, as far as frequency of inspection, I would feel more comfortable with more frequency. Exactly how you are going to get it under the circumstances, I don't know, but I just wanted to put plug in for more frequent inspections, and I think we have covered fairly adequately about the scope of inspections.

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DR. PIERONI: Consider ing the limited resources of the FDA, I go along with the proposed plan, but I would emphasize that we are speaking about Class II, and Class II includes the use, until we decided not to use, defibrillators and apnea monitors. They are not as important as an alarm clock, for example, but the point is these are obviously major items.

So, it is going to depend on the type of complaints that are received by the FDA, the severity of the complaints. Again, looking at the resources themselves, I would go along with the proposed plan.

MS. THIBEAULT: I also would go along with the proposed plan especially since if we believe in what we said just before break, that is, that the model of a limited inspection would find problems with a quality system if they were there, if those inspections were performed in a standardized way, and with vigorous application, then, there is no reason to increase the coverage because if we believe in that model, then, that model should work, and of course, that is based on the assumption that the quality and the consistent approach of the inspections would be there. I mean that is the assumption on which we build, saying, yes, this would work fine.

DR. ZABRANSKY: I certainly would not want to see the frequency decrease any further than what is the plan, which might occur as further cutbacks occur. Therefore, I think it is going to be very critical that certain key items be standardized for the inspection process, and again, to reiterate or to agree completely with what Anita has said concerning that, that these be rigorous and perhaps even a more limited inspection for these items if necessary, but they be carefully defined, because again, if you know what to look for in a specific plan, during a specific manufacturing process, you can identify the problems.

Any other comments?

Well, let's look at the last question. How should the Center approach serious problems with good manufacturing practices which may affect the safety and effectiveness of a device when the solution could be a recall or other action which might limit the availability of the device?

Do you want to explain that any further? This is much more philosophical than the others, if the other ones haven't been philosophical already.

MS. GILL: To me, it is a simple question except when I am faced with it, it is not quite so simple.

Some of the thinking behind this question is what we saw happening in Compliance sometime ago, some years ago,

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when we used an approach that looked at the MDR data, looked at some risk factors plus looked at the history of the manufacturer and found that certain key devices -- which I won't mention, Don -- defibrillators -- certain key devices, there were problems with them, issues that the Agency had with them, and the solution of that issue was the cessation of availability in some cases.

We were taken to task about that issue. We have tried different things including looking at the availability of products before we institute certain kinds of enforcement actions, but at times the problem is so critical that we are faced with a real tough decision, and that is, how do you make sure the problem that is available to the user is a good product and how do you reconcile the fact that if you take the only product or a manufacturer who has a substantial portion of the market away, you don't even have that product available regardless of how good or bad it is.

I mean these are the two things we are trying to balance, and I would just like to hear some discussion about that, as we go through this process, if we do find some very serious problems with some of the Class III devices, and it requires some decision that suggests removal, how should we approach that.

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MS. SMITH: I am thinking back several years ago. I had a chance to work in the OR in Moscow, downtown Moscow, working side by side with a surgeon.

DR. ZABRANSKY: Moscow, New York?

MS. SMITH: Moscow, Russia.

DR. ZABRANSKY: All right, because there is a Moscow, New York.

MS. SMITH: There certainly is. Thank you for making me clarify that. No, this is downtown Moscow in Russia, and that was an experience to be sure, but I recall the intravenous infusion for this young lad, which was green actually, the fluid was green, and as it was infusing into him, he had massive, massive septicemia. They had no antibiotics to treat it. The young man died.

When I am looking at a serious problem, such as that, I see that absolutely, truly, no fluid would have been better than that fluid for this young man, and so I guess I would use that when I am saying that serious problems must be dealt with quickly, very quickly, promptly, efficiently, and fairly, and please, with the consumer in mind.

I think that can be done fairly to the industry, as well, to get it off the market, to make the changes, and get it back on the market as quickly as possible, and the whole thing is efficiency.

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DR. CORNWELL: I will save my most opinionated answer for last, which is everything else we have done before this is a waste of time in determining how frequent an inspection, how extensive the scope should be, if after all of that, after all that effort, after all risk analysis is applied, we get to the teeth of the matter, which is identifying problems. If you identify problems and you leave them on the market, don't act on it, then, all previous efforts are a waste of time.

So, I think if serious problems are identified that affect public safety, then, they should be removed, quite simply.

MS. ALDRICH: It seems like situation where FDA has to make an expert judgment on the greater of the two risks, you know, is the risk that the device represents in the condition in which it is available, a more serious risk than not having the device available, and that has to be extremely situation-specific, and it would have to depend on the specific risks that the device represents versus the nonavailability of the device, and I don't think that anybody could give generic recommendations on that.

I mean I can imagine a whole host of variables.

DR. ZABRANSKY: I think the big issue here is the definition of the word "serious," how serious is serious.

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Again, for the more senior people in the audience, you might remember the I.V. problems that we had back in the late sixties and the early seventies, where a large number of people died from one company's I.V. product, and four years later we had the same thing again occur with another company's product from a different type of approach, and both situations were faults either with manufacturing and/or design.

The second one only involved about eight deaths. The first one I think involved about 80, 80 deaths nationwide. You learn from these things, and the ability to act on and recognize what a serious problem is, so I do feel that the FDA must retain its situation to be able to initiate and force a recall, and the users, the rest of us out there, have to be able to use them and the other public health facilities in the case with the I.V. fluids, it involved the Centers for Disease Control, and they must be given the same leeway to act on these things.

The devices must be recalled immediately when something is identified as serious, and I don't know, you know, who is going to define that seriousness. Are you going to define it by number of deaths or just by the morbidity rate? I don't know, but it is an issue that is going to continue to occur as we develop new and more and

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different types of invasive devices and diagnostic techniques, and so forth.

MS. THIBEAULT: That is a really difficult question you have asked us here. There is all kinds of things obviously that could be the problem. Let's say that it is a problem with the design of the device, it has an inherent design problem which affects safety and effectiveness.

At that point, there is nothing that can be done, and if the patient is at risk or any patient is at risk, I guess I go back to one of the colleagues that says you have to balance what the benefit versus the risk is, and, of course, you always have to be conservative on the patient's side, and frequently it is not a design problem, it's a manufacturing error, something going wrong in the production or in the control of production.

What I have seen in my experience is that some of these items can be quickly repaired, fixed, a fix can be put in relatively quickly. The manufacturer understands how to do that. Sometimes it behooves us to kind of work in concert with each other.

I would say with all due respect to Lillian and the Agency, that sometimes we get in each other's way when we are trying to accomplish the same goal, and sometimes I

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have seen where manufacturers -- and I am going to say, what, the majority of the manufacturers are out there trying to do their best, trying to make the patient safe, trying to help treat the patient with whatever problems that they are having, and they want to fix whatever it is, and they want to fix it quickly.

Unfortunately, sometimes there are regulatory barriers to doing that quickly, and so I guess I would be advocating some sort of maybe rethinking of maybe pursuing other ways of working together in concert when that kind of situation occurs, so that both goals are met without stumbling over each other's kind of feet as we waltz through the process of fixing it.

Manufacturers do it all the time in-house. They do what is called reprocessing, they do rework, they do repairs based on the fact that their system found the problem before it was distributed, and sometimes when that didn't occur, and the problem did get distributed, they still know how to do that quickly and efficiently.

So, I would say that it warrants some kind of mutual looking at the issue in a way that says, okay, what are available, what are our actions, and how can we support each other instead of tripping over each other as we are getting through the process.

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DR. PIERONI: I think a quick answer would be to couple the severity of the disease with the efficacy of the device. I will give an analogy with a nondevice, with HIV, with AIDS. Here, we have a disease that was uniformly fatal, and now FDA was pushed a little, but they did expedite a cocktail that is saving lives, and I have patients alive today who would have been dead just a few years ago.

We know these drugs have toxicities, there is nontoxic drug, so you really have to look at the severity of the disease, and you have to look at how effective the medication/device is, in this instance, it would be a device.

If you look at something, such as a Swan-Ganz pacemaker, which is not listed here, there is a lot of controversy in the literature going on right now with people actually dying more because of the Swan-Ganz than are living.

You look at something else like the implantable pacemaker, we know it is saving lives if it is functioning appropriately. So, again, it is fine balance, as has been mentioned, but again if you have got a severe disease, you have no other alternatives, and you have got an effective

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device, by all means use it unless you find that there are areas of great concern about the safety of the patient.

DR. HUGHES: I think for the FDA not to take the appropriate action under the circumstances that seem to be outlined here, would be setting a very dangerous kind of a precedent for other manufacturers.

If you see that a particular device is not meeting the requirements of the good manufacturing practices, naturally, you use as much diplomacy as possible, I guess, under the circumstances of it being a somewhat, let's say, rare device, because limiting its availability would have some adverse impact on patients, but you can't shirk your duties as a regulator if indeed there are problems with a device and if a manufacturer happens to be unwilling to follow along with the suggested remedies.

Also, I would like to make mention that it seems to me that most, virtually all medical devices have some sort of -- there is some sort of competitive nature to it or a competing product, so it seems to me that even limiting the availability of one particular device, that doesn't mean that it not going to be totally unavailable, maybe some other type of device that may not be quite as effective, for example, maybe having to substitute a porcine valve for

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patients needing valve replacements rather than some sort of mechanical valve.

Nonetheless, other competing products or therapies are available, so if there is indeed a problem, a GMP problem, the FDA needs to take effective action.

MR. BARTH: I think everyone has responded very appropriately, I agree with all of that. It seems to me that where you have a serious problem, the manufacturer may be your greatest ally in moving to resolve the serious problem. You may want to contain that problem, and the manufacturer knows where the devices are.

You may want to contain the distribution chain, and the manufacturer knows who is in that chain. You may want to stop the shipments at the factory level, and so you will need help from production folks in quarantining. If it goes back further than that, you may be talking to management and design folks about baseline problems.

In any case, it seems to me that FDA usually gets the attention of top management right away on what they consider to be a serious problem, in other words, it is no longer an FDA host or the departmental person, it goes right to the top of the management in the organization, and they are recruited as allies, and it seems to me in a serious problem, there may even be a mandate for an independent,

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objective view of getting at the systemic root cause and seeing that that is eliminated. That may mean hiring a consultant who is well known and acceptable to both parties, and that kind of an action.

No one in industry would disagree with any of those kinds of steps when serious problems arise. They are there to be dealt with very, very quickly, and using all the resources available.

DR. ZABRANSKY: I think that from the comments you have heard today, that we do recognize that you have a financial problem, as do we all, and we do support the efforts that the Agency is making regarding the inspection process and how this is going to be addressed, and how this is going to affect us.

I think the problem, if there was an issue here that there was a major, that could be contentious, it has to do with the model itself. It was definitely reservations upon all of us as how that model is going to be designed. I think we all felt that the data that went into it perhaps is not sufficient, in other words, we need more variables, but at the same time, by adding more variables it is going to make it harder, much harder to decide which devices are going to be -- where you are going to draw the line as far as the more detailed inspection is concerned.

I know that this is providing a background for much further work that you are going to be doing. I was wondering if there is any last comments for what we used to say the good and welfare of the group, that the panel would like to add.

DR. PIERONI: I would just mention Don used the term I believe "inspection overkill." I suggest we take that word out of the transcript.

DR. ZABRANSKY: Anybody from the audience would like to make any comments?

Allen.

DR. HUGHES: I just want to say that in putting together a model, as the FDA has done, I think you should use it as a guideline, yet not become too dependent upon models, such as these. What you are doing is you are looking retrospectively, you are looking at some sort of trend from the past, and using that to, in some sense, to make some sort of prediction towards the future, that is, you are not exactly predicting, but you are using it as a guide to where to put your resources in inspection in the future.

I just want to highlight that a number of things, a number of factors change over time, making it very difficult to take historical data and predict just where the

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problems may lie in the future, that is, management changes, you know, we have a lot of restructuring of corporate entities, mergers, acquisitions, new personnel coming in, new philosophies, all this sort of thing going on.

So, given that, just because a manufacturer has done a good job in the past, doesn't mean that everything is going to stay status quo throughout. At the same time, I do think that good performance in the past should reap some sort of reward, some sense of reward, but at the same time you need to take all of that with a grain of salt and with a very careful watchful eye on the situation.

MS. SMITH: I would just like to really for the record commend all the hard, hard work that I know went into this, and that we, I think as a committee, recognize that it is a work in progress, but that progress is being made. So, I commend you certainly, Lillian, and I commend the efforts of Kim. She is not here, but she has put a lot of hours into putting this together and also the future.

I do hope that you would keep the committee informed as things change and move forward on this. I would love to be kept informed and involved as much as possible, and thank you all for working with me, as well.

DR. ZABRANSKY: Anita.

MS. THIBEAULT: I would also like to echo Linda's statements and say that the amount of documentation that we got for review showed a considerable amount of work and actually a lot of -- you could see that a lot of thinking went into the development of this approach, and it wasn't easy to come up with what to look at and how to weigh it and how to put it together into some sort of a final number that would give you some inclination as to what was important and what was not, and I think that was a great effort, and I think that the Agency should be commended for that.

DR. ZABR ANSKY: Lastly, I would like to suggest, you know, we mentioned here, although it was not part of the plan, is the efforts on the part of the inspectors have to be more unified or more consistent in what they are doing, and I think the outcome issues, perhaps we don't know what they are now, but we can make some projections as to what outcomes we are looking at or want to see, and therefore, based upon that, you know, then, look at the feedback as to whether those outcomes have been achieved.

Then, you will know whether you are successful with your new model, whichever design it is going to have.

Thank you very much for your attendance, your promptness, your comments. I think it was a very

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participatory group, everybody had something to say, and  
thank you for your hospitality.

The meeting is adjourned.

[Whereupon, at 3:00 p.m., the meeting was  
adjourned.]