DEPARTMENT OF HEALTH AND HUMAN SERVICES

FOOD AND DRUG ADMINISTRATION

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TISSUE REFERENCE GROUP PROGRESS WORKSHOP

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Wednesday, August 29, 2001

9:30 a.m.

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P R O C E E D I N G S

DR. SOLOMON: Good morning. Welcome to the FDA's Tissue Reference Group workshop. I'd like to introduce my coworkers. First of all, I'm Ruth Solomon, with the Human Tissue Staff in the Office of Blood, CBER, at FDA.

Here we have Joe Wilczek from the Office of Blood is helping us with the AV stuff. Mark Melkerson from the Office of Device Evaluation in CDRH. Suzanne O'Shea from the Ombudsman's Office. Joanne Binkley from the Office of OCTMA, whatever that stands for. It's our Office of Congressional--

MS. BINKLEY: Communications.

DR. SOLOMON: --Communications, Training, and Manufacturers' Assistance. And, lastly, Areta Kupchyk, who is from the Office of the Chief Counsel.

I would just like to remind you, if you haven't already signed in, at the end of the program if you would sign in, that would be helpful.

Before I get started, I would like to thank the American Association of Tissue Banks, AATB, for their generosity in allowing FDA to use this room.

This is the first public meeting that FDA has had to describe its Tissue Reference Group, and it's the first step to try to make the TRG process more

understandable. A notice for this workshop appeared in the Federal Register on August 14th.

It mentioned that transcripts will be available in 15 working days. You can find the transcripts on the CBER web site, or you can contact the Freedom of Information Office at the address listed. By the way, we didn't make handouts of the slides, but the slides will also be on the CBER web site.

FDA has heard and received comments about the TRG, both in comments to the dockets for our proposed tissue rules and also in other public meetings. Some of the comments we have heard is, there is no document available to the public describing the TRG; the TRG process is not transparent enough; our TRG meetings should be announced in the Federal Register and open to the public; the TRG "decisions" should be available to the public; and, also, TRG makes class-wide decisions without public input.

So we are here today to provide information about the TRG process and to discuss some of the issues listed on that slide. The objectives for today's workshop will be, first, to give a history of the TRG and what the purpose of setting it up was; to describe the TRG process which is discussed in our SOP; to describe

the Request for Designation process contained in Part 3 of 21 CFR.

We will give an overview of information disclosure and describe the Freedom of Information Act process. We will give some information about human cell and tissue-based products regulated as medical devices. And then at the end we will have about a half-hour to answer questions, and please note I put generic questions, because questions specific to any particular product would not be appropriate for this forum. And we will also get your feedback on how the transparency can be improved.

Phil Noguchi, who is the Division Director of Cell and Gene Therapy in CBER, in the Office of Therapeutics, was not able to be here today. He and I are the co-chairs of the TRG. Phil was called to the Hill for some hearings today, so I'm going to be giving his talk on the history of the Tissue Reference Group.

The Tissue Reference Group was first described in our document called "A Proposed Approach to the Regulation of Cellular and Tissue-based Products," which published in February of 1997. In that document we set up the Tissue Reference Group, and as you can see from the slide, we said:

"The agency is setting up a Tissue Reference Group to assist in making jurisdictional decisions and applying consistent policy to human cell and tissue-based products. The agency hopes thereby to resolve expeditiously any scientific or regulatory questions that arise as to where and how such products should be reviewed. The Tissue Reference Group will consist of three Center for Biologics (CBER) persons and three Center for Devices employees. It will provide a single reference point for all tissue-related questions received by the Centers or the Office of the Ombudsman"--the Ombudsman's Office.

Just to give you a little history, the TRG began meeting the next month after the proposed approach published, so in March of '97. We actually discussed a product and made our first recommendation in July of '97. Between '97 and the present, we have had six meetings with sponsors who came in voluntarily to present information to us.

One date I left out was July '98. Our SOP was developed and went into effect. We have also initiated an internal set of meetings called TRG rounds, and we have had three of these. This gives us an opportunity for the two Centers, Center for Biologics and Center for

Devices, to get together informally and to share information about particular products.

And the majority of inquiries that the TRG has had come directly from sponsors who contact the TRG. We have had other inquiries coming through the Ombudsman's Office, through the Request for Designation, RFD, process.

In March of this year the Center Directors asked the TRG to do a self-assessment, and we were to discuss and answer the following questions: What is working about the TRG? What is not working? What is the usefulness of the process to industry as perceived by FDA? Is the process sufficiently open? And is the investment of time and resources worth the benefit?

What is working? We felt that the TRG had provided the public with an interpretation of FDA regulations at a time when these regulations are evolving. For instance, we have two proposed rules out there that have not yet been finalized on selling tissue-based products, and we have one rule that has been finalized, the registration and listing rule, which also discusses the whole concept of regulation-based risk.

One of the things we thought is not working is that we are aware that we have been criticized for not being more transparent. Under "Is the process

sufficiently open?" we said that we could make improvements, and some of the things that were discussed were to have meetings with you as we're doing today; to perhaps open a docket for discussion of a particular class of products; or we could even draft a guidance on a particular class of products. All of these are potential things, and we'd like to hear more from you during the question period about how you think we can become more open.

Next I'm going to talk about the TRG process itself. There are some seats available up front for those standing in the back. The Tissue Reference Group, there is quite a bit of information about us on the CBER web site, and the web site address is, as you see, www.fda.gov/cber/tissue/trg.htm. A broader web site that contains this information and other information about the Tissue Action Plan is basically the same address. www.fda.gov/cber/tissue/tissue.htm.

And on these web sites we describe the Tissue Action Plan, which is our way to move forward to implement the proposed approach to the regulation of human cell and tissue-based products. Under the Tissue Action Plan web site you will see a link to coordinating scientific and regulatory policy, the TRG, and that has five additional links under it that you'll find helpful.

The TRG, we said that we would draft operating procedures and make them available to the public. We did draft operating procedures. They are part of CBER's Manual of Standard Operating Procedures and Policies, SOPPs, and the Tissue Reference Group SOP is No. 8004. It became effective on July 28, 1998. You can find this SOP through the web sites I've given you already, or a more direct way to get to it is to go through www.fda.gov/cber/regsopp-8004.htm. The SOP describes the process that the TRG follows, and the July 28th version is being revised and updated. It's not yet on the web site but will be shortly.

The TRG composition, as I mentioned before, we have three representatives from the Center for Biologics, and one of these representatives is actually the Center's product jurisdictional officer. Then we have three representatives from the Center for Devices and Radiologic Health, including that Center's product jurisdictional officer.

We also have an Executive Secretary, and a liaison from the Ombudsman's Office attends our meetings regularly. And then we have other FDA staff as needed to provide product expertise, depending upon the product that we're discussing. They also attend the meetings.

And, again, the function is to provide a single reference point for questions about HCT/Ps. The TRG considers questions and makes recommendations regarding jurisdiction, policy, and regulations related to human cell and tissue-based products, and TRG tries to promote consistency in the implementation of the Tissue Action Plan.

Where do we get our agenda items from, and the products to discuss? There are two main ways these come to us. Either a sponsor can call or write in to our Executive Secretary, and this is the web site for to contact her. It can also be reached, as I said before, through the other, more general web sites, but it's basically /tissue/trgcont, for contact, .htm.

The other way that we find items to discuss is that the Ombudsman's Office receives a request for designation, and when it involves a human cell and tissue-based product, the request is forwarded to the Center's product jurisdiction officers and to the TRG.

The TRG meetings are routinely held twice a month. The agenda and accompanying information about the particular HCT/P being discussed at that meeting are distributed by the Executive Secretary prior to the meeting. The information may contain confidential information, such as a sponsor who is developing a new

product and would like advice on how it will be regulated by FDA.

At the TRG meeting, the product information that we receive from the sponsor is discussed. If more information is needed, the Executive Secretary contacts the sponsor or manufacturer, and the additional information, whenever it is sent in, is discussed at the next TRG meeting. Also, a sponsor may request to meet with the TRG to present information in person.

How does the TRG go about its deliberations to come up with a recommendation to the Center Directors? First, we ask ourselves the question, "Does the product meet the definition of a human cell and tissue-based product, as defined in 1271.3(d)?" This section is part of the registration and listing final rules which published in January of this year and became effective in April.

The definition says that an HCT/P are articles containing or consisting of human cells or tissue that are intended for implantation, transplantation, infusion, or transfer. "Transfer" is the term that's applied to reproductive cells and tissue.

And in that definition we say we do not consider a human cell and tissue product, the following items are not considered HCT/Ps: Organs, whole organs, are

regulated by a different Federal agency; that's HRSA. Blood or blood components, they have their own regulatory path. Secreted or extracted products from a cell or tissue. Bone marrow, which is regulated both by HRSA and FDA. Any ancillary products used in the manufacturing of the HCT/P. Animal cells, tissues, and organs, which again have their own pathway, they are xenotransplants. And in vitro devices. So those are items that would not come under the umbrella of our proposed and final rules, and therefore the TRG would not discuss such products.

The next question we ask ourselves in our deliberations is, "Is the HCT/P regulated solely under Section 361 of the Public Health Service Act, as described in 1271.10?" This is, again, a section in the registration final rule. And registration solely under Section 361 carries with it the fact that no premarket submission and approval of that submission are required, but these products do have to follow certain donor suitability requirements and GTP requirements, once those go into place.

So Section 1271.10 describes four criteria that a product would have to meet in order to be regulated solely under Section 361:

The HCT/P is minimally manipulated;

And the HCT/P is intended for homologous use only, as reflected by labeling, advertising, or other indications of the manufacturer's objective intent;

And the manufacture of the HCT does not involve the combination of the cell or tissue component with a drug or device, except for a sterilizing, preserving or storage agent, if the addition of that sterilizing, preserving or storage agent does not raise new clinical safety concerns with respect to the HCT/P;

And the fourth criteria is that the HCT/P does not have a systemic effect or is not dependent upon the metabolic activity of living cells for its primary function. And there are two exceptions, though, actually three exceptions: except if for autologous use, allogeneic use in a first degree or second degree relative, or reproductive use.

So, once having answered the question of whether the product can be regulated solely under Section 361 or whether the product is going to be regulated as a biologic product, a drug, or a device, after having made that determination, separating tissue from everything else, the next question we would ask ourselves is, is the HCT/P a biologic product, a drug, a medical device, or a combination product? And, in addition what Center should have the lead?

You may wonder how we answer these questions. Some of the things that we consider are the definitions of biologic product, drug, or medical device. Does the product meet the definition? We would also consider precedents. How have we regulated similar products before?

And in the case of combination products, which give us the most headaches or are most challenging, we would think about what is the primary mode of action. And in Part 3, as will be discussed later, if the primary mode of action is structural, we say that the Center for Devices would regulate it, and if metabolic, the Center for Biologics.

However, that distinction has not always been helpful to us or terribly clear, and we also take into consideration which component of the combination product plays the major role in achieving the intended use. Also, we use the Memorandum of Understanding, the MOU that has been developed between CBER and CDRH in 1991, and I should mention that that is undergoing discussion and may change, but it's coming up for review.

The TRG, we don't actually take a vote but we try to arrive at a consensus recommendation about how the products should be regulated. Then a letter is drafted by our Executive Secretary for comment by the TRG members

within seven working days. After comments are received and the letter incorporates the comments, the letter is forwarded to the Office of the Chief Counsel for clearance, and then to the Center Directors for signature, so that any correspondence that you would get from the TRG would have the Center Directors' signatures on it, Dr. Zoon and Dr. Fiegal.

If the TRG members cannot reach a consensus recommendation, then we bring the product to another group called the Tissue Action Plan Core Team. This is a group that meets monthly, and it consists of upper management from both CDRH and CBER, including Office Directors and Center Directors. The TAP Core Team then tries to reach a consensus recommendation. If the TAP Core Team cannot reach a consensus recommendation, the Center Directors themselves meet and resolve the issue. We've had one case that had to actually be taken directly to the Center Directors.

The second method of reviewing an item is through the Ombudsman's Office. A Request for Designation comes into the Ombudsman's Office, and you'll hear more about this procedure later. As I said before, RFDs that concern HCT/Ps are forwarded to the Center's product jurisdiction officers and to the TRG. Perhaps I should mention the names of the current Center product

jurisdiction officers. In CBER it's Sherry Lard, and in CDRH it's Eugene Berk. Also, our Executive Secretary currently is Martha Wells.

The TRG deliberates, as I've just explained, and we send recommendations back to the Centers' product jurisdiction officers, who then incorporate the TRG comments into the Center's comments, and then that is forwarded to the Ombudsman's Office. In the case of an RFD, the letter that goes out has the signature of the Ombudsman.

In terms of time lines, the TRG attempts to respond to inquiries directly from sponsors or manufacturers in 60 calendar days of receipt. Also, if we receive an RFD from the Ombudsman's Office, we consider that the RFD has strict time constraints that are written in the CFR. Their time constraints are, they have to get out a letter within 60 calendar days of receipt, and so TRG considers that time line.

If you contacted the TRG directly, as I mentioned was one of the mechanisms, and you disagree with the conclusion reached in the Center Director's letter that you receive, you have the option to now file a Request for Designation with the Ombudsman's Office, and then the Ombudsman will make the final decision. If you have filed an RFD and you disagree with the

designation that the Ombudsman has made, there is a regulation that tells you in Part 3 that you may request that the Ombudsman reconsider, and you would file a written request within 15 days.

Lastly, some additional information about the TRG process. We take minutes at each meeting. The minutes usually contain confidential information. The agendas and the meeting minutes are maintained on the Tissue Action Plan intranet site. That is an internal web site. A data base of all the TRG recommendations is maintained on this same internal web site.

On the external web site that is accessible to the public, we publish an annual TRG report or update which lists the products we have discussed in a very generic fashion. We cannot mention the name of the product. And that is available to the public, and it is updated yearly.

This you can find on the web site, the external web site. In FY 2000 it will tell you that the TRG made recommendations on the regulatory approach to be applied to the following products: an ex vivo cultured cartilage and periosteum tissue product which we considered to be a biologic; and a particulate fascia lata product administered in a syringe, which we considered a tissue regulated under 361.

And I just want to also mention that inquiries that involve trade complaints are usually forwarded to the respective compliance office at CBER or CDRH. If they need input from the TRG, we then provide that input, but our main function is not to be involved in trade complaints. Also, inquiries concerning products already clearly designated as biologics or devices are usually directed to the division, to the appropriate division, and would again not be discussed at the TRG.

Next I would like to present Suzanne O'Shea from the Ombudsman's Office, who is going to tell you about the Request for Designation process.

MS. O'SHEA: Hi. I'm Suzanne O'Shea from the Ombudsman's Office. I'm going to tell you a little bit about the Request for Designation process that Ruth told you about initially, and first the reason just why the Ombudsman's Office is involved in this process at all. We are in the Commissioner's Office. We're not associated with any Center, and we started out--so we call ourselves neutral, then, at least as far as the various Centers go. We don't have a vested interest in any particular outcome.

So about 10 or 12 years ago the RFD process was invented really to help with combination products. This really wasn't invented with tissue in mind at all, but it

sort of works pretty well with that. And the main gist of it was to, when companies developed products that were combinations of drugs or devices, the question was, which center should review the product.

So in the beginning of the Request for Designation process, the main question that we answered was the assignment of the agency component with primary jurisdiction. That was obviously whether CBER, CDER, or CDRH, was the main question that we were going to answer in that process. In general, we decided that when the product is a drug, then CDER would review it, and when it was a biologic, CBER would review it, but that's not even always true because CBER reviews some devices.

The real tricky part, as we have mentioned, was when we had combination products. And those, then we looked at the primary mode of action of the product to decide whether the device part of it was really doing the main thing or the biologic part of it was doing the main thing, and then we tended to go, to assign the product to that particular Center. But again, nothing is hard and fast in this world, so there's always exceptions to everything.

When FDAMA came along, we were then required to give a classification of a product, which is to tell what kind--we were doing these in our letters anyway, pretty

much, but now we are required to tell what kind of a product it is, a drug, device, biologic, combination product, and now we can even say whether it's a tissue in some cases, and the statutory provisions under which this product will be reviewed and regulated. And again, the tricky part comes when it's combination products, that in those cases we can be a little more flexible in what statutory provisions we'll use to regulate a particular product.

A Request for Designation, the main, the most interesting features about this whole process are that the company makes a recommendation. When they request a product to be designated, they make a recommendation on the Center that it would go to, the kind of product that it is, and the statutory provisions that it would be reviewed and regulated under.

We have a very strict 60-day time clock, and the hammer in that is that if we do not issue a letter answering these questions within the 60-day period, then the company's recommendation automatically takes effect, which is a big hammer for us, that we get these out. And that is really industry's opportunity to say what they think, and what they think this thing ought to be.

A Request for Designation is appropriate when a product's assignment and classification are unclear or in

dispute, and that, I'll talk a little bit more later about how that works in connection with the TRG, but that is in our regulations. And the next question, then, is how do you find out whether the way a product is reviewed and regulated is unclear or in dispute?

We have listed three ways up there. As Ruth mentioned, I think the main way to start is to contact the TRG, and they can give you their answer and their view on that. Another way is to contact the Center product jurisdiction contacts, and I've even given you their phone numbers up there. You can call them. Sometimes products have already been decided, types of products have already been decided, and the Center contacts can give you a quick answer.

We also have the inter-Center agreements that Ruth mentioned. There are three of them, CBER-CDRH, CDRH-CDER, and CDER-CDRH one. All three Centers have crossing, inter-Center agreements. They are available on the Ombudsman's home page, and the address is up there. They probably, in all honesty, wouldn't be all that helpful to tissue questions because they were written before tissue really got too involved. But, as Ruth mentioned, they are constantly undergoing thinking about revising them, so they may become more useful as time goes by.

The process that we follow when we get a Request for Designation--or, first, the process for requesting a Request for Designation is to submit a written request to our office. The address is up there. The information that is required is just some background information about the manufacturing of the product, what it would be intended to be used for, whether there is any other similar products on the market, things like that, but that's all spelled out in the regulations. And of course you are very free to call our office, and that's our phone number up there, and really anyone in the office can probably help you if you want to talk about what kinds of information would be useful or where we are or how to do this or anything like that.

Then, once we get a Request for Designation, we send it on to the Center product jurisdiction contacts, and when the Request for Designation refers to an HCT/P, we also send it on to the TRG. The Center contacts get back to us with the Center positions, the official Center position on how each Center thinks this product, what it is and how it ought to be regulated.

As Ruth was explaining, then, the TRG then also gives its recommendations to the Center contacts, and then they incorporate the TRG recommendations, and then we come back to our office with the final Center position

on a particular product. And the Ombudsman issues the letter, taking into account the two Center positions and the company's positions, and past practice and things like that, and issues a letter to the company, hopefully within 60 days, telling the answer.

And, as Ruth mentioned earlier also, there is a period that you can request reconsideration from the Ombudsman's Office if you're not happy with that decision, and that has gone on a time or two, when companies will come back and tell us all the reasons why we're wrong in our earlier decision. You can't submit new information in that request for reconsideration, but that is also a possibility.

Now, the real question here is, how does this process then relate to what the TRG does? We work together. As Ruth mentioned, if the TRG came up with a decision that a product is not a tissue, and the Center Directors issue, sign the letters saying it's a regulated product under the Food, Drug and Cosmetic Act or the PHS Act, then you could submit an RFD to our office, arguing the point that it should just be regulated under Section 361, and then that would be sort of in a sense an appeal of the Center Directors.

You can also use the RFD process to challenge the Center Director or TRG decision that a certain

product will be regulated in a certain way, and that, then the Ombudsman would issue an answer on that question.

Can you come directly to the Ombudsman's Office without going to the TRG first? Yes, you can, and as Ruth explained, we would, if it was an RFD that the TRG would be interested in, we would refer that back to them, not necessarily for an answer, because once the Request for Designation comes in, our office would still give the answer, but we would certainly take TRG's views into account through the Center contact process.

I guess we would recommend that you go to the TRG first with these kinds of questions, and then at least you have two bites of the apple. If you're not satisfied with the TRG/Center Director's decisions, then you can always preserve that route through the Ombudsman's Office.

And that's RFD in a nutshell.

DR. SOLOMON: Chris Proctor, please see Vicki.

The next speaker is Joanne Binkley from OCTMA. I won't try to tell you again what that acronym means

MS. BINKLEY: Hi. Ruth asked me to come here this morning to discuss with you the disclosure of information that you provide to the agency, since many of you have never done this before, and the disclosure of

information the agency may create regarding one of your submissions or your products, and so briefly I'm going to go through the disclosure process and then get a little bit more specific towards the end.

There's many statutes that affect disclosure. The Freedom of Information Act is the primary one, and it's commonly known as FOIA.

The Trade Secret Act makes it a criminal act to knowingly disclose trade secrets.

The Privacy Act only applies to government systems of records where personal identifiers are used to retrieve the information. This act was enacted in the early '70s following the Watergate hearings, when Congress became aware of the President's secret enemy list, and that kind of generated this act.

The Health Insurance Portability and Accountability Act was recently enacted, and it is my understanding that at this time it does not apply to tissues.

There are many acts that have disclosure provisions in them, that are not specifically disclosure acts. For instance, the NCVIA, the National Childhood Vaccine Injury Act, has a disclosure provision. The Federal Advisory Committee Act has a disclosure provision that requires that documents made available to advisory

committee members also be made available to the public in a redacted format.

So that kind of gives you an overview of the acts that are involved. FOIA, which I said is the main act that we regulate disclosure under, the main statute, was enacted in 1966. Prior to FOIA, Section 3 of the Administrative Procedures Act provided the procedures for disclosure or, as it frequently was used, for non-disclosure.

Two of the requirements under the Administrative Procedures Act gave agencies almost unlimited grounds to withhold documents. The first one was, a burden was put on the individual requesting the information to show that they had a proper and direct concern, and the second was that the agency would disclose documents only when it did not otherwise find cause to hold the information as confidential. In FOIA you will see a difference, that the requester does not have to justify the request. There is no need for the requester to state their need to have this information.

Part of the groundswell for disclosure in the '60s was the perception that there was excessive secrecy on the part of the administration regarding the Vietnam War. Nonetheless, when the act was pushed through

Congress, President Johnson signed it with great flourish and commended the act.

In 1974 there were amendments added as a result of what was called the Watergate hearings, and some of you that are as old as I am will remember them, where John Dean testified that the entire Civil Service was exempt from FOIA. So the amendments went through and made it very clear that Congress intended that the entire Civil Service, with the exception of Congress itself, were not exempt.

The 1986 amendments provided broader protection for enforced information, and I'll go through when I get to that, when I get to that exemption.

The purpose of FOIA was to ensure that the government's operations are apparent, except where the disclosure would harm an individual, a corporate entity, or national security. Historically, much of what has evolved into American law came to us from Great Britain. In Great Britain, authority comes from the monarchy. Therefore, originally, copying their form of law, everything that was in an official file was an official secret.

In contrast, our authority in the United States comes from the people, and so it has been held that informed citizens are the best citizens, and so the

authority to govern comes from the citizens, and increased access to government information was felt to be appropriate. At the time of the enactment of FOIA, only Sweden had had a similar statute.

It should be noted, in addition to Congress, White House staff is also exempt from FOIA, although the Executive Office staff is not. Okay?

Basically, FOIA provides that every person has the same right to access to Federal records--again, that's where you don't have to justify your right to access--that are not protected by one of the exemptions to disclosure. FOIA contains six subsections, the FOIA statute. The first subsection is in regard to the categories of information that must automatically be disclosed, either through publication in the Federal Register or through agency reading rooms. The second section of the FOIA act are the nine exemptions from mandatory disclosure. I will briefly discuss each of them.

The first exemption is one that FDA seldom uses, as we don't usually have records that are classified as Secret.

The second exemption relating to internal personnel rules and practices, we do use rather infrequently. These are records related solely to the

internal personnel rules and practices of the agency. Courts have made an interpretation that there's two types of (b)(2) exemptions.

One is "low 2" where it's trivial matters, and Attorney General Janet Reno encouraged us to use our discretion and release those, and so for the most part we do. The other ones are more substantial internal matters which, if we disclosed them, would risk circumvention of a legal requirement. So basically, if the disclosure of a "high 2" document benefits somebody attempting to violate the law and avoid detection, the documents will be protected. Otherwise, agencies are encouraged to disclose those records.

The third exemption, information exempt under other laws, is triggered by Federal statutes, other Federal statutes. As I mentioned earlier, there are-- many other statutes have disclosure provisions in them. So to be an exemption 3 statute, the statute must require that the matters be withheld, and they can leave the agency with no discretion on withholding. In addition, they must establish particular criteria for withholding, or refer to particular types of matters to be withheld.

The courts have ruled that the Privacy, the Trade Secrets Act, and the Federal Device Amendments of 1976, 360(jh) are not exemption statutes.

(b)(4) is probably the most frequently cited, (b)(4) and (b)(5), probably the most frequently cited exemptions by this agency, and (b)(4) is the exemption to protect your confidential material: trade secrets, commercial, financial information obtained from a person that is privileged or confidential.

Trade secrets are commercially valuable plans, formulas, processes or devices used in making you product. To be a trade secret, there should be a direct relationship between the trade secret and the production process.

The key words in this exemption are "secret" and "confidential." If what you want protected is already out there in a journal article or some other format that you've made it public in, on your own web site, to the Securities and Exchange Commission, whatever, to your stockholders, whatever, and we become aware of that, we can no longer protect it. So that's something that you need to keep in mind when you're releasing information about your products, is you release it publicly once, it's public. Okay?

Commercial information includes information such as sales data, research data, technical designs, customer lists, supplier lists, profits and losses and financial data.

The third part of this exemption is usually more difficult to possibly understand and even also to use. It's information that is privileged and confidential or confidential. And the courts distinguish between information that is voluntarily submitted to the agency and that that is required.

The information that is voluntarily submitted to the agency, there is a lower threshold to be met for us to protect the information. That is, it can be released if it would--it can be protected if the submitter customarily would not release it. Okay? If it is required to be submitted, then it's exempt from disclosure only if it meets a standard of substantial harm to the submitter's competitive process. So there's a difference there between voluntary and required submissions.

The next exemption is another one that we frequently use. It's internal government communications. In order for documents to be exempt from disclosure under this exemption, they must be inter- or intra-agency documents that are privileged. And the most important privilege that we use is the deliberative process privilege, which is protected in order to encourage open, frank discussion on matters of policy between subordinates and superiors, to protect against the

premature disclosure of proposed policies before they are adopted, and to protect against public confusion that might result if the reasons and rationale for policies that were not adopted are made public.

Another privilege under here that's often used is the pre-decisional, and the Supreme Court recognizes that agencies are engaged in a continuing process of examining their policies, and therefore not all memoranda ripen into an agency decision, so those that don't are still considered pre-decisional.

The next exemption is for personal privacy, and that also is frequently used by the agency, and it obviously includes personal and medical files and similar files, the disclosure of which would constitute a clearly unwarranted invasion of personal privacy. So it's kind of a high threshold, and you will see this in a later exemption, that this threshold here is a little bit higher than one used in (b)(7).

Information pertaining to a single individual whose identity cannot be determined after deletion of the individual's name from the record does not qualify for exemption (6) protection, so medical records where we can redact the name, and it's not such a unique event that the individual would be identified, we can release. However, if the information in question concerns a small

group of individuals who are known to each other and easily identified from the details in the information, redaction of personal identifiers may not adequately protect their privacy.

And this comes into consideration for some of our newer therapies that are used in small numbers of people, where the identities of the people are known, and so it's causing us to reexamine redaction of names in releasing medical records. So I can tell you that some of these therapies and some of the trials that are ongoing right now, we would probably not release medical records when it's small enough that people may know who the individuals are.

The courts have held that even a modest privacy interest outweighs no public interest. Court language. What can I say.

(b)(7) are law enforcement records, and we do use this exemption also, not often, not as often as the (b)(4) and (b)(5), but we do use this pretty frequently. Records or information compiled for law enforcement purposes, the release of which could reasonably be expected to interfere with enforcement proceedings or would deprive a person of a right to a fair trial.

In order for release of a record to interfere with enforcement proceedings, the proceeding must be

either pending or prospective, and the release could reasonably be expected to cause some harm to the pending enforcement proceeding or related proceeding; not even that proceeding, but if there's another matter that's related, that's still pending. Or it may deter witness cooperation or prevent the government from obtaining data in the future. Any of those reasons can be used there.

If the law enforcement record, release of it could reasonably be expected to constitute an unwarranted invasion of personal privacy. And here the threshold is lower than in the other, in the (b)(6) exemption, it's "reasonably be expected" as opposed to "clearly" and so it is a lower threshold. Often law enforcement records requested by name are responded to by what we call "glomerizing" the request. We neither confirm nor deny the existence, and that's because to confirm that we have the record tells you already something that shouldn't be disclosed.

If the law enforcement--released of the record would disclose investigative techniques and procedures, and such disclosure would reasonably be expected to risk or circumvent the law, then we would withhold it. But if the procedure is commonly know, the investigative procedure is commonly known, it would not be protected, as disclosure would not risk circumvention.

If the records could reasonably be expected to endanger the life or physical safety of an individual, then it could be protected, and in this case we would even protect Federal employees' names if there is the possibility of a threat to that employee.

I should add under law enforcement records, and these are probably not--483's are not necessarily considered law enforcement records in all cases, but a 483 that is issued after an inspection is available immediately after it is shared with the sponsor or the firm or the manager there at the firm, and it's available immediately in a redacted format. In addition, warning letters are posted on ORA's web site, and so if you've got an inspection coming up, it's a good place to do some homework.

The last two exemptions, regarding financial institutions and geological information, we just don't use those. We don't have any need for them.

In 1993, Attorney General Janet Reno made a statement that allowed agencies to use discretionary disclosures of certain exempt information. This does not apply to (b)(4) confidential commercial trade secret information, nor does it apply to (b)(6) privacy information. It's more for the (b)(2) personnel records that the agencies have, and (b)(5) pre-decisional.

Okay. FOIA requires that certain agency records be made available for public inspection and copying in agency reading rooms, including--records that are made available this way are final opinions and orders rendered in administrative cases, specific agency policy statements, and certain administrative staff manuals that affect a member of the public. These records must be indexed by the agencies in order to facilitate the public's convenient access to them.

Records that have no precedential value and do not constitute the working law of the agency are not required to be made available in reading rooms. Published materials or materials offered for sale are also not required to be in the reading rooms.

The Electronic Freedom of Information Act Amendments, known as EFOIA, were implemented in 1996. These require that the agency establish another category of records to enhance the availability of reading room records. In addition to the three categories of records I just mentioned for regular reading rooms, EFOIA also added a fourth category of records to be available, and that is those documents that are frequently requested or that we anticipate will be frequently requested under FOIA.

Other provisions of EFOIA include making records available in the formats requested unless it interferes significantly with the agency's IT operations, and EFOIA also provides for access based on compelling need, expedited access based on compelling need.

There are times when agencies disclose records outside of FOIA, and this slide here has some examples. The Commissioner can make a discretionary disclosure. Court orders require us to disclose documents.

Congress, and I briefly want to mention Congress, because requests from the Chair of a congressional oversight committee for documents that contain (b)(4), (b)(5), (b)(6) materials are turned over in a non-redacted format. We usually do try to get the committee to agree that we can redact privacy information, the names of patients. And Congress, as I stated earlier, is not under the FOIA so they are not required to exempt this material then from further disclosure. Most of the time they don't, but they are not under the same rules that we are, so I just wanted you to be aware of that.

There are disclosure regulations. The general regulations implementing the FOIA act are in 21 CFR Part 20. In addition to that, there are specific regulations relating to biologic products in 21 CFR 601.50 and 51,

which relate to INDs. 601.70 has to do with post-marketing studies. 601.8 has to do with revocation of licenses; we publish those. And 640.120, which is evading me right now. Regulations specific to IND, disclosure of INDs, are also in 312.130, and the regulations on disclosure of devices are in the sections listed there.

In addition to the regulations listed on this slide, of particular interest to this audience are the disclosure regulations in the recently published 21 CFR 1271.37. Under this regulation, the following will be available for public information once it is compiled: a list of the registered establishments for human cells, tissues, and cellular and tissue-based products; a list of all products by establishments for these products; a list of all discontinued products; and all data or information that has already become a matter of public record.

We will be working with Ruth's group as they get this information compiled, to get this either up on the web or otherwise available publicly.

I briefly want to discuss how to make a FOIA request, because you can also make a FOIA request and get information that may be helpful to you. You need to make them, the statute requires that requests be made in

writing, and at this point it has to be a letter to the agency, and the address is on the next slide: The Food and Drug Administration, Freedom of Information Staff. Put the mailing address there, HFI-35, or it wanders around the agency for a month or two. 5600 Fishers Lane, Rockville, Maryland. And I've also included the fax number.

When you make a FOIA request, if you identify the records that you are seeking as specifically as possible, it will speed your request. Requests are triaged into three categories: the relatively easy ones; the ones that are going to take some amount of work; and the complex ones or very voluminous ones.

And so the relatively easy ones that we can get out quickly are--you know, we handle them on a three-tier basis, but obviously the ones that go into that track often can be handled by a less senior staffer in the office and get out quicker. And so if you're as specific as you can be, and don't ask for "any and all" on something because that really, right away those words immediately slow the request down, if you're specific as to what you want, you will get better service, I think.

Also, the FOIA act requires that you include your name and address, and it's optional if you include your phone or e-mail address, but it's very helpful to us

if you do include your phone or e-mail address so that we can call you and discuss your request, because sometimes the way you worded it, there is no document, or there may be 500 documents that fit that, and we don't want to bill you for processing those documents.

Separate your requests for each firm or product. That also may help reduce the time, because one may already have been redacted, and we can get that out and get that closed for you; and another one may require us to go through the process of reviewing it and redacting it, which is slower.

If you are limited on how much money you want to spend on this, a statement on the limitations that you're willing to spend is also helpful to include in there. And on this note I should mention that freedom of information is not free information. Commercial users pay for search, copy and review. The news media, education, and non-commercial scientific institutions pay for copying after the first 100 pages. And others pay for the search and copying time after the first 2 hours and 100 pages.

The FOIA contacts in the Department are Rosario Cirincione. He's the director there. In FDA the director of the FOIA staff is Betty Dorsey. In CBER, my immediate boss is Mary Meyer; she's the Director of the

Office of Communication, Training, and Manufacturers' Assistance. I'm the Division Director for Disclosure and Oversight Management. Lisa Banks is the branch chief for our Access, Litigation, and Freedom of Information staff, and the staff consists of four people. At this point we have a backlog of over 600 requests, and you can see with four people it's difficult, so the more specific you are, the quicker we can help you.

CBER also has a Manufacturers' Assistance group that may be able to help you with some things, for instance if you need documents or if you need some assistance that's more general than what Ruth's group would give you, and their number is 301-827-2000. It's the same number you can reach myself or Lisa at. We also have an 800 number, 800-835-4709. If you have any questions, we'll be happy to take them later. Thank you.

MR. MELKERSON: Good morning. I'm Mark Melkerson. I'm the Deputy Director for the Division of General, Restorative, and Neurological Devices. Under my purview I have the Orthopedics Branch, and the Restorative Branch which deals with tissue products, as well as the Plastic and Reconstructive Surgery Branch that deals with your wound dressings, interactive wound dressings. Within the Office of Device Evaluation, other divisions that deal with tissue-based products that are

regulated as devices will include our Cardiovascular Group, our Dental Group, and also our OB-GYN Group.

Today I'm going to kind of touch on product responsibilities, a little bit on examples of products that are regulated under our jurisdiction, and the human cell and tissue-based--and I'm going to use acronyms, and I'm sorry that in the government we have to use them, otherwise we feel like we're at a loss--so HCT/Ps will be used in the abbreviations here.

I'll touch a little bit on standards. The regulations between the Center for Biologics and the Center for Drugs and the Center for Devices vary on how we access or use standards. And then a little bit on information. I put these at the end of the slides just for your information. You can go refer to them. I'm not going to read through the web pages for you.

Between the Center for Biologics and the Center for Devices, we run through and make a designation. If it's considered a combination product with our Center as the lead, based on its primary mode of function, or it's a medical device designation, we're going to take the lead. And we go through these decisions through the TRG, and I'm going to actually look through some practical examples of where we go.

The definition for a medical device, the main one is the bottom point. I'm not going to read through these. These are what we work through with the TRG, but basically, "does not achieve primary intended purposes through chemical action or metabolized" is in the device realm.

Medical devices, and the devices that are up here are some of the ones that have been designated as medical devices after going through the process, and some of the things you will not see up there are bone void fillers. We had a meeting last August that talked about using bone products to make medical devices. Those were considered a homologous use, and will show up as tissues, no longer as medical devices. That was part of that discussion, so if you are interested, I guess it's the transcripts for the August meeting of 2000.

The devices that are up here, probably the most recent is the FocalSeal products and the Apligraf. These products tend to be a collagen matrix base, and either mixed with growth factors or cells, but the primary mode of action for the Apligraf was basically an interactive wound dressing, or some may want to call it a skin substitute.

The next slide actually, with our recent acronyms, would be total product life cycle, but it

basically is a development process that usually a sponsor would come through. It's your idea, your design, run through your bench testing, clinical testing, premarket, commercial use, refinement, and eventually your product goes on and you either tweak it or it goes out of use.

But the process that we're trying to do at the Center is actually get people to come in just after they get to their inspiration and their design, come talk to us before they get to their bench testing. You'll get yourself through the process a lot easier in that interactive process.

For the Center for Devices, we have three main modes of marketing applications: Premarket Notification; Premarket or PMA Applications; and Humanitarian Device Exemption, which are generally for products that it's similar to an orphan drug use, less than 4,000 cases per year.

In the Premarket Notification process, we identify it as a case-by-case approach, but if you are just saying "We're a product that's equivalent to something that's already on the market," you can do that in using same intended use, preclinical equivalents, your specs for your product. And every once in a while, if you're using a new technology, you may have to supply

either clinical or bench testing to supplement that other preclinical testing.

Under FDAMA it gives the authority to recognize standards, and under the Premarket Notification process we use that quite often. A sponsor will come through, and instead of having to run through a battery of tests or justify using a test, we try to move forward with recognizing test methods. And it allows you to declare conformity to them, in other words, "I conform to the test method," or "I conform to a performance standard." And that actually saves review time on our end. You just need to have that information available on file at your firm.

The standards program, for those that are in the tissue area, it's actually covered in two different groups, ASTM and ISO. ISO is more in a data gathering stage. They're trying to figure out what they're doing, whether they're going to be involved or not. ASTM has actually established a Division on Tissue-Engineered Product, and I'll throw up another acronym, TEMPs.

The Tissue-Engineered Group, you know, touching on the scope here, it's tissue-engineered products. Well, the TRG crosses over two Centers. Each Center has different authorities with relation to the standards, so one group may be very enthusiastic, the Center for

Devices, because our portion of FDA may have said we're supposed to encourage the use of and help develop standards in the consensus format. The Center for Biologics has a little more restriction. So in terms of interaction, we're involving each other but the scope of attempts is something that crosses over both Centers.

There's 10 groups that are in that division, and the ones that probably fall into the categories that cross over the two Centers, let's see, you'll probably run into --the biomolecules and cells are going to be Biologics. Where we cross over mainly are the bone void fillers and cartilage repair products.

Currently the standards, the Center for Devices hasn't recognized any, which doesn't help in our 510(k) review process, or they can be used in PMA or IDE as well. There have been three approved by ASTM, and two are nearing balloting.

If CDRH recognizes a standard, we put out a Federal Register notice identifying that. That is done at least once a year. Trying to work better in conjunction with Center for Biologics, the Center has actually formed a Tissue Engineering--and again, another acronym--Standards Technical Group. It's made up of, within the Center for Devices, our Office of Compliance, our Office of Device Evaluation, our Office of

Surveillance, and the Tissue Engineering Group actually will have a representative from the Center for Biologics involved. The Tissue Engineering Group will also seek comments and input from CBER during that process. So this has just started, in trying to make sure that we're working together between the two Centers within our limitations.

The Pre-Market Approval process has a little higher regulatory bar. It usually involves not only preclinical testing, both on the bench, maybe animal models, but it also generally requires clinical data be included. Again, it's a case-by-case approach. In other words, you have a new technology or a new indication, how do you move forward? You have to establish both safety and effectiveness, not just that I'm equivalent or I'm a "me too" under the Pre-Market Notification process. You actually have to show you're safe and effective. We also in the review process will look through your product manufacturer, your in vitro testing, your clinical performance, and your product labeling, and there may also be post-market surveillance information, as well.

In the product manufacture as it relates to a tissue-based product, we're going to be following the same types of inputs you would see in terms of sourcing, so your good tissue practices; how you process the

product; in-process and final tests, in other words, how do you validate your manufacturing process, your quality control, your quality systems; the lot-to-lot consistency. And a few other points; your impurities; what do you bring along in the manufacturing process.

Again, when you're going through our review process, make sure your products are in sync with either our guidance documents that are available on the web for those areas, or come in and talk to us before you spend a lot of time planning that information out.

In vitro testing, this is generally applicable both to synthetics as well as tissues, but we'll go through, and depending on whether or not there's a broad-based literature or supportive information for your particular product, we'll have various levels of inquiry into each of these areas.

Probably the main part of the PMA approval process is your clinical study design, and in the study design, again it's a very good process to come in and talk to us early. We also have a pre-IDE or presubmission look at information that we're open to, as well.

But when you're designing your study, the question comes up: Where do you want to go with your product ultimately, with your indications? It's much

easier when you're making your study design for your product, to focus in on a very specific indication for use, well-controlled, but then how do I go to a general, more broad indication? Make sure those are brought up in your discussions while you're coming through, looking at study end points, how to conduct a study, your duration, and data analysis.

The investigational studies for most products require an IDE unless they're a non-significant risk. For a significant risk product, generally which would include implants, requires both FDA and IRB approval. Non-significant risk, you can get away with just IRB approval.

Humanitarian Device Exemption, again, it's like our orphan products. They are--within the Orthopedics Group we've had a couple products go through recently which were actually combination products but drug/device combination products. We go through and follow almost the same procedure as a PMA, except you just have to show probable benefit, and that information is for a product area. It is limited in scope and indication.

As far as interactive processes between CBER and Biologics, I put up the web pages again, but we work, when we look at a device or regulate it as a product, we will work in conjunction and most of the review teams

will be combinations of both CBER staff as well as CDRH staff. So even if you are designated as a device, you are going to have review involvement from both Centers. We do that in a collaborative nature, and the process itself should be fairly transparent.

Guidance documents, what we try to do both for tissue-based products as well as our synthetic-based products, is actually come up with guidance documents. Again, these are done in conjunction between the two Centers and are available for your perusal. And these are going to be up on the web page, so I'm not going to go through and list them all.

The screening and donor availability products will come up both in terms of your choice of source material; you throw out your bovine sources, human sources, or porcine sources.

Special product information, the products that I discussed earlier that have been regulated as devices, which will kind of give you an idea and scope of both, what we've looked for both in terms of safety and effectiveness, both from a preclinical standpoint and a clinical standpoint, are available on the web page. And another acronym for you, Summary of Safety and Effectiveness.

These are PMA products. The web sites, there are actually links to those sites directly. If you go to the FDA web page, go for the Center for Devices, you can click on PMA approval or type in, in your search, just the name of the company.

As far as contact information, I identified as a process of devices regulated, our Restorative Branch Chief deals mainly with your orthopedic applications. That Branch Chief is Ted Stevens. If you have general questions on how do I initiate a study, how do I come in and meet with you, how do I get a presubmission, please make sure you contact Ted. From the skin or tissue sides, Stephen Rhodes. And if you're not sure where the products are, you can either contact Gene Berk, whose number was up earlier, myself, and if it goes to another division, we'll be glad to direct you in that vicinity.

Thank you very much for your time, and I guess we're ready for questions.

MS. KUPCHYK: My name is Areta Kupchyk. I'm with the Office of the Chief Counsel at FDA, and I've been asked to moderate the question and answer period. Don't ask me why they want a lawyer to do this.

I am a child of the seventies, which means my hearing has been totally destroyed by rock and roll, and for any--there are no microphones here.

MR. WILCZEK: Yes, there are. We have a rotating one.

MS. KUPCHYK: We have a microphone, so you don't have to yell on my behalf, and the microphone will come to you, so please wait until it is there before you start speaking, because I guarantee you, I won't hear the question.

Do we have any questions to start off? If not, I can start off with one question. Ruth, this is a question for Ruth. It's an easy one, Ruth, believe me. You said that the TRG would not decide or respond to inquiries about products that were already clearly designated as a biologic or a drug or a device. If someone doesn't know that and they write to the TRG, will the TRG respond or, will we just ignore the letter? What do you think?

DR. SOLOMON: We'll respond.

MS. KUPCHYK: I thought I'd start with an easy question. Now, I can think of more easy ones, but I think I'll probably bore you, so someone come up with a question, if you have any. If not, we can all go home and eat lunch early.

MR. WILCZEK: Yes, if you'll just raise your hand, I'll be glad to take the mike to you.

MS. KUPCHYK: I have another question. How many of you know what a 483 is? Joanne Binkley mentioned it. How many don't know what a 483 is? Okay. It's, you know, an acronym. Some people don't. A 483 is a form. It's called FDA Form 483, and it stands for lists of observational--inspectional observations. When you are inspected by FDA, at the end of the inspection, if there are thing that the inspector notices that are not in compliance, they'll write it up on Form 483, the inspectional observations, and they will go over that with you at the end of the inspection. So 483 has become the short-cut word, the short-term word for inspectional observations.

QUESTION: Hi. Dr. Solomon, could you please clarify it as to why the TRG's letter of recommendations are not made public on a monthly basis, such as the 510(k)'s or PMA's, if you could clarify that point, please.

DR. SOLOMON: I guess you're suggesting that perhaps they should be made public--

QUESTION: Yes.

DR. SOLOMON: --as an effort to increase the transparency.

QUESTION: Correct.

DR. SOLOMON: We would consider that but, as I mentioned, the letters contain confidential information. You can request a TRG letter through FOIA, and the confidential information will be removed or redacted. But we did talk about actually in our group asking sponsors, when they send letters, information in to us, perhaps they could send the total amount of information including confidential material, and then they could redact the information that they don't want shared. We could--we discussed also how the TRG letters could also redact information and possibly be posted, but--so we have considered these things, and we will continue to consider them. It's not that we haven't thought of them.

QUESTION: Thank you

MS. BINKLEY: Could I take (inaudible) as an answer (inaudible)?

MS. KUPCHYK: Could you speak more into the microphone?

MS. BINKLEY: One of the requirements under electronic FOIA is if we get three or more requests--not three or more. We tend to use that three or more. But if we get frequent requests for a document, then we should make it public on our electronic web site. And so we will be looking at this, and if we are getting frequent requests for these types of letters once they're

redacted, we'll start putting them up and hopefully start putting them up proactively then. So that is something we'll watch, and since you brought it up in my presence, I'll make sure it's watched.

MS. KUPCHYK: Let me just add that a company can submit a letter or a request to the TRG and waive confidentiality. You can say, "I don't care. All of this is public, don't worry about it." And in that case then we don't have to worry about redacting or trying to figure out what's commercial, confidential, trade secret, etcetera, and that will speed the process up.

QUESTION: My name is Andrea Shandley, and before I get to my question, I want to just throw my two cents' worth in. I've done some work on this, and my experience is that companies want everybody else's information to be released but their own requests come with a cautionary label, "Do not release," so that makes it a very difficult question.

My question goes to products that are regulated as tissues under the Part 1270. What--and I'll drag you into this--what is FDA's policy on the labeling for these products, and where is the authority to require the labeling regulation for products that aren't drugs or biologics?

MS. KUPCHYK: You're talking about 1271, not 1270.

QUESTION: Yes.

MS. KUPCHYK: Well, it's a proposed rule, it's not a final rule. Our authority is in the publication that was in the Federal Register. We listed what our authority is under 361. And I'm not sure what more I can tell you.

QUESTION: Okay.

MS. KUPCHYK: Yes, there's a hand back there.

QUESTION: Hi. Marjorie Monk. Is the only way that an issue comes before the TRG through a request from the producer of the new product?

MS. KUPCHYK: Ruth?

DR. SOLOMON: As I mentioned, another possible way might be for a competitor to snitch on the other guy and say, you know, "How come his product is out there as a tissue? Shouldn't it be a device?" But at the beginning of the TRG, we used to try to resolve those issues, but as I mentioned before, our current policy is that trade complaints like that would be referred to our Offices of Compliance at each Center.

MS. KUPCHYK: Let me follow up with a question. Do we ever make--on our own, decide to discuss a particular product without the request of a sponsor? We

know something is out there, or we know something is a device or a biologic, and we want to--we think it might not need to be regulated as a device or biologic and could be regulated in 1271. Would we, on our own, discuss it? Is that sort of what your question went to, as well?

MR. MELKERSON: Actually, we have done that in the area of the bone tissue products, last August in a public meeting, where we're looking at a class of product, and would it be regulated as a tissue or device? And the issue was related to products that, if you machine cut a piece of bone into something that looks like--and I'll throw out an interference screw for fixing ligaments in place, which are usually made out of metal or polymer, the answer was, that was considered a tissue because it was used in a homologous manner.

DR. SOLOMON: Regarding the bone dowel issue, I have to admit that when the TRG first started, we did issue a letter to a particular company, not realizing that it had class-wide implications. And we are very much cognizant of that now and will try, on decisions that affect a whole class of products, we will try to have public discussion before making a decision as to their regulatory status.

MS. KUPCHYK: Any other questions?

QUESTION: Along these lines, how are you handling combinations? There are various, for example, demineralized bone products that are combined with what some believe are materials regulated as devices, and how is that being addressed by the TRG?

MR. MELKERSON: Well, according to 1271, one of the, if you want to call it, factors that would cause you to be a regulated product are the combination of a tissue with a drug or device, and it can be a drug or device if it's a storage, preserving, or sterilization agent. One other exception to that would be if it's water or buffer.

MS. KUPCHYK: There was a question up here. I don't know if there still is. Right here.

QUESTION: Hi. My name is Kathy Joyce. I just wanted to ask a little bit more about the process. I'm just trying to figure out which is--is there one way that's better than the other, to go directly to the TRG or to go to the Ombudsman's Office? It seems like the Centers are involved, regardless of which way you go, which obviously they need to be. But is there an easier way? What's the best way?

MS. O'SHEA: From the Ombudsman's perspective, we would really I think recommend that you go to the Centers first, through the TRG or the Center contacts. A lot of things can be worked out just fine with them, and

as I said before, you know, you're right, there is sort of--it folds in on itself at some point, and you would start talking to the same people over and over. So I think I would recommend to go TRG first or the Center contacts first, and then if you want to get another view, you could come to the Ombudsman through the RFD.

MR. MELKERSON: Just a follow-up on the Center contacts. If the decisions have already been reached, the Center contacts will actually know that ahead of time, so by contacting them first you can get an idea of whether or not a similar product has already been taken to the TRG or the Ombudsman's Office. So they may actually be the best point of contact initially.

MS. KUPCHYK: Any other questions?

QUESTION: I would like to ask my question again and maybe be more specific. I'll be as generic as possible, but there are demineralized bone products, for example, that have components that are not just buffers. They offer structural properties or handling properties, some of which we know have been regulated as Class II or even Class III devices prior. I'm not naming names, but I think this group is probably familiar with that. Are these being addressed by TRG? Are you waiting for sponsors to come to you?

DR. SOLOMON: We have seen several of these products come through the TRG. This would be what we would consider a class-wide answer, because we want to try to be consistent and develop a policy that would apply across the board. So we have had internal discussion about demineralized bone combined with other stuff, and we are going to try to, I guess, really address it or address it as a class or release something in draft or perhaps have additional meetings on that. What I'm trying to say is, we haven't come to a decision yet.

MS. KUPCHYK: Any other questions? Well, going--

[Applause.]

MS. KUPCHYK: I do have one comment. You can't go yet. One comment was to ask the audience for ideas or suggestions about additional ways for the TRG to be more transparent, other than the ones that we've talked about here and that we're thinking about and considering, if you have any specific suggestions.

If you are bashful and would like to speak to us privately, that would be just fine also. We'll be here for a few minutes. And please, before you leave the area, if you would sign in--if you haven't already, there

is a sheet of paper outside--we'd appreciate it, and thank you again.

[Whereupon, at 11:15 a.m., the workshop was concluded.]