CBER Advisory Committees

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This presentation will discuss the CBER Advisory Committees.

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CBER has an advisory committee program in which outside experts advise and help the agency do its chores. The agency itself has considerable expertise, with some of the best scientists and clinicians.

However, it's difficult to keep up with the cross-cutting new technology in all areas, such as gene therapy, stem cell product, genomics, transgenic plants and animals, xenotransplantation, and some of the new vaccines. Companies may come in and ask the agency how they develop a product that they want to put on the market in three to five years with this new technology. Trying to design a roadmap is very difficult, so advisory committees are used. Issues and challenges for CBER in the regulation of novel products from new technologies, include: Increasing Workload; Human Genome projects, such as Genomics and Proteomics; Gene Therapy and Cellular Therapies; Xenotransplantation; Transgenic Plants and Animals; Cloning; Nucleic Acid Vaccines; Setting Standards/Controls, and Therapeutic Equivalence.

SLIDE 3
FDA's philosophy for using advisory committees is simple. The most sound basis for wise regulatory decisions is good scientific evidence, and the thoughtful advice of public-spirited experts who have taken the time to study, and listen, and learn the issues. So CBER will bring in experts from all over the country. It used to be from all over the world, but as you will soon see, these experts have to be U.S. Government employees. If they're not, they're processed to become U.S. Government employees, known as "special government employee", or SGE.

That really limits participation to U.S. citizens. However, the speakers at the advisory committees, and the people who contribute are, of course, from all over the world.

However, all advice from advisory committees is in the form of recommendations. There is no requirement for the agency to follow the recommendations of an advisory committee, but, in fact, it is most commonly followed.

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CBER has five advisory committees, which are listed on this slide. They range across the various product categories that CBER regulates. But five advisory committees staffed with experts is really not enough to solve all the problems the Center may have.

So frequently, the Center will go to other centers. In total, FDA has 33 advisory committees. Some of those advisory committees have subcommittees and panels. A large number of advisory committees are available to advise CBER and give recommendations. Sometimes in the case of a cross-cutting issue, there will be a meeting with several committees to give advice on a specific topic.

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Who is on the advisory committees? Scientific, clinical, and technical experts. In addition, there is always a statistician, a consumer representative, and an industry representative on a committee.

You may ask why is there both a consumer representative and an industry representative, if these are scientific and technical advisory committees?
It is believed that the more input received from different perspectives, the better, including input received from consumers and industry. An industry representative cannot vote, but he/she can sit at the table and enter into the discussions throughout the advisory committee meeting.

In addition to the scientific, clinical, and technical experts, there will be a patient representative, if it is a life-threatening illness such as cancer, HIV, and other life-threatening diseases.

Also required, are two experts in the particular disease or condition that the product is intended to treat.

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On average, there are about 12 to 17 members for every advisory committee.
In addition to advisory committee members, there is a pool of consultants. CBER has about 300 consultants. So, if there is a short question, or a need for targeted advice, an individual consultant may be asked for input. However, if there is a major issue for consideration, CBER takes the issue to a full committee, and receives the recommendations from the full committee.

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So how does CBER know when to take an issue to the full advisory committee?
The types of advice being sought from advisory committees are recommendations regarding the design of clinical trials, the development of guidelines, recommendations concerning post-marketing studies, and recommendations on whether the benefits outweigh the risks for the conditions posed on the label. CBER also does this for the review of research.

There is a strong research program in CBER, though the researchers also do review work and are commonly referred to as research-reviewers. It is the advisory committees which review their research, inasmuch as the committees are composed of experts in the various fields, and can provide substantive reviews of the research programs.

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And of course, CBER also does product approvals. Not all pending product approvals are taken to advisory committees, but many are.

What are the types of product approvals that would be taken to an advisory committee meeting? They have to be significant new products, those with significant potential for risk, compared to a normal therapeutic benefit; those with controversial efficacy; those under consideration for post-marketing studies; those that may be withdrawn from the market because of safety or questionable efficacy; and other products in which the public expresses a significant interest.

So, a routine product approval would never see the light of an advisory committee, but product approvals meeting the criteria listed here, would be taken to an advisory committee meeting.

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In addition to getting advice in advisory committee meetings, CBER uses the venue as an opportunity to serve as a public forum. The process is very transparent, so the public can see not just what advice FDA receives, but the process behind the advice, and the deliberation involved in it. There could be a closed meeting, or part of a meeting, when it's necessary to discuss trade secret information.

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Whenever possible, FDA holds open advisory committee meetings which, again, are public forums. Any member of the public can come and listen to the debate, and even participate in the meetings. Each of the advisory committees has approximately one hour for an open public hearing. Anyone can come and comment during that time. Also, in order to enable public participation, all the briefing materials sent to the advisory committee members must be added to the CBER website 48 hours before a meeting, if it is a product approval, or earlier if it is not a product approval.

This is done so the public can see the issues and information that the committee members are reviewing in their deliberations. It is a very public process.

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This slide shows a typical advisory committee agenda, for a single topic going before an advisory committee. Typically, there are two topics going on the same

day, but it's possible to squeeze in more. However, this is a typical schedule for a product approval, where only one product approval is on the agenda.

Basically, FDA would introduce the topic, and the sponsor would give the presentation. Equal time is generally allotted for both sponsor and FDA presentations. This example shows each presentation has been given 90 minutes. FDA's presentation would never be longer than the time allowed the sponsor. There is also at least one hour of open public hearing for the public to present their comments prior to the committee discussion.

Afterwards, there is a committee vote and adjournment. With this standard meeting format, the sponsor is given an equal opportunity with FDA to make presentations before the committee. The committee acts as an independent, outside body of experts, hearing both "sides" in order to provide its advice to the agency.

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Each committee has a chair. The chair will run the meetings. FDA has a full time person called the "designated federal officer", who may have responsibility for one or more advisory committees, and provides the administrative support for them.

The designated federal officer also is responsible for nominations for advisory committees, all the logistics, the scheduling of the meetings, the documentation, and adherence to the statutes and policies that govern advisory committees.

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The designated federal official is really the focal point for communication between the committee members, the press, the general public, FDA reviewers and, of course, the sponsor.

FDA reviewers do not speak directly to the committee members. They go through the designated federal official. When a sponsor brings an issue before an advisory committee, they are not allowed to contact the advisory committee members. All must go through the designated federal official in order to communicate and exchange information. So, the designated federal official is really the central link in the advisory committee program.

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Who is invited to serve on an advisory committee? They must be a full time government employee, or they are processed to become “special government employees'. In fact, most members are not full-time government employees, since most are academics.

When asked to serve FDA, a common question asked is "how much time is it going to take to serve?" The answer, except for filling out the paperwork, is that

they would be meeting possibly three to four times a year. When asked about the time needed for paperwork, the answer most often sent to the advisory committee members, is that the paperwork should be filled out in a week. There are about 21 different forms and, more importantly, the forms include all the rules and regulations involved in being an advisory committee member.

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If someone is just going to give advice, why does FDA have so many rules for a committee member? Because the person will be made an SGE, the paperwork they are asked to sign makes them acknowledge they are subject to criminal prosecution. Though the FDA has never criminally prosecuted an advisory committee member, the committee member is required, by law, to protect privileged information and ensure they have no conflicts of interest, or COI.

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Conflicts of interest are a very major concern regarding the advisory committee program. Some of the FDA regulated products, of course, involve a lot of money. Therefore, the FDA wants to make sure that advisory committee recommendations are impartial and fair.

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It is important to always have the public trust. No matter how good the advice is, if the public does not have confidence and trust in the advice that the advisory committee is giving, then the advice will not be as useful to the agency as it should be. So it's important that there be no conflict of interest issues, and that the public perceives the advisory committee process to be fair, since it is their tax dollars paying for the advisory committee meeting.

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What are the laws on COI prohibitions? The FDA advisory committee members may not participate in a particular matter's discussion -- and that is almost all the discussions going before an advisory committee -- if they have a direct, or an imputed financial interest that may be affected by the outcome of the meeting. The effect must be direct and predictable, and not speculative.

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That is what the rule says. But what really happens? FDA may contact a university and ask a professor to help the FDA in an advisory committee program.

The professor may have a few stocks and bonds set aside for retirement. FDA would ask the professor to disclose everything in the stock portfolio and that of their spouse or general partner. FDA also asks if the spouse or general partner is employed by industry. If this information shows a conflict of interest, FDA may not be able to use that person in an advisory committee program.

Though FDA likes to include people on the forefront of technology and doing research, these persons may have study grants and other funding contracts with regulated firms. FDA needs to be very cautious when, and if, using these people. And though the person's advice is really appreciated, FDA will need to weigh the 'excess baggage' this person may bring before allowing that person to sit in an advisory committee meeting.

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Each person potentially has something to disclose, so everyone is screened. Each person is asked to list all financial holdings related to an advisory committee meeting. FDA has three options moving forward. FDA can disclose it; can write a waiver for it; or can tell the committee member that their expertise is needed, but they are not permitted to participate at a given advisory committee meeting because of appearance of COI.

Remember, a lot of these things may not be an actual conflict of interest. It's the appearance of a conflict of interest that FDA screens for, in order to maintain the public's trust.

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Screening is not a one-time process. For every single meeting, the FDA re-screens advisory committee members to prevent any violation of title 18 of the United States Code, which restricts participation in an advisory committee meeting for any conflicts of interest. Members are screened for their own protection, because they would be in violation of a criminal law if they provided advice at an advisory committee meeting that would influence their financial wellbeing.

After an advisory committee meeting, the FDA may receive numerous e-mails indicating some background about a committee member that is of concern. FDA reviews any serious charges because it takes COI clearance at an advisory committee meeting very seriously. FDA does its best to make sure that advisory members do not have conflicts of interest.

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This presentation will not go into detail on the laws governing advisory committees. But advisory committees were in existence long before 1972, when the Federal Advisory Committee Act was passed.

The act was intended to limit the power of an advisory committee, and make sure it was open to the public. The law was amended in 1976, followed by the FDA Amendments Act of 2007. These are commonly known as the "sunshine laws."

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The Federal Advisory Committee Act also was enacted not only to control the operation of advisory committees and analogous groups, but also to control the growth in numbers of them. As a general matter, Congress has a very strong interest in those bodies giving advice to the government.

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FDA puts most of the information relevant to an advisory committee on a dedicated web page.

There is also a toll-free number for information on an advisory committee, or you can call the designated federal official.

Finally, you can subscribe to an automated e-mail list to learn information about the FDA advisory committees.

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Advice from an advisory committee lasts forever. Once the gavel goes down and the meeting is over, the committee is gone. You cannot go back and change it. When the gavel goes down, and the committee is not there anymore, FDA lives with their decisions.

These advisory committees are good, and very instrumental in getting good advice and giving the agency recommendations.

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This concludes the presentation, "CBER Advisory Committees".

We would like to acknowledge those who contributed to its development. Thank you.