

Overview: Office of Cellular, Tissue and Gene Therapies

SLIDE 1

This presentation is an overview of the Office of Cellular, Tissue, and Gene Therapies, or OCTGT.

SLIDE 2

This will review how OCTGT fits into the FDA, including the regulated products, policy development and outreach, and dialogue activities used to inform stakeholders of those policies. This will be a high-level overview. Additional details about OCTGT can be found in other presentations from this series.

SLIDE 3

FDA is made up of a number of Centers as listed on this slide. Some of the products regulated in OCTGT are combination products. The Office of Combination Products is located in the Office of the Commissioner. The purpose of this office is to make jurisdictional decisions and to facilitate communications between the Centers.

The Center for Biologics Evaluation and Research regulates vaccines, blood and blood products, human tissue and tissue products for transplantation, cell therapy, and gene therapy, donor screening tests for blood and tissue safety, devices.

The Center for Devices and Radiological Health regulates devices for treatment, implants, and diagnostic devices.

The Center for Drug Evaluation and Research regulates drugs, monoclonal antibodies and therapeutic proteins.

OCTGT is located in the Center for Biologics Evaluation and Research. CBER and OCTGT works closely with the Center for Devices and Radiological Health and the Center for Drugs Evaluation and Research.

SLIDE 4

The Center for Biologics is composed of 8 Offices. Three of these offices are responsible for product regulation: the Office of Vaccines, the Office of Blood and the Office of Cellular, Tissue and Gene Therapies.

SLIDE 5

There are three review divisions in OCTGT. The Division of Cell and Gene Therapies is by far the largest. This division contains both review and research/review scientists. The laboratory component conducts mission-relevant research as well as review of regulatory files.

The role of the division of human tissues is to regulate products that are defined as human tissues. The regulatory framework established by this division not only applies to the regulation of human tissues, but also affects the more highly manufactured products that are regulated in the other divisions.

The Division of Clinical Evaluation and Pharmacology and Toxicology consists of medical officers and toxicologists that are essential to the regulatory process.

The Immediate Office of the Director is composed of regulatory experts; those presentations are included in this series.

SLIDE 6

There is a wide variety of products regulated in OCTGT. A few examples are listed on this slide. There is a high degree of interest in cell therapy products. These products can range from therapeutic products derived from human embryonic stem cells at one end of the spectrum to expanded cartilage for articular cartilage repair at the other end. They also include cord blood for hematopoietic reconstitution, tumor vaccines, and immunotherapy for the treatment of cancer. Other products regulated in OCTGT are gene therapies, tissue products, and xenotransplantation products. Xenotransplantation and combination products will be discussed later.

Some devices are regulated in OCTGT. These devices include those used to make cells from tissues or combine cells and tissues and donor screening tests used to screen human tissues.

As you can imagine, sometimes these categories of products are not distinct. Often cell and gene therapies overlap, as in the case of gene modified cells.

SLIDE 7

The pre-market pathways for the categories of products in the previous slide vary depending on the product. This slide lists the pre-market review pathways available. Most of the products regulated in OCTGT are regulated as biologics and require an IND, or Investigational New Drug, for pre-marketing and a Biologics License Application for marketing.

Products regulated as a device would need an IDE, Investigational Device Exemption, and a PMA, Pre-Marketing Application, or an HDE, Humanitarian Device Exemption or a 510(k).

In the case where a product would be considered a combination product, or a product consisting of more than one regulated article, the Office of Combination Products will determine the pathway. This Office will look at inter-center agreements and precedents to make their determination. This is discussed in the presentation on product Jurisdiction. Information on this process can also be found on the FDA internet.

SLIDE 8

Human cells, tissues, or cellular-based products are referred to as HCTPs. The regulations for these products will be discussed in more detail later.

SLIDE 9

The legal authority used for the regulation of tissue-based products is the Public Health Service Act, which is aimed at preventing the introduction, transmission, or spread of communicable diseases.

A tiered risk-based approach covering a broad scope of cells and tissues is used to regulate these products. Tissue regulations are implemented through rulemaking. Some products are regulated purely as a human tissue -- in other words, only under the legal authority of the Public Health Service Act and some products need a pre-market review, a higher category of regulation.

Slide 10

Next let's discuss cell and gene therapy.

SLIDE 11

Examples of cell therapies include: pancreatic islets from allogeneic or other sources for the treatment of type 1 diabetes; stem and skeletal muscle progenitor cells for ischemic cardiac disease; hematopoietic reconstitution for treatment of malignancies, such as cord blood; and stem cells for metabolic storage disease, CNS indications and expanded autologous cartilage for joint repair. These are just a few examples of cell therapies. More details on cell therapy products are covered in another presentation in this series.

SLIDE 12

Gene therapies can either be transferred directly into a patient or delivered by way of ex vivo modified cells administered to subjects. This slide lists some of the various gene therapy vectors that have been seen. Another presentation in this series will discuss gene therapy in more detail.

SLIDE 13

Cell/scaffold combination products are also regulated in OCTGT.

SLIDE 14

Examples of cell scaffold products include: autologous or allogeneic cells, seeded on a collagen or synthetic, resorbable matrix for wound repair, cell

seeded scaffolds for cardiovascular repair, encapsulated pancreatic islets, and expanded, autologous cells on a matrix for cartilage repair.

SLIDE 15

Xenotransplantation is a product class that presents special concerns because of the potential for infectious disease exposure to not just the patient, but also a segment of the population that may come in contact with the patient. Therefore, a special policy has been developed to help prevent the spread of infectious disease from xenotransplantation products to the general population.

SLIDE 16

This is the Public Health Service definition of xenotransplantation. Any procedure that involves the transplantation, implantation, or infusion into a recipient of either live cells, tissues, or organs from a non-human animal source or human body fluid, cells, tissues, or organs that have had ex vivo contact with live non-human cells, tissues, or organs. Let us point out that this definition does not include highly processed animal tissue, such as bovine or porcine collagen matrices. These products are regulated as medical devices or as part of medical devices. Xenotransplantation policies do not apply to these products.

SLIDE 17

Now let's talk about the regulatory and scientific outreach and other forms of dialogue that take place in OCTGT.

There are a number of ways that OCTGT has dialogue with the public. There are product-specific confidential inquiries during the pre-submission process. Information on how to make a request for a product-specific confidential interaction with the Agency can be found on the website.

OCTGT often attends scientific meetings and gives scientific talks. This provides an excellent opportunity to dialog with the scientific community and to keep current on scientific issues that affect the products that OCTGT regulates.

Advisory committee discussions take place when independent, expert advice is needed on topics of interest. These kinds of committee meetings are public in general, but in some cases, there may be closed sessions. The discussions can be either on specific matters, that is, a specific marketing application, or on a general matter, such as scientific, technical, or policy issues. FDA may ask for advice on how to develop a certain kind of product or general safety issue.

The site visit program is an opportunity for FDA staff to visit a manufacturing establishment and learn how the establishment functions. The Office of Communications, Outreach and Development posts on the internet an invitation to sponsors to host an FDA visit to their facility for the purpose of educating reviewers. Staff members have visited tissue processing sites and cell therapy processing facilities as part of this program.

The OCTGT office also participates in many workshops and liaison meetings with industry, patient advocacy groups, and other government agencies.

SLIDE 18

As noted in the previous slide, sponsors may obtain FDA advice during the pre-application or the investigational phase for INDs and IDEs. Before a sponsor has a meeting with CBER, however, they must provide a meeting package containing background information on the proposed clinical trial and specific questions that they would like answered by the Agency. These meetings are confidential and typically product-specific. They can be used to clarify procedures and expectations of the Agency, or to resolve disputed issues.

This is a very active program. OCTGT has several of these meetings each week. Sponsors are encouraged to meet with the Agency at all stages of development, even before they think they are ready to submit an application.

In some cases, a sponsor might meet with the Agency a couple of years before they plan on submitting an application for a novel product. For example, the sponsor might discuss the kinds of data that will be needed to get their initial clinical study approved. Or, a sponsor may come to the FDA before they start animal studies to ask for advice on the design of animal studies.

Each Center has its own procedures for requesting and holding these meetings. For CBER, these are documented in CBER SOPP 8101.1, which can be found on the internet.

SLIDE 19

This slide shows some examples of Workshops that have been co-sponsored by FDA.

A meeting on animal models for treatment of acute radiation syndrome took place in September of 2008 in conjunction with our colleagues at the National Institute of Allergy and Infectious Diseases, or NIAID, at the National Institutes of Health. This workshop focused on animal models for the treatment of acute radiation syndrome, which is a particularly challenging area since the development of this type of product would most likely have a portion of its development done under the so-called animal rule. The animal rule is a mechanism for getting a product approved without a pivotal human clinical study, which, in this case, would be the most appropriate pathway for approval.

FDA also co-sponsored a workshop discussing clinical trial end points for acute graft-versus-host disease, after allogeneic hematopoietic stem cell transplantation. This topic is certainly of considerable interest due to the challenges in studying this graft-versus-host disease.

A workshop on therapeutic cancer vaccines, called Considerations for Early Clinical Trials based on Lessons Learned from Phase 3 Clinical Trials, was co-sponsored by FDA and the National Cancer Institute. For this workshop, FDA did a look-back at the phase 3 studies across the office, not just in cancer, but also in some of the other fields, to see if similarities could be found between the trials, and to tabulate lessons learned from these trials. Many of the phase 3 trials failed, so phase 2 data that was used to initiate the phase 3 studies was looked at. FDA and the cancer community discussed what might be done in phase 2 trials to better design phase 3 trials.

And finally, there was a workshop with the Juvenile Diabetes Research Foundation and NIH looking at beta cell transplantation, since there has been a lot of recent interest in renewable cell sources for beta cell transplantation.

SLIDE 20

OCTGT has a very active laboratory research program in the areas listed on this slide.

The most recent addition is the research program on human tissue safety. This is a challenging area of research. As the tissue rules were implemented, a number of questions arose concerning infectious diseases. This tissues-research program will assist in developing policy with respect to donor screening and donor testing.

SLIDE 21

References for the regulatory process for products regulated in the Office of Cellular, Tissue, and Gene Therapies, including guidance documents and standard Operating procedures, can be found at this web address.

Slide 22

This concludes the presentation, "Overview of the Office of Cellular, Tissue, and Gene Therapies."

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