

Script for CDRH Learn Module 1 - OOPD

Slide 1

Hello, my name is Eric Chen. I am the Director of the Humanitarian Use Device Designation program in the Office of Orphan Products Development. Welcome to CDRH Learn, the Center's resource for multimedia industry education. The title of this presentation is, "Office of Orphan Products Development." This presentation will provide industry with information that is comprehensive, interactive, and easily accessible with regards to the programs supported by the Office of Orphan Products Development.

Slide 2

After watching this program, you should have a better understanding of the Office of Orphan Products Development, the programs that are overseen by the Office, and the legislative basis and evolution of the Humanitarian Use Device, or H-U-D, designation and the Humanitarian Device Exemption, or H-D-E, programs.

Slide 3

Before we get into an overview of the programs in the Office of Orphan Products Development, or OOPD, I want to present a 'rare disease who's who at FDA' at a glance. This figure illustrates only a portion of the FDA. If you look to the lower left of this figure, you will see a star labeled as OOPD. Moving towards the middle along the dotted line, you'll see that OOPD is located in the Office of Special Medical Programs, which is housed under the Office of Medical Products and Tobacco. OOPD is situated outside of the FDA Regulatory Review Centers of CDER, CBER, and CDRH, because our programs work on all rare disease products issues including drugs, biologics, and devices. We also work with the Center for Food Safety and Applied Nutrition on medical foods related to rare diseases. We also work closely with the Office of Health and Constituent Affairs as shown on the left side of the diagram that assures patient preferences are taken into consideration when forming FDA's regulatory policy for rare diseases. If we go back to the CDER circle in the middle of the slide, within CDER is their Rare Diseases Program. This maintains consistency in the review of rare disease drug and biologic products. It also develops policy and procedures for the review of these treatments. We work closely with this group.

Slide 4

The challenge that exists in rare diseases is that only a portion of the 7,000 known rare diseases have approved treatments in the United States. This slide lists the number of currently approved products and represents FDA's

accomplishment as we've made real progress with the number of drug approvals and humanitarian use device approvals.

Slide 5

The OOPD mission is to promote the development of products, including drugs, devices, biologics, and medical foods, for the treatment, diagnosis, and prevention of rare diseases and conditions. These are products that demonstrate promise for rare diseases and other orphan conditions, such as those requiring pediatric device development. OOPD oversees programs that provide development incentives as well as coordinating cross-cutting rare diseases activities.

Our programs fall within two columns shown here as designation programs or grant programs. In our designation programs, we have our orphan drug, rare pediatric disease and humanitarian use device designation programs. In our grant programs, we have our orphan products grants, pediatric device consortia grants, and orphan products natural history grants. OOPD evaluates scientific and clinical data submissions from sponsors to identify and designate products for rare diseases and to further advance scientific development of such promising medical products. The Office also works on rare disease issues with the medical and research communities, professional organizations, academia, governmental agencies, industry, and rare disease patient groups.

We'll briefly discuss each program in the following slides.

Slide 6

We'll now discuss the Orphan Drug Designation Program in OOPD.

Slide 7

The Orphan Drug Designation program was authorized in 1983 under the Orphan Drug Act. The program provides a special status to a drug or biological product that is intended to treat, diagnose, or prevent a rare disease or condition. Orphan designation qualifies the sponsor of the drug for various development incentives of the O-D-A, including tax credits for qualified clinical testing, waiver of the marketing application user fee, and the possibility of 7 years marketing exclusivity.

Slide 8

The Orphan Drug Act defines a rare disease as any disease or condition which affects fewer than 200,000 persons in the United States; or more than 200,000

persons if there is no reasonable expectation that the cost of developing and making it available will be recovered from sales in the United States.

Slide 9

We'll now discuss the Rare Pediatric Disease Designation Program.

Slide 10

The Rare Pediatric Disease Designation program was created in 2012 to encourage the development of drugs and biologics for rare pediatric diseases. Under this program, a sponsor who receives approval for a drug for a rare pediatric disease may qualify for a priority review voucher of a subsequent marketing application for a different product. This priority review voucher means FDA will review and take action no later than 6 months after receipt of the new drug marketing application. This is compared to the usual 10 month review period.

For more information about this program, please visit the website link at the bottom of the slide.

Slide 11

We'll now discuss the Orphan Products Grants program.

Slide 12

The Orphan Products Grants program provides funding to support the clinical development of products for use in rare diseases or conditions where no current therapy exists or where the proposed product will be superior to the existing therapy. These grants apply to the clinical study of drugs, biologics, devices or medical foods to collect safety and/or effectiveness data that will result in, or substantially contribute to, market approval of these products. These grants are usually 3-4 years long and at any time the office is funding has 60-85 ongoing grants and funds about 10-15 new grants per fiscal year. For more information about this grant program, please visit the website listed on this slide.

Slide 13

We'll now discuss the Orphan Products Natural History Grants program.

Slide 14

The OPD Natural History Grant Program is the newest OOPD program and you may be wondering "What is a Natural History Study?"

A natural history study is a well-designed, well-thought out, and well-planned attempt to learn about what happens to people who are affected by a particular specific rare disease or condition. Most often, rare diseases have names and some information about their clinical manifestation. However, the majority lack a thorough understanding of the natural history of the disease or an understanding of the pathogenesis of the disease, or even treatments to target the disease.

The goal of the OPD Natural History Grants program is to help support studies that will advance rare disease product development through characterization of the natural history, identification of genotype, and development or validation of clinical outcome measures.

For more information about this grant program, please visit the website listed on this slide.

Slide 15

We'll now discuss the Pediatric Device Consortia Grants program.

Slide 16

The Pediatric Device Consortia grants program funds nonprofit consortia that stimulate projects for pediatric device development. The consortia provide expertise to innovators of pediatric devices by providing them with various services, including legal, funding advice, and clinical study planning. For more information about this grant program, please visit the website listed on this slide.

Slide 17

We'll now discuss the Humanitarian Use Device Designation program.

Slide 18

This regulatory program supports device development for rare diseases. There are two key, and similar sounding terms that are important to understand with this.

First, we have the Humanitarian Use Device, or H-U-D. This is a medical device intended to benefit patients in the treatment or diagnosis of a disease or condition that affects or is manifested in not more than 8,000 individuals in the United States per year.

The second key term is the Humanitarian Device Exemption, or H-D-E. This is the premarket submission that allows an H-U-D to be marketed once a demonstration

of safety and probable benefit has been satisfied by FDA. The H-U-D/H-D-E Program was created by Congress to provide an incentive for the development of devices for the treatment or diagnosis of diseases affecting small (rare) patient populations.

The Humanitarian Use Device and the Humanitarian Device Exemption Program can be broken into two distinct parts. I will describe in more detail the program and how the laws and regulations are written, interpreted and implemented in the subsequent slides.

Slide 19

Let's take a step back and look at what is written in the law. The law was created in 1990 under Section 520(m) of the Food, Drug and Cosmetic Act and recently updated in the passing of the 21st Century Cures Act. The purpose of this program was to "...encourage the discovery and use of devices intended to benefit patients in the treatment and diagnosis of diseases or conditions that affect not more than 8,000 individuals in the United States."

Slide 20

As usual, a regulation intends to further clarify a Law. In this case, the relevant regulation is 21 CFR 814.100a. The current regulation clarifies the term "fewer than 4,000 individuals" and states that the H-U-D/H-D-E program was established "...to encourage the discovery and use of devices intended to benefit patients in the treatment or diagnosis of disease or conditions that affect or are manifested in fewer than 4,000 individuals in the United States per year." This per year interpretation serves the primary purpose of the law to provide such incentive to the program and will be discussed in more detail in another module. Note that regulations are developed after the law has been changed at the time of taping this module, the regulation had not been updated to the "no more than 8,000" individuals in the United States per year threshold.

Please note that this definition differs from that listed in the Orphan Drug Act for Orphan Drugs. The number cited in 21 CFR 814.100a and corresponding population estimate, is important when submitting the HUD application to the Office of Orphan Products Development for H-U-D designation. This is further discussed in subsequent modules that we encourage you to view.

Slide 21

In order to have a better understanding of current legislation governing the H-U-D/H-D-E program, it is important to understand its history.

As I mentioned previously, in 1990, Congress passed the Safe Medical Devices Act (or SMDA), which created the program as an incentive for the development of devices targeting diseases affecting small (rare) populations. At that time, sponsors were not permitted to sell any devices approved through the H-U-D/H-D-E pathway for profit (i.e., could only sell them for the cost of research, development, fabrication and distribution).

The Food and Drug Administration Modernization Act of 1997 (FDAMA) made some revisions to the program. Among other things, the law required FDA to issue an order approving or denying an HDE within 75 days after receiving an application. It also provided an exemption to allow an H-U-D to be used without IRB approval in emergency situations (more on IRB review in presentations to come), and it eliminated the requirement that the sponsor must obtain approval for continued use of the device every 18 months. It also removed the sunset period for new HDE approvals.

Slide 22

In 2007, the Food and Drug Administration Amendments Act (FDAAA) was passed. In order to motivate the development of pediatric devices, FDAAA allowed devices labeled for use in a pediatric population or sub-population and approved under an H-D-E after September 27, 2007 to be eligible to be sold for a profit. These devices could be sold for profit as long as the number of devices distributed in any calendar year did not exceed the annual distribution number (or A-D-N) for the device, which is a number calculated by FDA. If the number of devices distributed exceeds the ADN, the sponsor can continue to sell the device but just not for profit for the remainder of the year.

Additionally, as a check on postmarket safety, FDAAA added a requirement that the FDA's Pediatric Advisory Committee (PAC) would conduct an annual review of H-D-E approved pediatric devices permitted to make a profit to ensure that the H-D-E remains appropriate for the pediatric populations for which they are approved.

Slide 23

In 2012, the Food and Drug Administration Safety and Innovation Act (FDASIA) expanded the ability to make a profit to H-D-E approved devices intended for adult populations without undermining the pediatric incentive. It also changed the definition for the annual distribution number. In addition, sponsors of

devices that received HDE approval prior to FDASIA may ask FDA for the ability to make a profit, if they meet the eligibility criteria.

In 2016, the 21st Century Cures Act provides FDA with the authority to use 8,000 as the limit when determining if a device qualifies for the H-U-D/H-D-E program. It also removed the requirement that a H-D-E sponsor always use a local institutional review board. The change will allow for use of centralized models.

Slide 24

The regulation explains that the H-U-D/H-D-E pathway has a two-step process. First, a sponsor must obtain H-U-D designation from OOPD. Once the HUD designation is received, the sponsor may then submit their H-D-E marketing application to the review divisions in either CDRH or CBER. The review divisions evaluate the data to support safety and probable benefit which is discussed in more detail in the subsequent H-U-D/H-D-E program modules. Please refer to these modules for more information about the H-U-D and H-D-E review and post-market process and requirements.

Slide 25

In Summary, OOPD's mission is 'to promote the development of products, including drugs, devices, biologics, and medical foods, for the treatment, diagnosis, and prevention of rare diseases and conditions.' OOPD manages three designation programs, the orphan drug, rare pediatric diseases, and humanitarian use device designation programs. The office also manages three grant programs, the OPD grants program, pediatric device consortia grants program, and OPD natural history grant program. The H-U-D/H-D-E program allows for a pathway to market for medical devices intended to treat or diagnose diseases that occur in small (rare) populations.

Slide 26

If you have questions regarding the programs administered by the Office of Orphan Products Development described in this presentation, please contact us via email or telephone using the information show on this slide. For further reference, you may also refer to our website located at the link on this slide.

Slide 27

Thank you for watching the "Office of Orphan Products Development" presentation. Please consider watching the entirety of the H-U-D and H-D-E program modules to develop a complete understanding of these programs.

CDRH provides multiple opportunities for industry education. CDRH Learn provides over 80 online modules which provide a wide-range of CDRH education that can be accessed via the link provided on this slide. Device Advice is text-based education, please use the link above to access the guidance document. In addition, the Division of Industry and Consumer Education (DICE) provides live agents to answer industry questions. Please either contact us via email or at the phone numbers provided above. For more information, please visit our webpage.

Thank you for your attention.