What is an Investigational Device Exemption (IDE)?

Lynn Henley

SLIDE 1

Hello. My name is Lynn Henley. I represent the IDE Program Office within the Office of Device Evaluation at the Center for Devices and Radiological Health. Welcome to a presentation introducing IDEs, or Investigational Device Exemptions.

SLIDE 2

This presentation is not intended to be all-inclusive. The objective is to highlight some of the critical components of the IDE program. Today I am going to discuss the purpose of an IDE submission; different types of IDEs; study determination or pre-submission; what an IDE does and does not permit; when manufacturers or physicians should seek an IDE; significant risk determinations; diagnostic studies; and IDEs within the product development process.

SLIDE 3

1) What is an IDE? You may be wondering what exactly is meant by the term, "Investigational Device Exemption." The term refers to a regulatory submission that permits clinical investigation of devices. This investigation is exempt from some, but not all, regulatory requirements for medical devices. The name stems from the following description:

2) What is an exemption? "An approved investigational device exemption (IDE) permits a device that otherwise would be required to comply with a performance standard or to have premarket approval to be shipped lawfully for the purpose of conducting investigations of that device." Therefore an IDE exempts an unapproved device from the applicable law for shipping into interstate commerce.

Please note that during this presentation I will be using the terms "investigation of a device," "clinical investigation," "investigation," and "study" interchangeably.

SLIDE 4

The Federal Food, Drug, and Cosmetic Act, referred to as the FD&C Act, is the statutory law passed by Congress. The Code of Federal Regulations is a codification of the rules published in the Federal Register by Federal agencies, including FDA. The Code is divided into 50 titles which represent broad areas subject to Federal regulation. Title 21 covers Food and Drugs, which pertain to the Food and Drug Administration.

The parts of 21 CFR listed here are those with the most relevance to IDE regulation: Part 812, which outlines the IDE regulations; Part 50, which deals with human subject protection and informed consent, Part 54, which describes how investigators should disclose their financial interests; and Part 56, which delves into the responsibilities of Institutional Review Boards. As you proceed with your clinical investigation, you may need to refer to these sections of the CFR.

SLIDE 5

Section 520(g) of the Federal Food, Drug, and Cosmetic Act states that the purpose of an IDE is, "To encourage discovery and development of useful medical devices for human use, to the extent consistent with the protection of the public health and safety and with ethical standards, while maintaining optimum freedom for scientific investigators in their pursuit of that purpose."
This purpose expands upon FDA's mission, which is protecting and promoting public health.

SLIDE 6

The purpose of an IDE is to allow an investigational device to be used in a clinical study to collect safety and effectiveness data for a marketing application. An IDE also permits a device to be shipped lawfully so that it can be studied in a clinical investigation.

SLIDE 7

The IDE regulation stipulates that all clinical investigations that are subject to the regulation must be approved before they can begin; it assigns responsibilities to all participants in the clinical study; and mandates that all subjects in the investigation be given informed consent.

SLIDE 8

We will now describe the difference between an investigational device and investigational use. An investigational device is defined as still in the developmental stage; it is the object of a clinical investigation to determine safety and effectiveness; and is not considered to be in commercial distribution. Investigational use of a device refers to clinical evaluation of an already legally marketed device for a new intended use or a new indication for use.

SLIDE 9

IDEs come in many forms. They may be early feasibility or traditional feasibility during the exploratory stage; if the study is evaluating safety and effectiveness for a marketing application, it would be deemed a pivotal study. An early feasibility study is a limited clinical investigation of a device early in development, typically before the device design has been finalized, for a specific indication (e.g., innovative device for a new or established intended use, marketed device for a novel clinical application).

It may be used to evaluate the device design concept with respect to basic safety and device functionality in a small number of subjects (generally fewer than 10 initial subjects) when this information cannot be readily provided through additional nonclinical assessments or appropriate nonclinical tests are unavailable.

Information obtained from an early feasibility study may guide device modifications. An early feasibility study does not necessarily involve the first clinical use of a device. The early feasibility category also includes first in human studies. A first in human (FIH) study is a type of study in which a device for a specific indication is evaluated for the first time in human subjects. A traditional feasibility study is defined as a clinical investigation that is commonly used to capture preliminary safety and effectiveness information on a near-final or final device design to adequately plan an appropriate pivotal study. As compared to an early feasibility study, more nonclinical (or prior clinical) data are necessary for approval to initiate a traditional feasibility study; however, a traditional feasibility study does not necessarily need to be preceded by an early feasibility study. A pivotal study is a clinical investigation designed to collect definitive evidence of the safety and effectiveness of a device for a specified intended use, typically in a statistically justified number of subjects. It may or may not be preceded by an early and/or a traditional feasibility study.

CDRH also makes available several types of expanded access to investigational devices during the device development process. Emergency use is intended for life-threatening situations. Although prior FDA approval is not required or given, the IRB chair must provide concurrence prior to use of the device. However, FDA must be notified within five working days after the sponsor learns of the use of the product.

Compassionate use is appropriate for a serious condition when there is no alternative. It may be requested before or during an IDE. It is usually requested for a single patient, but in some cases a small group may be studied under an IDE.

Treatment use of an investigational device is intended to be used for a life-threatening or serious condition during or after an IDE when no comparable or satisfactory alternative is available.

Continued access is intended to extend the investigation while the marketing application is prepared. It allows collection of additional safety and effectiveness data if there is a public health need for the device and preliminary evidence exists that the device is likely to be effective and that no significant safety concerns have been identified.

SLIDE 10

This graph depicts the stages of device development during which each type of expanded access may be requested.

SLIDE 11

If an IRB is uncertain whether a study is exempt, significant risk, or non-significant risk, FDA will make a determination. In these cases, the sponsor submits a draft protocol and details about the device to be investigated in the form of a Pre-Submission. This process presents an opportunity for the sponsor to get feedback on their study from the review division that will eventually be evaluating their marketing application, if applicable. FDA will issue a determination letter within approximately 60 days. This decision is binding for both the sponsor and the IRB.

SLIDE 12

IDEs are exempt from regulations pertaining to misbranding under section 502 of the act; registration, listing, and premarket notification under section 510; premarket approval under section 515; performance standards under section 514; good manufacturing practice requirements under section 520(f) except for the requirements found in 820.30; color additive requirements under section 721; a banned device regulation under section 516; restricted device requirements under section 520(e); and records and reports under section 519.

SLIDE 13

Approved IDEs are not exempt from regulations pertaining to adulteration; labeling; prohibition on promotion and/or marketing, commercialization, prolonging the investigation, representing the device as safe and effective; and import/export requirements. You may find more information about these regulations in the Federal Food, Drug and Cosmetic Act under Section 501 as well as in 21 CFR 812.5, 812.7, and 812.18.

SLIDE 14

Studies which are subject to the IDE regulation are those intended to support a marketing application, those for collection of safety and effectiveness information, and sponsor-investigator studies of an unapproved device or a new intended use of an approved device, even if no marketing application is planned.

SLIDE 15

This chart helps determine how to determine whether your study needs an IDE and, if so, whether your study is significant risk or non-significant risk. First you must determine whether your study is subject to the IDE regulation. If it is exempt, you do not need to send in an IDE. If it is subject to the IDE regulation, you need to determine whether it is significant risk (SR) or non-significant risk (NSR). Significant risk studies are subject to the full requirements of the IDE regulations, whereas non-significant risk studies are subject to abbreviated requirements.

Please note that study risk determinations take into account not only the device but how the device is used in the study and other procedures in the study which may increase the overall risk of the study.

SLIDE 16

Studies that are exempt from the need for an IDE include pre-amendment or pre-1976 devices; 510(k)-cleared or PMA-approved devices, if used in accordance with approved labeling; in vitro diagnostic devices (most of the time); consumer preference testing; combinations of legally marketed devices; and custom devices, which are rarely granted this exemption. CDRH's Office of Compliance can assist sponsors with determining whether a device meets the custom device criteria. The criteria may be found in 21 CFR 812.3.

SLIDE 17

Section 906 of the Food, Drug and Cosmetic Act addressed the practice of medicine issue by stating, "Nothing in this Act shall be construed to limit or interfere with the authority of a health care practitioner to prescribe or administer any legally marketed device to a patient for any condition or disease within a legitimate health care practitioner-patient relationship." This means that a legally marketed device can be used outside its approved indication by a physician to care for a patient, as long as it is not used in a clinical trial.

SLIDE 18

If a physician uses a device under the practice of medicine, he or she should be well-informed about the product, use firm scientific rationale and sound medical evidence, and maintain records on its use and effects. An IDE is not required; however, the institution may require IRB review or approval and informed consent. The prohibitions related to unapproved uses of legally marketed devices still apply.

SLIDE 19

Studies involving basic physiological research are exempt from an IDE. These studies are investigating a physiological principle and the sponsor has no intention of developing the device for marketing purposes. They would only use the device to address the research question. The device itself is not being studied, and no safety or effectiveness data are being collected on the use of the device. There is no IDE needed; however, IRB approval and informed consent should be obtained.

SLIDE 20

If the study is not exempt from the device regulation then, you must determine whether the study is significant risk or non-significant risk. IRBs usually make this determination. If the IRB or sponsor do not want to make the risk determination, FDA can assist with the process. However, if FDA makes the determination, that decision is final.

SLIDE 21

A significant risk study is defined as presenting a potential for a serious risk to the health, safety and welfare of a subject and is an implant, used in supporting or sustaining human life, or of substantial importance in diagnosing, curing, mitigating, or treating disease or preventing impairment of human health.

SLIDE 22

Examples of significant risk studies include evaluation of a marketed biliary stent for use in the peripheral vasculature, evaluation of an unapproved radiofrequency ablation device for treatment of primary hepatic neoplasia, and most studies of extended wear contact lenses.

SLIDE 23

In the case of significant risk studies, the sponsor submits the IDE application to FDA. FDA then approves, approves with conditions, or disapproves the IDE within 30 calendar days. If FDA does not respond within 30 days, the IDE is considered "deemed approved." The sponsor then obtains IRB approval. After both FDA and the IRB approve the investigation, the study may begin.

SLIDE 24

Each IDE submission should include only one indication. If a sponsor sends in an additional study for an IDE, that study will receive a new 30-day review clock. If the review results in "approved with conditions," this means that the study may begin, but that certain conditions have been stipulated and must be met by the sponsor. Most IDE review decisions consist of either "approved" or "approved with conditions."

SLIDE 25

In the case of non-significant risk studies, the sponsor presents the protocol to the IRB and a statement as to why the investigation does not pose significant risk. If the IRB approves the investigation as NSR, the study may begin. Abbreviated IDE requirements apply in this situation, including labeling, IRB approval, informed consent, monitoring, reporting, and prohibition of promotional activities. No IDE submission to FDA is necessary.

SLIDE 26

Examples of non-significant risk studies include most functional MRI studies, a study of a non-invasive blood pressure measuring device, electro-encephalography studies, and most studies involving daily wear contact lenses.

SLIDE 27

When an IDE is required for in vitro diagnostic studies, the same principles of significant risk versus non-significant risk apply. Studies are generally of a therapeutic nature, where the IVD device is used to select or assign patients. The use of IVD test results to assign different study arms may result in either significant risk or non-significant risk.

Correlation studies, where IVD test results do not impact patient management in those studies, are generally exempt from the need for an IDE. In vitro diagnostic tests, including any combination of equipment, disposables, software, procedures, or algorithms, used in clinical trials outside their cleared or approved intended uses are considered investigational devices by FDA. However, though in vitro diagnostic tests used in such a manner are investigational devices, this does not imply that such a use automatically requires an IDE.

SLIDE 28

Companion diagnostics involve both IDEs and Investigational New Drug applications, or "INDs." With these products, the sponsor may submit an IDE to CDRH or device validation information in an IND to the Center for Drug Evaluation and Research, also known as CDER, or the Center for Biologics Evaluation and Research, or CBER. There is no need for both applications, as CDER or CBER will consult CDRH when appropriate.

SLIDE 29

In regard to Clinical Laboratory Improvement Amendments, or CLIA, we would like to point out that results reported from human testing are subject to CLIA. CLIA regulates clinical laboratory practice, while the FD&C Act regulates the medical devices used in clinical laboratories. Patient-specific investigational in vitro diagnostic data, for example that reported and used to select subjects for trials or to assign or alter subjects' clinical management, must be generated in compliance with CLIA.

SLIDE 30

IDEs play a key role in the product development process. A medical device begins with a concept, develops into a prototype, goes through preclinical and clinical testing (where IDEs come into play), premarket review and clearance or approval, manufacturing, marketing, commercial use, and, eventually, obsolescence. At CDRH we refer to this as the Total Product Life Cycle. As we pursue FDA's mission to promote and protect public health, we look forward to working with our commercial partners throughout this cycle to bring innovative products to the American public.

SLIDE 31

FDA has published a helpful information sheet on significant risk determinations available at the web link shown here: "Information Sheet Guidance for IRBs, Clinical Investigators, and Sponsors." You may also consult "Device Advice", which is a comprehensive source of information on IDEs via this web link. "CDRH Learn" is a series of videos on many subjects pertaining to several aspects of device regulation available via this web link. It is especially helpful in the area of IDE sponsor responsibilities, investigator responsibilities, roles of Institutional Review Boards, and in Bioresearch Monitoring.

SLIDE 32

Our staff is ready to help you with your IDE questions. Contact us at 301-796-5640. Thank you!
