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Medical Device Clinical Trials – How Do They Compare with Drug Trials?

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Note: The views expressed in this article are those of the author and do not necessarily represent those of the employer, GxP Lifeline, its editor or MasterControl Inc.

It seems like the clinical research world is often thought of in terms of pharmaceuticals. Clinical trials are often referred to in Phases, such as "a Phase 2 study of a new drug" or "a Phase 3 randomized clinical study with a placebo control." Although clinical trials for medical devices have many similarities to those for pharmaceuticals, there are some necessary differences in the way the trials are designed and carried out. And in some cases, for medical devices, clinical trials may not even be required!

Clinical Trial Classifications

New drugs are studied carefully in Phases, starting with an introduction to a small number of healthy subjects (Phase 1), toward use in large populations with the disease or condition indicated for treatment (Phase 3). Even slight modifications in the chemical composition of a new drug can result in unanticipated effects (both positive and adverse) that must be studied in a controlled setting. Phase 1 studies often start with fewer than 50 subjects, and Phase 3 trials can have thousands. In order to determine the rare side effects, including interactions with other drugs, they must be studied in these large populations.

However, for medical devices, especially those that require a surgical implant, it is not appropriate to insert the devices into healthy subjects. Instead, device trials may initially be conducted in a smaller "pilot" population with the disease or condition being studied, before moving into the larger "pivotal" population. The total number of subjects needed to show safety and effectiveness is often only one or two hundred, rather than thousands needed for drug trials.

In either case of drug or device, after approval there is often a requirement for long-term data. For drug studies, this is considered Phase 4, and in device studies, this is considered a Post-Approval Study. A comparison of trial classification is summarized in Table 1.

Table 1. Clinical Trial Classification

Drugs	Devices
Phase 1: • Aimed at safety and tolerance • Healthy volunteers (20-100 subjects) • Determine dosing and major adverse effects	Pilot: • Smaller population with disease or condition (10-30 subjects) • Determine preliminary safety and performance information
Phase 2: • Aimed at safety and effectiveness • Small population with disease or condition (50-200 subjects) • Confirm dosing and major adverse effects	Pivotal: • Larger population with disease or condition (150-300 subjects) • Determine effectiveness and adverse effects
Phase 3: • Aimed at safety and effectiveness • Large population with disease or condition (100s to 1000s of subjects) • Determine drug-drug interactions and minor adverse effects	
Phase 4: • Post approval study • Collect long-term data and adverse effects	Post-Approval Study: • Collect long-term data and adverse effects

Clinical Trial Design

Clinical trial design may include randomization to ensure there is no bias for treatment outcomes. Randomization, which places subjects randomly into either the treatment or control, ensures that Investigators could not choose subjects who would likely have better outcomes to be in the study group, while those who would likely have worse outcomes go into the control group. Many times, the controls used are previously- approved drugs or devices, in order to show how the new product compares to current therapies.

For many drug trials, the control is a placebo, rather than current therapy, depending on the therapy being studied. In medical device studies, it is often unethical to use a placebo, and for many devices it would be impossible! For example, if a subject enrolled in a study of an artificial hip, the subject could not be given a placebo, or “sham” operation and be withheld treatment for the diseased joint.

Another common way to design a trial is to use “blind” or “double blind” controls. A blind study means the subject is unaware of which treatment group they are assigned to, and double blind means both the subject and the physician are not aware of the treatment being provided. With new drug trials, double blind trials are commonly used. However, as one can imagine, it is nearly impossible to blind subjects or investigators with a device trial. Of course there are exceptions, but they are rare.

Clinical trials need a way to measure the success of a new product. For drug trials, standard follow-up might collect blood pressures, heart rates, ECGs, etc. to determine the effect the drug has on the body. But in device trials, there is a way to actually visualize the performance of the device through imaging. There will likely be at least one imaging modality used to enable the sponsor to see the device and ensure it is still functioning appropriately. Table 2 summarizes some similarities and differences in the design of clinical trials.

Table 2. Study design for new drugs and medical devices.

New Drug Clinical Trials	Medical Device Clinical Trials
Randomization is common	Often no randomization
Control group	Control group
Large populations Includes placebos	Small populations
May compare to other approved therapies	Rarely uses placebos
Ability to “blind”	May compare to other approved therapies
Difficult to visualize	Difficult to “blind”
	Visualization often included

Clinical Trial Requirements

When studying new drugs, a clinical trial is required in every case. Minute changes to the composition of a drug may result in unexpected effects. However, when studying medical devices, clinical trials are not always required, and whether or not one will be conducted depends on a risk assessment. For example, a tongue depressor and an adhesive bandage are considered medical devices. They pose little risk to human subjects, and therefore do not require a clinical trial. On the other hand, a drug-eluting stent, or a new material for a hip replacement, introduce higher levels of risk and may require a clinical trial. Medical devices can be broken out into Classes, with Class I being Minimal risk, Class II being Intermediate Risk, and Class III being Substantial Risk. Class III devices always require a clinical trial, and some Class II devices do as well. This is summarized in Table 3.

Table 2. Study design for new drugs and medical devices.

Class	Class I	Class II	Class III
Examples	Tongue Depressor	Shoulder Prosthesis	Drug-eluting Stent
Clinical Trial?	NO	MAYBE	YES

Regardless of which is being studied, many of the regulatory requirements are the same, covering electronic records, informed consent, financial disclosure, and IRB requirements (21 CFR Parts 11, 50, 54 and 56). For those regulations specific to drugs or medical devices (21 CFR 312 or 21 CFR 812, respectively), there are also many similarities. Of course, there are some differences to consider, and the key differences can be broken into four categories: agreements, adverse event reporting, training, and product reimbursement. For more detail on this topic, please see our whitepaper.

In summary, there are differences in the way clinical trials are organized and designed for drugs and medical devices, when clinical trials are required. Regarding the regulatory conduct of the trials, the differences are in the details. Understanding these differences and implementing strategies to address them can lead researchers to successful clinical trials. For a quick reference on the similarities and differences, download our infographic.

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