

## Life Sciences 101? Exploring Clinical Trials — Initiation of a Human Study

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Before a new drug, device, or biological product may be commercially distributed in the United States, it must be shown to be safe and effective for its intended conditions of use.

A variety of non-clinical analyses, including laboratory (“bench”) development and animal testing, commonly precede the administration or application of an investigational drug or device to humans. The non-clinical evaluations assess, for example, how a compound will interact with the body (e.g., how it will be absorbed, distributed, metabolized, and excreted). Toxicological assessments of adverse events, dose lethality, carcinogenicity, reproductive consequences, etc. also are carefully considered.

The Food and Drug Administration (FDA) has some regulatory expectations for the performance of non-clinical analyses. However, the agency becomes substantially more involved when an investigational drug, device, or biologic sponsor desires to test a product in human subjects. Generally, the sponsor must submit an Investigational New Drug (IND) application or an Investigational Device Exemption (IDE) application to FDA, supplying:

- Product information (e.g., component and design specifications, analytical methods and test results, manufacturing process controls);
- Discussion of prior human and non-human experience with the investigational product;
- Description of the study protocol to be implemented, and rationale for the overall investigational plan;
- Personnel information (e.g., investigators who will perform the study; monitors who will oversee performance of the study; persons responsible to review and evaluate collected safety information); and
- Commitment to conform to applicable regulatory requirements.

When an IND or IDE is first submitted, the sponsor typically must wait 30 days to initiate the proposed study. During this time, FDA has an opportunity to review

the information package and judge whether (i) clinical trial participants will face unreasonable risk, (ii) the study is adequately designed to test a scientifically legitimate hypothesis, and (iii) other human subject protection and public interest criteria are satisfied. Strictly speaking, FDA does not “approve” the initiation or pursuit of a clinical study; instead, the agency allows a protocol to proceed via non-objection. At any time during the 30-day review period or thereafter, FDA may place a trial on “clinical hold,” pending the resolution of perceived deficiencies.

In addition to, and distinct from, FDA authorization, a clinical trial sponsor generally must obtain affirmative approval by a relevant Institutional Review Board (IRB) prior to initiation of a human clinical study.

Most drug, device, and biological products are developed through sequential studies. In so-called “Phase I” trials, researchers test an experimental product in a small group of people (e.g., 20-80 people, often healthy volunteers) to evaluate the drug’s safety, determine safe dosage ranges, and identify side effects. “Phase II” trials test a larger group (e.g., several hundred subjects) to further analyze safety and to preliminarily determine whether patients are responding to the treatment. “Phase III” trials test a larger group (e.g., several hundred subjects) to further analyze safety and to preliminarily determine whether patients are responding to the treatment. “Phase III” trials commonly test an investigational product in several thousand people to confirm data observed in earlier trials and to compare the product against placebo and/or active controls. Finally, “Phase IV” refers to post-approval studies; these commonly are designed to enhance information about product risks, benefits, and use in real-world settings.

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