

Orphan Drug Development Guidebook

Milestone: Human PoC

PoC: Proof of Concept

Purpose: Efficacy and side effects

While preclinical research answers basic questions about a drug's safety, it is not a substitute for studies of ways the drug will interact with the human body. "Clinical research" refers to studies, or trials, that are done in people. As the developers design the clinical study, they will consider what they want to accomplish for each of the different Clinical Research Phases and begin the Investigational New Drug Process (IND) / Clinical Trial Application (CTA) / national regulatory applications, a process they must go through before clinical research begins.

The First in Human (FIH) is the first clinical trial where the drug tested previously in animal is for the first time tested in normal volunteers (healthy people). In most cases, 20 to 80 healthy volunteers or people with the disease/condition participate in this first study (or set of studies) aiming at providing initial safety and tolerability information. This set of studies in healthy volunteers is collectively called "phase I". However, if a new drug is intended for use in cancer patients or if the administration of the drug poses risks to the healthy volunteers (e.g. in the case of most biotechnology products), researchers conduct phase I studies in patients with that type of cancer/rare-disease/etc.

Phase I studies are closely monitored and gather information about how a drug interacts with the human body. Researchers adjust dosing schemes based on animal data to find out how much of a drug the body can tolerate and what its acute side effects are.

As a phase I trials continue, researchers answer research questions related to how it works in the body, the side effects associated with increased dosage, and early information about how effective it is to determine how best to administer the drug to limit risks and maximize possible benefits. This is important to the design of phase II studies.

In some cases, the phase I and II may be condensed.

- *Study Participants (Phase I):* 20 to 100 healthy volunteers or people with the disease/condition.
- *Length of Study:* Several months
- *Purpose:* Safety and dosage

In phase II studies, researchers administer the drug to a (small) group of patients with the disease or condition for which the drug is being developed. The scope of phase II studies is to

provide the first evidence of biological activity, efficacy and safety in the intended patient population, as well as to selected the best dose(s) to be further studied in phase III.

Typically involving a few hundred patients, these studies aren't large enough to formally demonstrate whether the drug will be beneficial, or to accurately predict product's safety. In rare diseases, phase II (or combined phase I-II) studies might be much smaller, sometimes only a few dozens of patients or even less.

Researchers use data gathered in phase II to refine research questions, develop research methods, and design phase III research protocols.

- *Study Participants (Phase II)*: Up to several hundred people with the disease/condition.
- *Length of Study*: Several months to 2 years
- *Purpose*: Efficacy and side effects