Annex I of ISO 14155:2020 (International Organization for Standardization) helps define the various stages of clinical investigations for medical devices as well as the types of study designs. The following flowchart summarises Annex I, to assist those working in this domain, to better understand what each type of clinical investigation (CI) entails and facilitate with the medical device study designing process.

**Types of Study Design**

- **Exploratory**
  - First in Human or Early feasibility CI are exploratory
  - Might not have a pre-specified statistical hypotheses
  - Can be conducted to generate a hypotheses which is confirmed in subsequent CI
  - Helps plan further steps of design development
  - for example
    - Need for design modifications
    - Parameters for pivotal CI

- **Confirmatory**
  - An adequate controlled CI
  - Hypothesis of primary endpoint are stated in the CIP before the start of the CI
  - Sound confirmative statistical testing is applied

- **Observational**
  - Draw inference of possible effect of an intervention on subjects but no subjects are assigned to intervention groups. Only data during the normal course or clinical practice is collected.

**ANEX 1 - ISO 14155:2020**

**Medical Device Clinical Investigation (CI) stages**

- **Pre-Market Clinical Investigation**
  - An exploratory clinical investigation
  - Used to capture preliminary information on medical devices at an early stage of product design, development and validation
  - Might not require pre-specified statistical hypotheses but design of this CI and its outcomes can be more straightforward if statistical considerations are provided
  - Helps plan further steps of design development

- **Post-Market Clinical Investigation**
  - A CI done after market approval of a medical device
  - Intended to answer specific questions to device performance, effectiveness and safety
  - Post market CI can be a part of post-market clinical follow up (PMCF)
  - Note: if a marketed device is investigated for new indications other than those described in its labelling, then the requirements for a pre-market CI apply
Traditional Feasibility CI

A CI commonly used to capture preliminary performance, effectiveness or safety information

Done when the medical device is near-final or final device design

Done to plan an appropriate Pivotal CI

More non-clinical or prior clinical data is expected for this CI

because

the near final design takes place later in development than an early feasibility CI

This CI does not need to be preceded by an early feasibility CI

First in Human (FIH) CI

Medical device is evaluated for the first time in humans

Early Feasibility CI or Proof-of-Concept CI

This is a limited CI of a device early in its development

before the device design is finalised

Medical device has a specific indication

for example

innovative device for new/ established technology

Marketing device for novel clinical application

Done to evaluate device design concept with regards to clinical safety, performance and effectiveness

Done in a small number of subjects

Done when the information can’t be provided by non-clinical assessment or when the non-clinical tests are unavailable

Information gathered in this study can guide device modification

An early feasibility CI does not necessarily involve the first clinical use of the device

which means

We could have, for example, compassionate use studies prior to the early feasibility study (first clinical use)

Interventional CI

A pre- or post-market CI

Assignment of subject to a medical device is decided in advance in a Clinical Investigation Plan (CIP)

Diagnostic or monitoring procedures to collect data on S&P of device are pre-specified in a CIP in addition to those used in a normal clinical practice

Non-Interventional CI

A post-market CI where the medical device is used according to labelling

Assignment of subject is not decided in advance but falls under current clinical practice

No diagnostic/ monitoring procedure defined

Epidemiological methods used to collect data

Burden to Subjects