b) Study designs to accommodate multiple investigational products and/or indications

Traditionally, Clinical Development consists of clinical studies going through sequential phases (I to IV) where **one Investigational Product (IP)** such as a Drug, Biologic or Device is evaluated to assess its safety and efficacy in **one indication**. This is a costly and lengthy endeavor. It often takes more than a decade to gain marketing approval for a new prescription medicine[3]. So, to expedite Clinical Development and reduce cost, new study designs are emerging as alternatives to the traditional linear study phase approach.

Umbrella
X Drugs → 1 Indication

The **Umbrella** design where **multiple IPs** are being tested in **one indication** may be perceived as the least disruptive to current CDM practices. It is potentially possible to collect similar Safety and Efficacy data across IPs for the same indication. However, some variations of the eCRF may arise from differences across the IPs being tested. As an example, the use of different routes of administration where local site reactions need to be collected for injections and topical IPs, which is not required for other modes of administration. Additionally, the safety profile and duration of effect of each of the IPs may also require longer safety follow-up for one IP compared to the others. Many variations could be handled with traditional data capture systems with flexible designs leveraging branching logics, dynamic forms, derivations, etc. Additionally, to avoid unintentional unblinding, CDM must perform a thorough protocol operationalization assessment (e.g. how to handle local site reactions for a study with Injectables and Systematic Drugs) that would require specific data handling (e.g. use of an unblinded data scientists or unblinding evaluating investigators) and system configurations.

Basket
1 Drugs → Y Indications

Basket design where **one IP is** tested across **multiple indications** addresses some of the challenges of the Umbrella design (e.g. the variation in IP route of administration). However, it introduces new complexities such as handling of different efficacy endpoints. This would affect the design of the eCRF, eCOA and external data streams.

Platform
X Drugs → Y Indications

The **Platform** design where **multiple IPs** are tested across **multiple indications** will inherit the complexity of both Umbrella and Basket designs. This design may be more beneficial in Phase I allowing fast screening of IPs.

Additionally, to leverage the strengths to the above designs, some Clinical Research organizations may foresee benefits (e.g. economically, to reduce site burden, etc.) in designing roll-over trials where patients completing pre-defined milestones across all studies within a program are “rolled over” into one single Umbrella, Basket or Platform long term follow-up study.

In all cases, careful attention needs to be given early in the process when performing the risk assessment, to identify critical processes and data as well as designing and testing the end to end data collection and processing tools. It is also important to realize that these three designs will dramatically impact the set-up of the randomization systems with corresponding emergency unblinding procedures.