Recipharm

STRATEGIES FOR FIRST IN HUMAN (FIH) STUDIES

HOW TO CHOOSE THE RIGHT FORMULATION

There are multiple stages of drug development which are both challenging and time consuming. Constant efforts are being made to shorten the time needed to reach clinical development.

Identifying and understanding the physicochemical properties of a molecule is crucial to choosing a formulation strategy and ensuring the fastest route to clinic. Drug substance preformulation studies are the primary stage of formulation development, this includes looking at a selection of salt and polymorph solubility at different physiological pH, partition coefficient, ionisation constant, dissolution behaviour, moisture absorption rate, solid and solution state stability and flow properties.

Along with this data, the biopharmaceutical classification system (BCS) of a molecule plays a crucial role in the selection of a suitable dosage form for its intended use and in-vivo performance. When preformulation data is available it is time to define the formulation strategy for first in human (FIH) studies.

The main approaches for oral administration are described below.

DRUG IN BOTTLE (DIB)

DESCRIPTION

- API dispensed in bottle
- Reconstituted at the clinical site to form suspension or solution

ADVANTAGES

- High dosing flexibility
- Fastest to clinic
- Minimum development and GMP manufacturing required
- Simple and cost effective
- Suitable for BCS I and III molecules

DISADVANTAGES

- Not suitable for poorly soluble drugs
- Taste could be an issue
- Matching placebo is difficult
- Withdrawal volume to be verified
- Bridging study required at later phase of development

DRUG IN CAPSULE (DIC)

DESCRIPTION

- Drug filled in capsule

ADVANTAGES

- Less time consuming than a formulated dosage form
- No taste problems
- Faster development than full-scale formulation development
- No excipients API compatibility testing needed
- Blindings can be easily achieved

DISADVANTAGES

- Not suitable for poorly soluble drugs
- Low dosing flexibility
- More time consuming than DIB
- Stability plan for API and finished product required
- Bridging study required at later phase of development

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FORMULATED DOSAGE FORM

DESCRIPTION

- Tablets
- Simple dry mix powder or granules of different excipients with API in capsules

ADVANTAGES

- Automated manufacturing process
- Potential for using similar formulation through all phases of clinical studies and into commercial manufacturing
- Opportunities to enhance bioavailability

DISADVANTAGES

- Higher development effort and cost than DIC
- More API required
- Low dosing flexibility

Our dedicated team offers an end-to-end service from early stage formulation development to commercial manufacturing of various oral solid dosage forms. Our areas of expertise include:

- Experience in preformulation of different molecules
- Experience in managing various stages of clinical formulation development from Phase I to Phase III clinical studies
- Ability to handle various dosage forms such as immediate and modified release tablets and capsules, powder or pellet in sachet, powder in capsule, powder in bottle, oral solution, oral suspension and various topical formulations including ointment, cream and gel
- Quality by Design (QbD) based formulation development
- Optimisation of formulation and process variables by employing a Design of Experiment (DOE) approach
- A complete development package, comprising formulation development, analytical method development and validation, manufacture of clinical trial material (CTM), stability studies and scale-up into commercial production
- Supporting analytical chemistry development and stability studies
- Manufacture of clinical batches from gram to kilogram scale including QC, packaging, labelling and QP release
- Experience in handling DIB and DIC formulations as well as formulated dosage forms

About Recipharm: Recipharm is a leading contract development and manufacturing organisation (CDMO) headquartered in Stockholm, Sweden. We operate development and manufacturing facilities in France, Germany, India, Israel, Italy, Portugal, Spain, Sweden, the UK and the US and are continuing to grow and expand our offering for our customers.

Employing around 9,000 people, we are focused on supporting pharmaceutical companies with our full service offering, taking products from early development through to commercial production. For over 25 years we have been there for our clients throughout the entire product lifecycle, providing pharmaceutical expertise and managing complexity, time and time again. Despite our growing global footprint, we conduct our business as we always have and continue to deliver value for money with each customer's needs firmly at the heart of all that we do. That's the Recipharm way.

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