FRESENIUS KABI

Product Partnering

Your Partner for Development & Manufacturing for Clinical Trials

The validity of clinical trials depends crucially on being able to safely apply the trial results to the commercial version of the drug. The manufacturing process used to make the drug used in the trial must be stable and scalable. Fresenius Kabi Product Partnering offers first-class support in developing production processes for clinical trial drugs that avoid problems in the subsequent transfer to commercial scale. Drawing on Fresenius Kabi's decades-long track record of successful development of sterile pharmaceuticals, we provide made-to-measure solutions from galenic development to implementation of a stable manufacturing process, scale-up, and finally manufacturing of GMP batches for clinical and commercial use.

STEP 1: Primary Containers for Clinical Trials

We have implemented and qualified numerous primary container closure systems for use in GMP batches for clinical trial and market supply, including:

- Glass vials: 2–100 mL
- Glass bottles: 50–1000 mL
- Glass ampoules: 1–20 mL
- Pre-filled syringes (glass and polymer): 0.5–50 mL
- Bags (PVC-free): 50–1000 mL

STEP 2: Formulation Development for Sterile Pharmaceuticals

Our highly trained and experienced scientists will collaborate with you to work out a development strategy that will lead to a stable product formulation. Depending on the critical quality attributes of your substance, we can offer one of the following formulation types:

- Aqueous solution
- Emulsion
- Liposomal formulation
- Suspension
- Lyophilization

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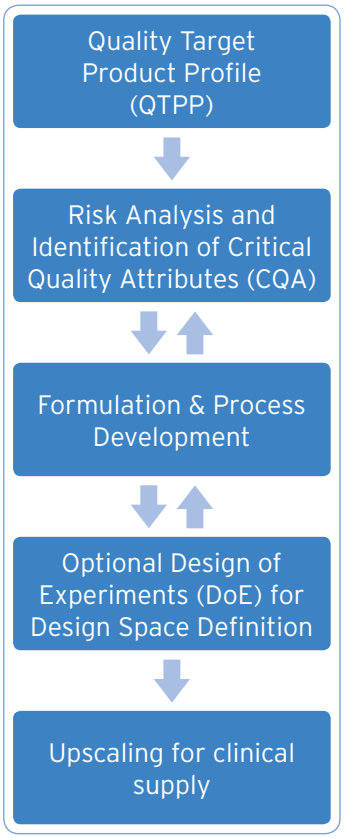
STEP 3: Process & Product Development for Sterile Pharmaceuticals

Incorporating early input from our commercial manufacturing sites, we set up initial manufacturing methods at lab scale. We then use sophisticated assays to optimize process parameters to arrive at a process that can be scaled up without problems and that assures consistent product quality following the logic of Quality by Design (QbD).

- Testing and definition of critical quality attributes
- Implementation of a lab-scale manufacturing process, including in-process controls
- Scale-up from lab scale to clinical trial scale and/or commercial scale, ensuring consistent product quality
- Implementation of sterility using aseptic filling or terminal sterilization
- Developmental studies on product stability include:
  - ICH and/or ambient light photo stability
  - Stress stability
- Compatibility studies for product contacting parts
- Compatibility studies with primary container closure system include:
  - Stress stability studies using different primary container closure systems
  - Extractable & leachable studies



STEP 1 & 2 & 3: Analytical Method Development

Accompanying the development and scale-up of the manufacturing process itself, we also support you in developing and validating the analytical methods needed for raw materials and finished product. In the first instance, analytical methods are implemented in our on-site labs. We can also call on a range of qualified, competent outside partners to develop and implement your analytical methods.

STEP 4: Clinical Trial Supply (Phase I–IV)

Our pilot plant in Graz, Austria and our commercial manufacturing plants are fully compliant with international quality standards (including FDA-GMP, EU-GMP), offering production for preclinical and global clinical studies in various container closure systems. Our plant in Neufahrn, Germany is the ideal partner for aseptic compounding and can also offer blinding of study medication for clinical trials.

- FDA & EMEA-approved plants for clinical trial supply in the US and Europe
- Procurement of raw materials from qualified suppliers
- cGMP batch sizes: From small to large scale batches
- Filling in existing qualified primary container closure systems
- Aseptic filling or terminal sterilization of product
- Secondary packaging and blinding of study medication for clinical studies
- Analytical analyses of raw materials and finished product according to agreed specifications
- Technical release by Qualified Person
- ICH stability studies
- Support documentation for submission

After having established a successful manufacturing process for your clinical trial supply, we support you in generating validation and registration batches to obtain market authorization of your product.

CONTACT INFORMATION

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