

# Technologies for Sterile Products with Complex Formulations at Fresenius Kabi

The increasing medical need for drugs with highly specific, well-understood modes of action and minimal side-effects has important effects on pharmaceutical manufacturing. Nowadays many new drug substances are either highly potent and/or biological, and often very cost-intensive. All of these aspects pose special challenges from a manufacturing perspective. In addition the effort needed to achieve safety and containment, efficiency of use of the active pharmaceutical ingredients (APIs), and stability of the final products has grown steadily.

Fresenius Kabi Product Partnering is excellently positioned to meet these challenges. We offer services for manufacturing of sterile products using APIs of various chemical qualities, of biological origin, and in different potency ranges. With deep expertise in different drug formulation technologies such as aqueous solutions, emulsions, liposomes, suspensions, and lyophilization, we can reliably develop ways to keep APIs stable and to facilitate their clinical use. Complementing our range of formulation options is a full portfolio of primary containers, including bottles, vials, bags, and pre-filled syringes.

Furthermore we can draw on extensive experience in regulatory affairs in Europe, the US, and Asia. In this way, we can offer you support from early development to launch of the product in your target markets.

## Certifications of Fresenius Kabi Manufacturing Sites

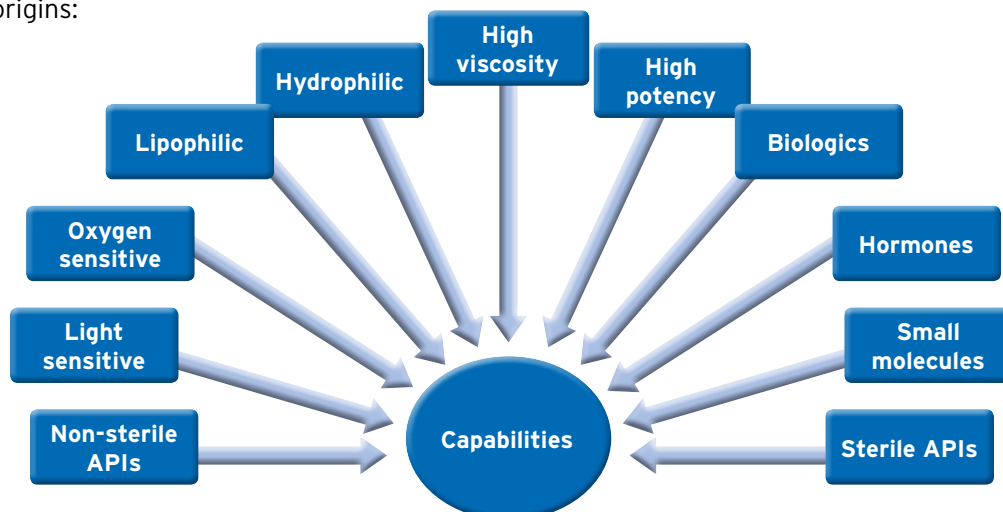
Our manufacturing sites have been certified and approved by numerous authorities, including:

- ISO 9001 and ISO 14001 certification
- FDA (US)
- GMP (EU, WHO)
- ANVISA (Brazil)
- Korea
- Taiwan
- Gulf states

Besides the certifications for manufacturing pharmaceutical products worldwide, we also have the capabilities to manufacture medical devices.

## Handling Different APIs

Our manufacturing sites have been certified and approved by numerous authorities, including: The Fresenius Kabi manufacturing sites are able to handle and formulate APIs with a wide range of physical and chemical attributes and origins:



## Manufacturing Capabilities at Fresenius Kabi

To formulate your API in accordance with its physicochemical attributes, we can provide you with the following technologies:

### 1) High-potency APIs:

- Weighing and compounding of high-potency APIs in a weighing isolator under nitrogen atmosphere for oxygen protection
- Handling of sterile APIs under aseptic conditions in a weighing isolator with a VHP generator
- Direct and sterile connection to mobile tanks



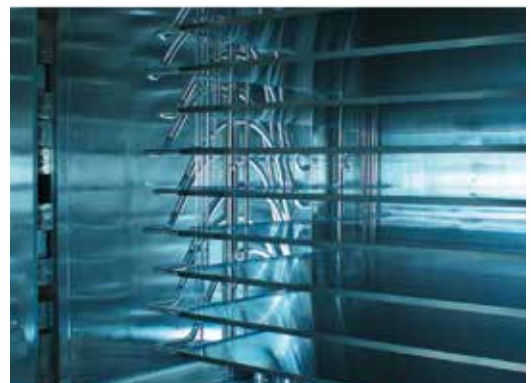
### 2) Equipment

- Compounding in mobile tanks if required
  - Batch sizes: 4-500 L
  - Port system for secure transfer from weighing isolator
  - High potent and sterile compounds
  - Full CIP/SIP options
  - Fully automated system including audit trail
- Multi-use equipment, dedicated equipment, single-use bags for bulk solutions
- Filling of delivered bulk solutions (delivered in tanks or frozen bags)



### 3) Formulation

- Aqueous solutions
- Emulsions
  - Phospholipids made by Fresenius Kabi
  - New preparation unit for the handling of high potent compounds in a weighing isolator
  - Flexible batch sizes up to several thousand liters
- Liposomal formulation
  - Phospholipids made by Fresenius Kabi
  - High-pressure homogenizer
- Suspensions
  - Aseptic compounding and filling
  - Carboy with recirculation to maintain suspension during filling
- Lyophilization of aqueous and liposomal formulations
  - Shelf area: Currently 19 m<sup>2</sup> but with extendable lyophilization capacities



## Filling Processes at Fresenius Kabi

To fill your product according to its critical attributes into the appropriate primary container closure system, we can provide you with the following technologies:

### 1) Technology

- Filling lines qualified for aseptic filling
- Terminally sterilized products
- Availability of different dosing systems
- Mobile tanks or fixed piping from compounding tanks to filling line

### 2) Filling lines include:

- New high speed state-of-the-art aseptic large volume parenteral (LVP) filling line
  - 50-500 mL glass bottles
  - Closed reduced access barrier system (RABS) including vaporized hydrogen peroxide (VHP) sterilisation
  - 100% IPC filling volume without reduction of speed
- New high speed state-of-the-art aseptic small volume parenteral (SVP) filling line
  - 2-50 mL glass vials
  - Closed RABS including VHP sterilisation
  - Dual dosing system
  - Freeze dryer fully integrated into the aseptic SVP filling line
- Aseptic filling and terminal sterilization of bags
  - Filling of bags with different formats and materials
  - Filling in low-leachable Fresenius Kabi freeflex® bags: An innovative and flexible container concept, without plasticizers and adhesives; proven compatibility with more than 40 drugs
  - Dedicated filling line for aseptic filling
- Aseptic filling line for pre-filled syringes
  - Use of sterile primary packaging components
  - Nested syringes, ready-to-fill
  - Closed RABS
  - Stoppering with vacuum or positioning pipe
- Filling of ampoules

### 3) Primary container closure systems:

- |  |               |
|--|---------------|
| ➤ Glass vials:                           | 2-100 mL      |
| ➤ Glass bottles:                         | 50-1000 mL    |
| ➤ One-chamber bags:                      | Up to 2000 mL |
| ➤ Multi-chamber bags:                    | Up to 4000 mL |
| ➤ Glass ampoules:                        | 1-20 mL       |
| ➤ Glass and plastic pre-filled syringes: | 0.5-50 mL     |



## Secondary & Tertiary Packaging

To package your filled product according to your requirements, we offer the following secondary and tertiary packaging technologies/materials:

- Labelling
- Fully automated packaging lines for SVPs and LVPs
- Packaging in cardboard boxes
- Pouches for pre-filled syringes - with or without oxygen protection
- Blistering of pre-filled syringes - with or without oxygen protection
- Data matrix code implemented, if required
- Tamper-proof sealing
- Track and trace
- EUR/US pallets

## Logistics

Besides the services for contract manufacturing, we also offer the following logistics services:

- Procurement of raw materials and packaging materials from qualified suppliers
- Worldwide shipping and distribution under controlled conditions as required for your product

## CONTACT INFORMATION



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