INSIGHT

cmo@fresenius-kabi.com

Contract Manufacturing in the U.S.

Stefan Czvitkovich, PhD
Director
Contract Manufacturing Sterile Pharmaceuticals

Dear valued customers,

Over the past decade, Fresenius Kabi has become a household name for providing contract manufacturing services in the pharmaceutical industry. To be reliable as a global partner, we understand that being close to both our customers and manufacturing sites is vital for establishing long-lasting and successful relationships.

In this edition of Insight, we highlight the contract manufacturing services offered by our Fresenius Kabi U.S. sites and introduce you to our newly formed U.S. team with members located at each manufacturing site to support you also locally in the U.S.

Fresenius Kabi operates three pharmaceutical manufacturing sites in the U.S. They are located in Melrose Park IL, Grand Island NY, and Wilson NC. These sites have the ability to manufacture sterile liquid injectables ranging from price competitive standard solutions in high quantities to complex products with specific manufacturing requirements, for example for use with disposable equipment with high yield and quality requirements and for either U.S. or global markets. The containers for fill/finish range from glass and plastic vials to pre-filled syringes and PVC-free proprietary **free***flex*® bags.

To satisfy increased market demands and also to stay ahead with state-of-the-art technologies and regulatory requirements, Fresenius Kabi is currently making investments for expansions in all three U.S. sites and decided to make Fresenius Kabi Contract Manufacturing a central pillar for its future strategy in the U.S.

To support all our new and existing partners directly in the U.S. to the best level, we have formed this year a new U.S. team with Courtney Torchia-Roman located in Melrose Park, IL, Erin Crawford in Grand Island, NY, and Wanda Mason in Wilson, NC. All three have all previously held different positions within Fresenius Kabi and have extensive knowledge of the local manufacturing sites. A big welcome to Courtney, Erin, and Wanda to the Fresenius Kabi Contract Manufacturing U.S. team!

Due to the global COVID-19 restrictions in travel, we are also improving our virtual presence and the ways you can get in touch with us more efficiently via our website https://cmo.fresenius-kabi.com/.

We are very much looking forward to meeting you and discussing with you customized solutions for your products and to supporting all our new and existing partners in these challenging times.

With all the best wishes,

Stefan

IN THIS ISSUE

MEET THE CONTRACT MANUFACTURING TEAM
for the U.S. plants

Franz Kainz, PhD

Vice President
Global Contract Manufacturing
Sterile Pharmaceuticals & Medical Devices

Stefan Czvitkovich, PhD

Director
Contract Manufacturing Sterile Pharmaceuticals
Region North America

Erin Crawford

Manager
Contract Manufacturing Sterile Pharmaceuticals
Grand Island

Nicholas Baraie

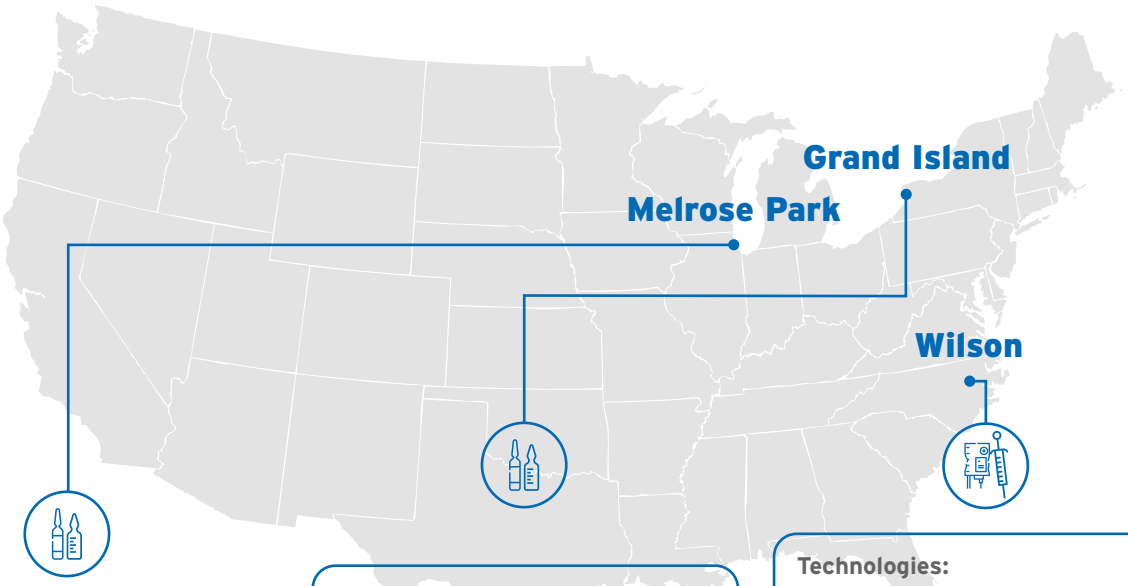
Manager
Contract Manufacturing Sterile Pharmaceuticals
North America

Courtney Torchia-Roman

Manager
Contract Manufacturing Sterile Pharmaceuticals
Melrose Park

GET IN TOUCH: cmo@fresenius-kabi.com

MANUFACTURING LOCATIONS | USA



Technologies:
- Aseptic liquid filling
- Lyophilization
- Terminal sterilization
- Isolator contained dispensing; disposable product path (SUS)
- Cold filling
- Highly Oxygen sensitive products
- Cytotoxic line
- High Potency capabilities

Products:
- Anesthetic/analgesic
- Oncolytic
- Critical care

Glass: Vials (2-200 mL)

Plastic: -

Certificates:
- US-FDA
- Canada-Health Canada

Technologies:
- Aseptic filling
- Lyophilization
- Terminal sterilization
- Glass and plastic vial capabilities
- Oxygen sensitive products

Products:
- Anti-infectives
- Standard solutions
- DEA schedule II and IV-controlled drugs
- Critical care
- Anesthetic/analgesic
- Oncologic

Glass: Vials (2-200 mL)

Plastic: Vials (3-200 mL)

Certificates:
- US-FDA
- Canada-Health Canada
- DEA

Technologies:
- Aseptic filling with in-line E-beam decontamination
- Formulation available in 100% Single-use-system, fixed and/or mobile tanks with CIP/SIP
- Terminal sterilization
- Automated inspection of product filled syringes, stopper/plunger, tip cap

Products:
- Anesthetic/analgesic
- Diluents/standard solutions
- DEA schedule II and IV-controlled drugs
- Critical care

Glass: Pre-filled syringes (0.5-3 mL)

Plastic: Pre-filled syringes (5-10 mL)

Certificates:
- US-FDA
- Canada-Health Canada
- DEA

WILSON, NC

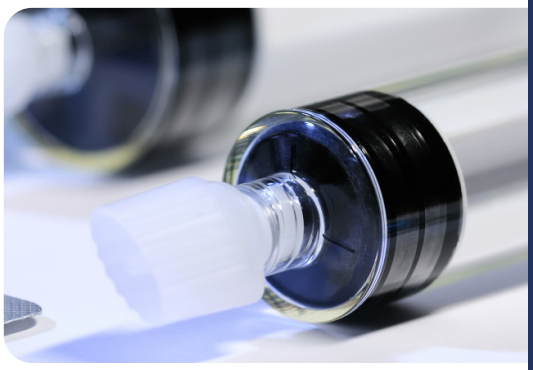
Our Fresenius Kabi U.S. center of excellence for prefilled syringes (PFS) is in Wilson, which is located in the eastern part of North Carolina. The Wilson site is a world-class facility with state-of-the-art, fully automated syringe technologies that are focused on the production and distribution of complex and critical drugs in ready-to-administer delivery systems and diluents, both for Fresenius Kabi and contract manufacturing partners.

The Wilson site specializes in the formulation, syringe filling, and packaging of aseptic and terminally sterilized drug products and diluents with the advantage of being able to offer large-scale quantities and flexibility in the syringe portfolio and sizes. PFS drug products and diluents are produced on fully automated manufacturing, inspection, and packaging lines in a continuous process under controlled conditions. This highly automated and state-of-the-art manufacturing facility, half of which is dedicated to prefilled syringe production, has a unique capability and capacity to launch additional tens of millions of new and existing commercial PFS drug products including biologics, highly active compounds and products (maximum OEL = 0.1 µg/m^3), and products that are sensitive to temperature, light, and/or oxygen.

Highly active compounds and products and biologics are able to be formulated and filled using disposable single-use system technologies with completely disposable and/or dedicated product contact parts for reduced exposure levels. Products sensitive to oxygen can undergo nitrogen-filling technologies with light-protected palletization to achieve maximum shelf life and market value.

The site in Wilson has the capacity to fill and finish more than 100 million units of ready-to-administer product in PFS anually

including anesthetic, analgesic, antiemetic, anti-inflammatory, and a host of modifier and inhibitor therapeutic classes. These pharmaceuticals are filled in various configurations of syringes (Luer lock and/or staked needle), and are inspected and packed in various configurations such as nested syringes of unlabeled bulk, as labelled and blistered (singles and/or sheets), cartoned as cases, and/or are kitted with additional product(s).



This manufacturing facility is implementing additional automated state-of-the-art PFS manufacturing lines, suitable also for larger PFS formats up to 10 mL, flow-wrapped packaging, as well as IV bags and standard solution bags based on Fresenius Kabi's **free***flex*® platform. These implementations will create a unique possibility to launch products across multiple platforms specific to various product and customer requirements.

To support you with a global supply of your product, our Wilson plant has been inspected by domestic and international agencies

and will be capable of serving the worldwide market in the future, including key markets like the EU and China. In 2020 and 2021 the plant achieved ISO quality and environmental certification ISO ISO14001 and ISO50001.

We are proud to offer our partners the possibility of filling their solutions into syringes and **free***flex*® bags in Wilson, North Carolina. Please get in touch with us to find the perfect solution for your formulation and filling and finishing needs.

GRAND ISLAND, NY

The Grand Island site is located just over ten miles from Buffalo, NY and a few minutes from the spectacular Niagara Falls. Buffalo is in the Western New York region of the northeast U.S. The Grand Island plant has been under Fresenius Kabi ownership for the last 12 years. Only recently, Fresenius Kabi has invested more than $ 200 million in its Grand Island plant to extend its overall manufacturing capacity.

The site currently holds the capacity of more than 200 million units anually, embodying the company's commitment to „caring for life" with each patient dose.

At this time, the main markets are the U.S. and Canada with projects to expand to the European market ongoing. The vials shipped from here include both plastic and glass containers and range in size from as small as 2 mL to as large as 200 mL. The site's products include mostly critical care and anesthetic and analgesic medications.

Today, the plant consists of two production facilities that manufacture IV drugs and one newly developed production facility that is dedicated to monobactam products.

The site's production facilities hold approx. 300.000 ft^2 including for advanced technologies with restricted access barrier systems, handling and filling of controlled substances, and a dedicated area for monobactams.

The site focuses on controlled substance production and logistics, lyophilization, and sterilization.

Lastly, the fully automated monobactam facility in development contains 19,000 ft^2 (1,765 m^2) of manufacturing space with one lyophilization line and isolator technology.

As can be seen, the site can offer significant capability for customers when it comes to sterile diluents and lyophilization. The site has also invested in the infrastructure and processes needed for controlled substance production and logistics.

With a cross-functional team of more than 800 employees across five shifts, the plant is constantly improving and advancing. Examples include the addition of larger formulation tanks to scale up batch size, automatic cleaning processes for equipment, in-line depyrogenation tunnels, automated visual inspection recipes, and packaging serialization. The site has also assembled a team which continues improvements such as the planned implementation of an electronic batch records aid in the batch release process occurring at the highest level of compliance.

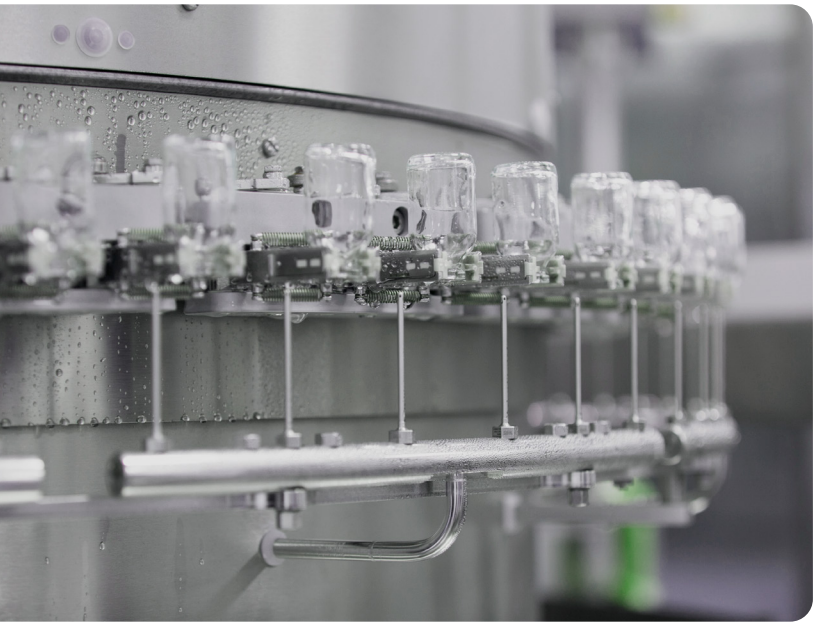
We are committed to sustainable production, which is evidenced by all three U.S. plants obtaining the ISO 14001:2015 Environmental Management Certificate in 2020. The Grand Island site is targeting achievement of the ISO 50001:2018 Energy Management Certification in the near future as well.

The Grand Island team's collaboration and passion are vital to the product launch process. We embrace the opportunity to learn and grow our technical capabilities together and look forward to partnering with you for your contract manufacturing needs!

MELROSE PARK, IL

Do you have a developed parenteral injectable product in glass vials (2-200 mL), and are you looking for a high throughput facility to partner with for Phase 3 and/or commercialization? Then, the Fresenius Kabi Melrose Park site is for you. Melrose Park is a suburb of Chicago and is located five miles away from the O'Hare International Airport. The facility has more than 12 years history within Fresenius Kabi, and currently produces a wide range (250 finished products) of parenteral injectable medicines for the treatment of critically and chronically ill patients.

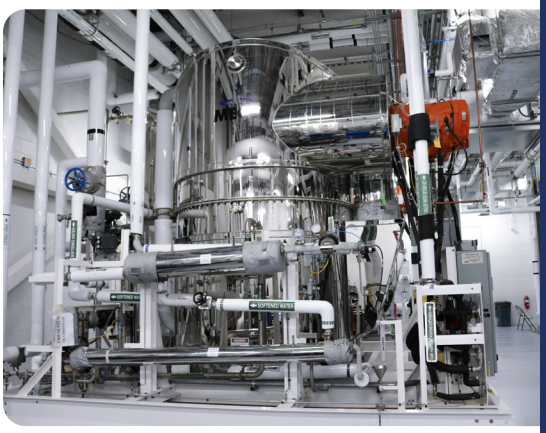
The new facility is equipped with a state-of-the-art urban manufacturing campus, fully-automated aseptic filling lines and advanced isolator technology, as well as expanded lyophilization capabilities and formulation areas.



Fresenius Kabi is currently completing a $ 250 million investment project to expand capacities at its Melrose Park site with annual capacities in future of more than 250 million units.

Multiple integrated aseptic filling lines in connection with lyophilizers with automated loading are being installed in the expansion, including one cytotoxic line, one highpotent/ hormone line and multiple general product lines to increase overall manufacturing capacities. This additional capacitity will significantly enhance the annual output as of today, with multiple aseptic lines and lyophilizers in place in the existing site for the supply of life-saving drugs filled in vials for distribution in the U.S. and Canada.

We offer also filling and finishing services for highly potent products in a multiproduct facility using effective separation with smart HVAC and architecture design and new disposable single-use system technologies with fully disposable and/or dedicated product contact parts for the reduced risk of cross contamination.



Additionally, we offer technologies required for filling advanced complex parenterals such as emulsion processing, cold filling, oxygen reduction, metal-sensitive, and other sophisticated technologies.

The site is also home to GMP compliant semi-automated and automated inspection processes, and five packaging lines, two of which are fully automated, and all are installed with serialization and aggregation equipment to meet DSCSA requirements.

We are committed to sustainable production, with certification efforts of all U.S. plants sustainable production commitment to obtain ISO 14001:2015 (Environmental Management) cert ISO 50001:2018 (Energy Management) certification, planned this year.

The Melrose Park team is passionate about our "caring for life" philosophy and bringing value to our customers and their patients through high-quality products. We are excited to learn about your contract manufacturing needs and be *Your Partner for Solutions!*

LYOPHILIZATION AND DILUENTS

With more than 30 percent of the FDA-approved parenteral drugs and a steady increase in injectables requiring lyophilization, the Fresenius Kabi Contract Manufacturing organization is dedicated to support both our new and existing partners' drug product portfolios. Our U.S. based state-of-the-art facilities offer lyophilization and sterile diluents for reconstitution in various containments and volumes.

Lyophilization, defined as the freeze-drying process of a liquid product after it is frozen and placed under a vacuum, has three interdependent processes; freezing, sublimation (primary drying), and desorption (secondary drying). The process simplifies aseptic product handling while enhancing the stability of the product in a dry state through the removal of water without excessive heat. Products with instability in solution are manufactured as a lyophilized form. There are a multitude of lyophilized product advantages including extended shelf life (typically two to five years) while maintaining drug potency, room temperature storage conditions and ease of transport due to the reduced weight and volume of the finished product.

As lyophilized drug products require diluent for reconstitution, Fresenius Kabi Contract Manufacturing is proud to provide sterile diluent to our partners in both pre-filled syringe and vial formats through our plants in Wilson,Grand Island and Melrose Park.

In addition to PFS, we offer sterile diluents in a variety of vial formats and volumes.

We offer manufacture of diluents in 1-10mL pre-filled syringes (PFS) and vials, as well as larger volumes upon request.

Choosing the right partner is critical to the success of your product development and commercialization. When your complex formulation cannot be sterile filtered or terminally sterilized, let our aseptic fill & finish, lyophilization, and sterile diluents (filled in PFS out of Wilson and vials filled out of Grand Island and Melrose Park) contract manufacturing services provide you with the solution.

Taken together, we can combine large-scale fill & finish services for both complex lyophilized parenterals and their associated simple diluents, making us the ideal one-stop-shop for your next outsourcing project for these complex sterile pharmaceuticals.

FIND OUT MORE ABOUT OUR CAPABILITIES

Find out more: https://cmo.fresenius-kabi.com/wilson-usa

Find out more: https://cmo.fresenius-kabi.com

CONTRACT MANUFACTURING

cmo@fresenius-kabi.com
https://cmo.fresenius-kabi.com