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CONTRACT MANUFACTURING // N°01 // 2020 //

INSIGHT

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Your Partner for Solutions

Franz Kainz, PhD
Vice President
Global Contract Manufacturing

Dear Readers,

With our new Insight edition, we intend to shed light on the combined portfolio of cutting-edge bag technology suitable for IV drugs and diluents associated with transfer sets, which we, Fresenius Kabi Contract Manufacturing, formerly known as "Fresenius Kabi Product Partnering", are proud to offer to you.

Our new slogan "Your Partner for Solutions" represents our wish to support our third-party customers in the development and manufacturing of sterile solutions and pharmaceuticals by providing innovative solutions with our unique portfolio of technologies for sterile pharmaceuticals and medical devices. We have also launched our new website *cmo.fresenius-kabi.com*, providing you with further insight into our capabilities for sterile pharmaceuticals and medical devices.

Over the last fifteen years, Fresenius Kabi's contract manufacturing business has become a globally recognized provider for sterile fill & finish services, fulfilling the needs of medium-sized to large pharmaceutical companies searching for a true "one-stop shop" experience. Whereas our customers are handling the market authorization and commercialization of the product, Fresenius Kabi takes over the entire manufacturing process, starting from the initial process and product development, up to the commercial manufacturing of the sterile drug product and the associated medical device, including sourcing of all raw materials and packaging of the final product for global supply. Our success is based on our technology platforms, which include the broad range of containers such as IV bags, prefilled syringes, vials, ampoules, and bottles as well as process technologies such as the handling of highly potent APIs and disperse systems such as emulsions, liposomes, and suspensions.

In this Insight edition, we would like to give you an overview of Fresenius Kabi's manufacturing facility in Halden, Norway, as your potential plant to manufacture your next IV drug or diluent filled in the award-winning **free***flex*® bag technology, a PVC-free bag also suitable for oxygen-sensitive drug products with a sterile overpouch or filled in PVC-free plastic ampoules made with polypropylene. The Halden production plant is considered a competence center for the filling of IV drugs in bags and blow-fill-seal technology, based on decades of experience and state-of-the-art in-house technologies suitable for global supply including the USA, Europe, and Asia.

I would like to conclude by thanking all of our partners for their continued business and support. We look forward to working together with you, side by side, to help you achieve your next objectives and to truly be "Your Partner for Solutions".

We would love to hear from you,

Franz

IN THIS ISSUE

TRANSFER DEVICES
Important Excipients for Modern Drugs

Fresenius Kabi Contract Manufacturing is an experienced single-source partner for business-to-business customers. In fact, it is our goal to be a full-service provider to our customers and thus support you throughout the entire life cycle of your product, from the early stages of development to full commercial maturity and beyond. As a contract manufacturer, we strive to make our client's every idea become a reality. With extensive experience in adapting manufacturing processes, assembly strategies, and packaging formats, we are dedicated to providing our partners with tailor-made solutions to meet the unique requirements of their products and businesses. Fresenius Kabi Contract Manufacturing Devices is a leading manufacturer of sterile disposable products for drug application. Using validated manufacturing methods, we produce high-quality, sterile infusion and transfusion sets, subcutaneous applications for insulin therapy, and sets for enteral nutrition, as well as a comprehensive range of accessories for each of these applications.

Quality Standards

Our quality management system is designed to ensure compliance with all applicable national and international requirements, as well as to meet the expectations of our partners and customers. For us, it is a matter of course to undertake regular quality improvements across all operations.To countervail potential negative consequences for the environment, it is of the utmost importance to use materials that make the most efficient use of resources and that minimize waste disposal. To do this while fulfilling increasing demands on performance, for example for migration-free and light-source protective infusion devices, we make use of the latest know-how.

Facilities

With production locations in Błonie (Poland) and Nanchang (China), we are able to manufacture the product in the best fit area and optimally connect our global partners to the resources they need. Our production services range from partially to fully automatic mass production. The manufacturing capabilities comprise tube extrusion, injection molding, and sterile finished products, and include all the common manufacturing methods (manual and fully automatic assembly) of plastic medical products. Our production locations maintain EO (Ethylene Oxide) sterilization installations and have their own distribution depots.

Infusion Therapy

Infusion therapy is one of the most important therapeutic measures in inpatient and outpatient medical care. Needless to say, we are, among other things, the right partner when it comes to infusion therapy systems. We develop special application systems for the most diverse medicines or pump systems. We can offer the complete development range supported by our 3D construction, including tool manufacture and injection molding. Taking on full-range project processing in our company with our downstream sterilization manufacturing guarantees fast and above all smooth handling of the project for our customers.

Transfer device

Transfer device

free*flex*® adapter

free*flex*® adapter

Extra-Spike Plus 5 µm KP

Transfer Devices

To achieve optimal clinical results for the sake of your patients' health, we ensure that our application systems safely transfer or mix sterile substances and other liquids in closed systems, for example medication and nutritional and blood components. As for infusion therapy, Fresenius Kabi offers various spike systems from simple double-sided plastic spikes and Luer lock combinations, which can be used on a large variety of containers, to covered needle spikes, which are surrounded by a plastic housing to provide extra protection against injuries.
The basic devices are not dedicated to special containers. However, we offer dedicated transfer systems as well, which provide a fixed and stable snap connection to the bag port or vial cap. This feature is especially important in the application of cytotoxic drugs. Should you, for example, discover the **free***flex*® IV bag to be the proper container system for your business, we are the perfect match for suitable transfer devices. You can benefit from our convenient one-stop shop philosophy and entrust us with anything you need for the purpose of drug delivery and its preparation. Fresenius Kabi Contract Manufacturing Medical Devices supplies a broad portfolio of compatible products with well-thought-out designs and features such as easy and intuitive utilization and safety precautions. **free***flex*® compatible transfer devices include the Extra-Spike Plus 5 µm, the cannula transfer device FK micro, and two varieties of the **free***flex*® transfer adapter. All of these medical devices are made of PVC-, latex-, and DEHP-free materials.

Alternatively, our team of development engineers is ready to take on any challenging development task to create a customized transfer device for your application and the corresponding container – thus providing the optimal solution for your requirements. Get in touch with us to find the perfect solution for your medical devices.

Basic Transfer Devices	**Dedicated Transfer Devices for Fresenius Kabi Containers**	**Dedicated Transfer Devices for Diverse Containers**
Variable usage with many different containers Examples: • Basic form with double-sided plastic needle • Micro spike for small vials with needle-free Luer lock connection to the syringe	Connection with a dedicated container Examples: • KabiPac® adapter • **free***flex*® adapter	• Connection with a dedicated container and bottle • Customized development

CLINICO MEDICAL SP. Z O.O. BŁONIE, POLAND

Manufacturing Plant for Medical Devices

Since its acquisition in 2005, the Clinico Medical Sp. z o.o. production site has been part of our structured and effective manufacturing network within Fresenius Kabi. The plant with focus on medical devices is located in Błonie, Poland, in the Lower Silesia region, and employs more than 1,500 people.

This dynamically growing production unit uses state-of-the-art machinery and equipment, providing Fresenius Kabi customers and contract manufacturing partners with products that comply with the highest quality standards.

The range of medical devices manufactured at the Błonie plant is impressive, from infusion and transfusion sets, all the way to numerous system accessories such as transfer devices. In addition, it includes sets for enteral feeding, insulin, and special oncology therapy (e.g. ports, class III, implants). More than 1,200 different finished products can be manufactured in Błonie.

As we offer customized solutions to our international customers, we are proud that we can draw on the long-standing expertise in Błonie.

In particular, the plant specializes in injection molding (including high cavity and 2k techniques), fully automatic assembly, tube extrusion, thermotransforming packaging, and EO product sterilization.

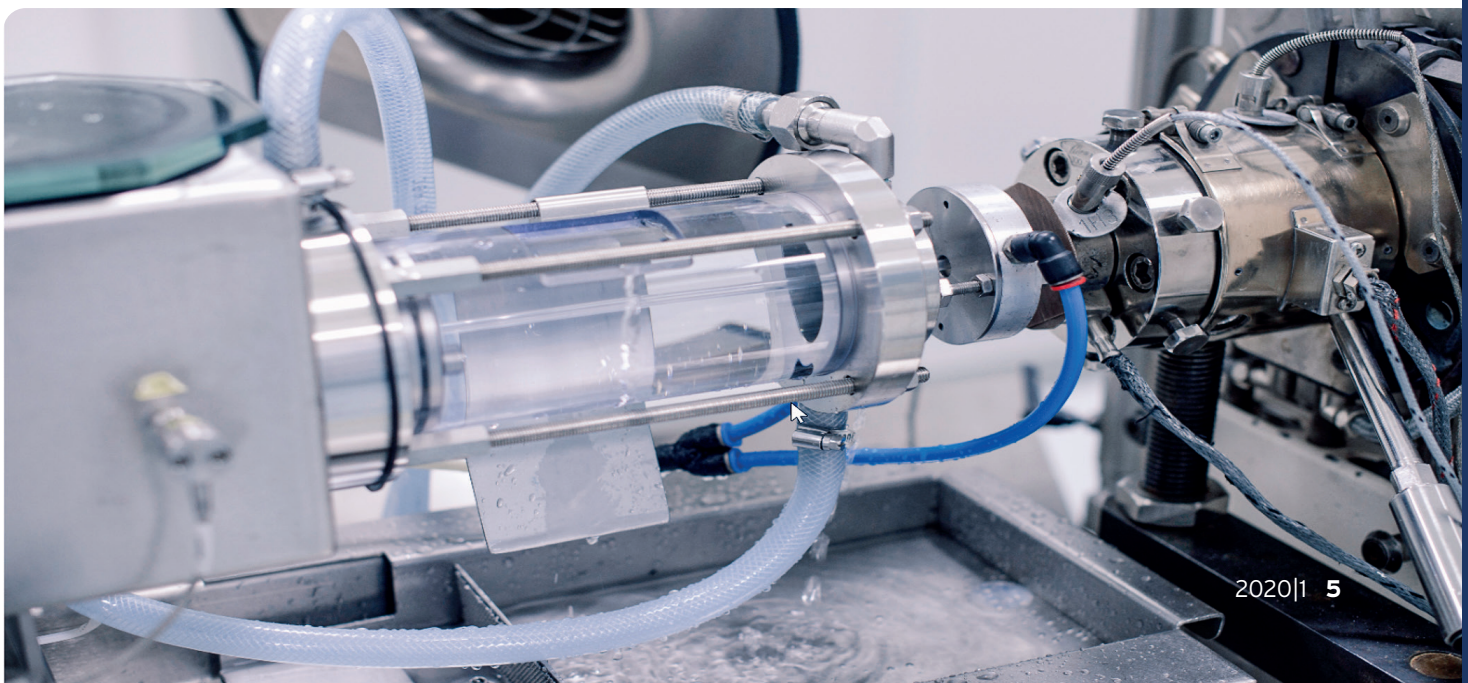
Our clients can benefit from optimized supply-chain costs, advanced technologies, and highly competent staff, which make Clinico Medical Sp. z o.o. a valuable and reliable partner.

The production unit consistently expands its manufacturing capacity and technical capability to implement high-volume customer projects by making purposeful investments.

In the last five years alone, more than 50 million euros have been invested in capacity extension and new technology.

With the currently ongoing expansion, the available clean-room space, for instance, will exceed 9,000 square meters (approx. 97,000 square feet) with ISO 7 and 8 areas. The new logistics hub, established in 2018, allows direct worldwide shipment and is one step to improving the availability of products for our customers. Furthermore, the plant has its own microbiological lab as well as a state-of-the-art technical lab to support the research and development of new products, which also facilitates the qualification of products and equipment. Following our road map of progress, we intend to further invent and implement fully automated assembling and packaging methods.

Besides our customer focus, we are committed to including environmental aspects in our investment activities. In fact, we are operating with trigeneration technology, or combined cooling, heat, and power (CCHP) processes, at the Błonie site to contribute to the reduction of CO_2 emissions. More precisely, we produce the electricity needed for our processes using our own cogenerator, which is much more eco-friendly than conventional procedures.



FRESENIUS KABI NANCHANG, CHINA
Manufacturing Plant and I&D Center

The production site of Fresenius Kabi Nanchang Co. Ltd., which belongs to the Pharmaceuticals and Devices division of Fresenius Kabi, is located in Nanchang City, Jiangxi Province, People's Republic of China. Nanchang is the third largest city in central China and is ascribed to the Nanchang State Economic and Technological Development Zone.

Previously known as Clinico, the plant was built in 2003 and acquired by Fresenius Kabi in 2005. Today, the dynamically growing plant covers an area of 65,000 square meters (approx. 700,000 square feet), employs about 1,000 people, and is certified by TÜV and CFDA China with ISO13485, ISO9001, CE, and MD GMP.

This manufacturing site has profound expertise in the efficient manufacturing of high-volume disposables. More than 150 different finished products are produced in Nanchang and delivered worldwide. Its extensive product range comprises application-device disposables and active devices.

In terms of application-device disposables, the major product categories are enteral nutrition sets, dedicated pump sets, infusion and transfusion sets, IV extension lines, transfer systems, and the respective accessories. With regard to active devices, the Nanchang plant produces infusion and nutrition pumps in order to meet the increasing demand of the domestic and international markets. In addition, volumetric and syringe pumps enhance the active-devices portfolio.

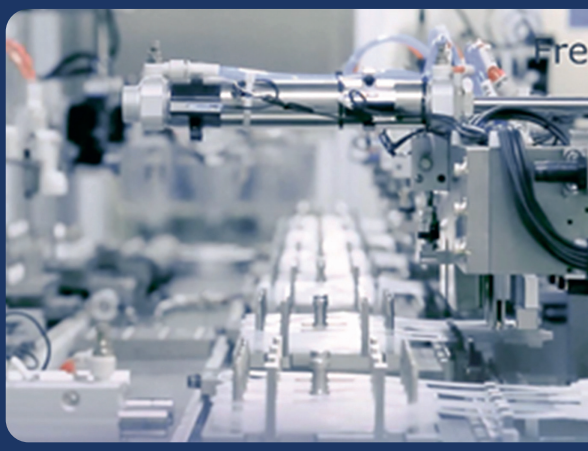
The plant specializes in injection molding, tube extrusion, automated assembly processes, thermoforming packing, and EO sterilization.

In fact, it operates its own state-of-the-art laboratory for physical testing and analysis and a clean-room of ISO Class 8 with an area of 5,288 square meters (approx. 57,000 square feet). Also, its central hub location ensures direct supply for the Asia-Pacific market and provides fast and convenient service for all customers.

Fresenius Kabi Nanchang is constantly expanding. In 2018, for instance, an I&D center with 50 highly qualified engineers to support the innovation and development of active devices and application-device disposable products was established.

Moreover, to expand its manufacturing capacity and technical capability, the Nanchang plant has been striving to increase its automated assembly processes rapidly in the last few years. Several manual assembly steps were upgraded to a higher technological level. The production of IV and EN (Enteral Nutrition) sets, for example, has been advanced to fully automated assembly lines. This increased automation consistently ensures a high level of product quality and efficiency.

The 2018 expansion enabled the Nanchang production site to reach a big milestone in achieving further market growth. In the course of this, space restrictions were eliminated. To optimize lean material flow in the future, the whole plant is currently under reorganization. With the completion of a new finished-goods warehouse, the Nanchang plant will have finalized the CNN project, which started in 2017. This strategy will strengthen the competitive position of Fresenius Kabi Nanchang, as it will result in new technologies, I&D competencies, and an even broader product portfolio.



With our philosophy "Your Partner for Solutions", Fresenius Kabi Nanchang is committed to our customers, as well as to our corporate, social, and environmental responsibility.

Looking forward to the future, Fresenius Kabi Nanchang will continue to seek improvement of processes and products to better serve our customers around the world.

IN THE SPOTLIGHT: freeflex® IV bags

Fresenius Kabi builds on its broad range of expertise in flexible container technologies for infusion and clinical nutrition therapy.

As the originator of many container technologies that include the IV bag platform **free***flex*®, we wish to highlight the characteristics and advantages we offer to our partners to fill & finish their products in our PVC-free bags.

IV bags are widely used in hospitals and health-care clinics all over the world. Plastic is preferred over glass as a packaging material for many types of pharmaceutical dosage forms due to its unbreakable, lightweight, and leak-resistant characteristics. Furthermore, plastic containers are chemically inert and corrosion resistant. They are additionally collapsible and can be easily molded or remolded. [1-3]

Fresenius Kabi's IV bag technology is the **free***flex*® container system. These IV bags are made of polyolefinen, an inert plastic material consisting of polypropylene (PP) and thermoplastic elastomer, free of PVC and latex. **free***flex*® bags are approved for various infusion solutions and are compatible with more than 140 drugs based on internal Fresenius Kabi studies and published data based on containers with comparable polyolefinen materials. [4-7]

free*flex*® are available in the size range of 50 to 1,000 mL with one or more separate ship-shaped ports made of PP. Their arrow and color coding facilitate the identification of the injection and infusion ports, and the tamper-evident flip-off covers protect them from external contamination. Tests have shown that the infusion port is compatible with all IV sets commonly available on the market. The container concept of **free***flex*® offers a strictly closed system for drug reconstitution to guarantee maximum sterility while ensuring intuitive and safe handling. [8-10]

The package concept of **free***flex*® bags consists of a primary bag to hold the solution and a secondary bag as physical sterile protection. The secondary PVC-free film is clear and flexible; it protects the primary bag mechanically and against water loss through vaporing. The overwrap is easy to open and has excellent transparency to allow visual inspection. **free***flex*® bags are sterilized in their overwraps at 121°C.

Leading independent hospital physicians and pharmacists in France have awarded freeflex® the top accolade for innovation. It is representing Fresenius Kabi's solution to the increasing complexity of drug handling and infusion protocols.

It is designed to simplify user handling and maximize patient safety. From the crystal-clear, non-PVC, phthalate-free bag and patented leak-resistant technology to the easy-to-handle bag design, every element of this innovative and flexible container system makes **free***flex*® the perfect choice for safe infusions.

free*flex*® bags are produced by Fresenius Kabi in many facilities around the world, including Fresenius Kabi Norge AS in Halden, which, as described below, is a competence center for the filling of IV drugs in bags based on decades of experience and state-of-the-art technologies.

The advantages of using freeflex® bags include:

Easy handling:

The shape of **free***flex*® is optimized for both strength and convenience and has soft edges that will not cut hands or gloves.

Excellent drug compatibility:

free*flex*® bags demonstrate high drug compatibility standards and have been tested with more than 140 drugs including antibiotics and cancer drugs. [11]

Environmentally friendly:

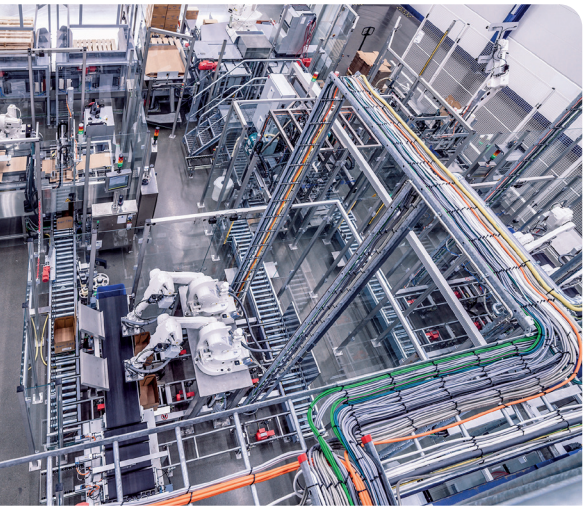
free*flex*® bags can be recycled to minimize the environmental impact through the product life cycle.

HALDEN PLANT IN NORWAY

Center of Excellence for freeflex® IV Bags

Fresenius Kabi's center of excellence for **free***flex*® IV bags is located in Halden, in the southern part of Norway, and builds on over 40 years of experience with more than 20 years of history within Fresenius Kabi. The plant focuses on the production and worldwide distribution of IV drugs and standard solutions, both for Fresenius Kabi and contract manufacturing partners.

The Halden plant specializes in the fill & finish of plastic containers that can be manufactured in-house through blow-fill-seal technology, has the advantage of a diverse container portfolio, and offers size flexibility.



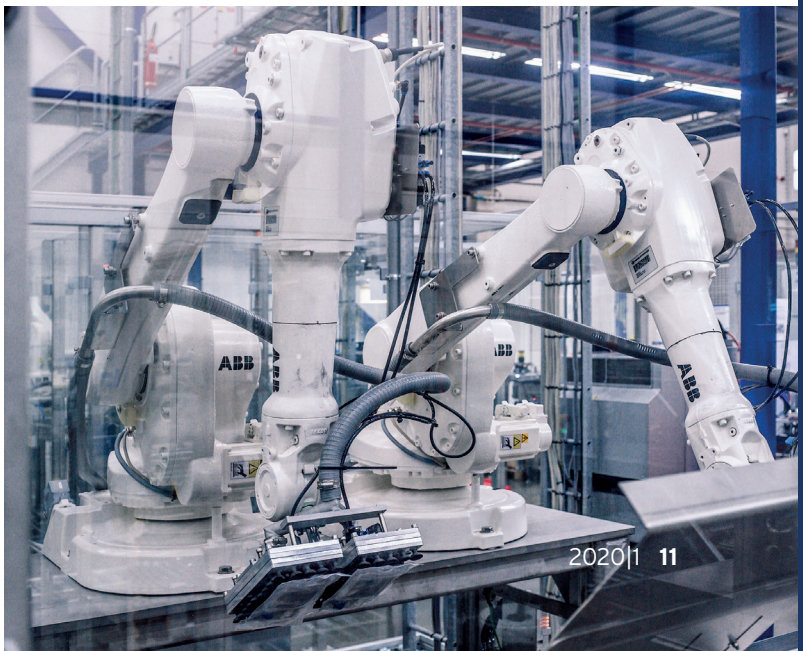
IV bags are produced in automated production lines, and all steps (bag production, filling, overwrapping, sterilization, and packaging) are carried out in a continuous process under clean-room conditions. In Halden, we produce 100 million units of water-based drugs for infusion, injection, rinsing, and disinfection every year. We fill these pharmaceuticals in various plastic containers, such as IV bags (50 to 1,000 mL), polypropylene (PP) ampoules (10 to 30 mL) and vials (10 to 20 mL), and polyethylene (PE) bottles (125 to 1000 mL).

This manufacturing facility is highly automated and equipped with state-of-the-art manufacturing lines, half of which are dedicated to **free***flex*® bag production. The plant has recently implemented an in-house preprint machine, which offers a unique option to launch products with a multicolored print design on the primary bags. **free***flex*® bags can now be wrapped in different types of overwraps according to product and customer requirements. Light-sensitive products can be packed in aluminum overwraps, with black or multicolored printing. We also fill oxygen-sensitive drugs in **free***flex*® IV bags, where we combine nitrogen-filling technologies with the aluminum overwrap for the best protection of the drug product with a shelf life comparable to glass containers.

Halden produces more than 50 million units of polypropylene (PP) ampoules and vials each year.

The products are manufactured with blow-fill-seal technology that uses an automated multistep process to form, fill, and seal containers in an uninterrupted sequence of operations that are carried out in one contained compartment. Based on the product and customer requirements, the ampoules are packed directly into cartons, or in a sterile blister pack, with black or multicolored printing.
To support you with a global supply of your product, our Halden plant has been inspected by various medical authorities, including the US FDA, to serve the worldwide market, including key markets like the EU, the US, China, Japan, Brazil, and Australia.
The plant holds ISO quality and environmental certification as ISO 9001: 2018, ISO 13485: 2019, and ISO 14001: 2018.

We are proud to offer our partners the possibility of filling their solutions into our **free***flex*® bags in Halden, Norway! Please get in touch with us to find the perfect solution to your fill & finish needs.



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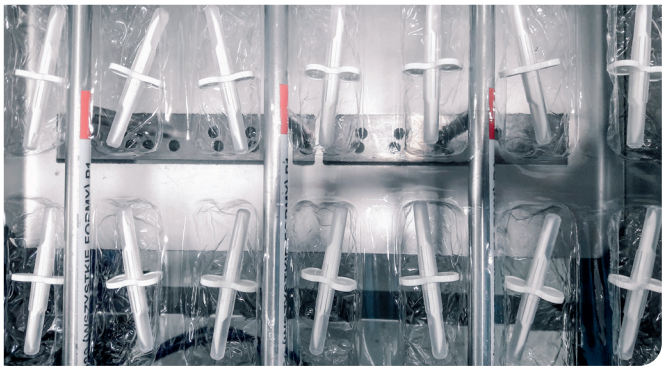

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Fresenius Kabi Contract Manufacturing is the contract manufacturing platform of Fresenius Kabi, providing partners with easy access to the expertise of more than 20 manufacturing sites worldwide. Capabilities include the fill & finish of sterile pharmaceuticals in a wide variety of containers, as well as sterile devices and APIs.

Insight is a publication of Fresenius Kabi Contract Manufacturing.