O-COM

THE OPTIMA MAGAZINE

All-round service, artificial intelligence, time-to-market

Full focus:

Holistic solutions for the future of your production

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Your turnkey partner – **today and tomorrow**

Gerhard Breu
Chairman,
Optima Pharma Division

Dear Reader,

More than ever, the dynamic market requires maximum flexibility and perfect quality. Why you can count on Optima as your top partner?

Because we believe partnership is the key to success. Because we use our industry knowledge and our technological expertise to drive your success. And because we provide you with complete, integrated solutions from a single source - bringing your newly approved pharmaceutical and biotech products to market in record time.

Our new slogan "Your home for turnkey" embodies this idea and anchors its strategy in the company.

Read about: A successful turnkey project for the perfect drug process, how INCOG has fast tracked the launch of its pharmaceutical product in record time with Optima, and much more in this c-com issue.

Would you like to look into the future? So would we! That is why we are working intensively on artificial intelligence and its potential for pharmaceutical production. Another important step towards the future: sustainable machine and packaging solutions. Read about the ideas and trends Optima is realizing in this area in the interview with my colleague Dr. Stefan König, Managing Director of the Optima Group.

Enjoy reading!

Yours,
Gerhard Breu

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Service

Optima Pharma's service department is re-organizing itself. The goal: to further increase customer satisfaction.

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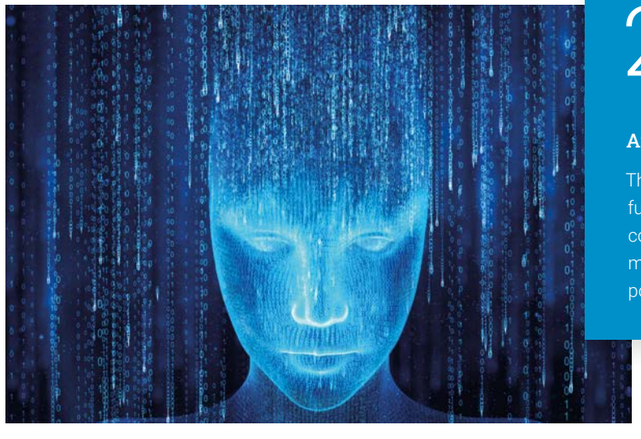
CSPE

Time is short. Especially when a new turnkey filling and capping line for vials with isolator is installed and commissioned in the immediate vicinity of a pharmaceutical production facility. An example of how the CSPE process shortened the on-site work phase at a customer by approximately two months.



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Artificial intelligence

The mandatory Annex 1 promotes the pursuit of further increased pharmaceutical safety: What contribution can new automation solutions make to this? And do these solutions have a positive effect on skill shortage?

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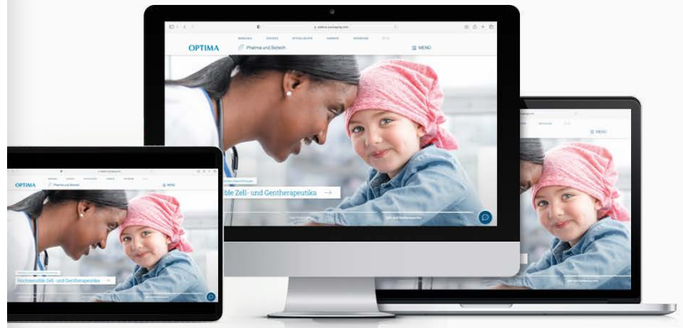
The big website relaunch

Content growth of up to 1,000%: Optima's new website offers a state-of-the-art design and even more targeted information for customers and prospects. Whether they are seeking information on aseptic filling, isolator and containment, freeze-drying or cell and gene therapy – visitors to the site will find information on all of Optima's solutions for the pharmaceutical and biotech industry. They will also find additional information on our sustainability efforts, service portfolio, success stories and interviews with Optima experts.

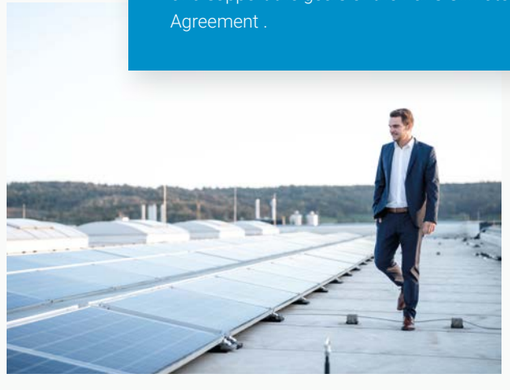


OPTIMA on course for growth

Optima is strengthening its claim as a technology leader and strategic partner and can look back on another successful business year 2022. Optima has retained the flexibility of a family company and combined it with the performance strength of a group. That is why the company now has over 7,000 customers, from start-ups to large company groups. Optima generates the majority of the revenue abroad, with exports accounting for over 85 percent. About 3,000 people are employed worldwide at 20 locations. Over 2,500 in Germany and over 2,000 of these in Schwaebisch Hall.

Shaping a sustainable future

Sustainability is part of the Optima Group's corporate DNA. This results in valuable practices, such as conducting regular sustainability management ratings, including those from EcoVadis, to identify opportunities for improvement early on. As part of the Carbon Disclosure Project (CDP), the grouap provides environmental data for better transparency. In addition, Optima focuses on CO_2 reduction targets based on the Science Based Targets initiative (SBTi) methods that are proven effective and support the goals of the Paris Climate Agreement .



Clear approach with new company mission statement

To provide orientation for the many new employees and customers, Optima updated its mission statement. "We care for people" defines a clear mission, vision, principles and values. With its technologies and solutions, Optima makes a valuable contribution to improving health and safety and creating a better quality of life. The vision is to be the best partner for filling, packaging and production systems for challenging products. The group has also committed to the values that characterize the daily cooperation within the team: reliability, partnership, commitment, focus on solutions and a human approach.

Milestone for strategic turnkey approach

Optima Pharma focuses on consistently aligning its processes to the needs of its customers. The greatest benefit of working with Optima is that all solutions are provided from a single source. This approach marks another major milestone in system integration: METALL+PLASTIC GmbH will become OPTIMA pharma containment GmbH on October 1, 2023. Our three Optima Pharma Division sites in Schwäbisch Hall, Radolfzell, and Mornshausen, coordinate to provide an integrated total solution. We offer filling machines, isolators, and freeze-dryers, all from one partner, which is unique in the industry.

With the new slogan, **"Your home for turnkey"**, Optima Pharma further expresses its claim and thus anchors the strategic positioning in the company more strongly than ever: Optima is your expert, partner, and home for turnkey. Optima Pharma assures competence, safety, and reliability.

→
By synchronizing service areas across locations, maintenance operations for the individual line components can be optimally planned and stay in step with each other. System availability continues to rise.

One **team**, one **product**, one **point of contact**

Optima Pharma's support service is undergoing reorganization to boost customer satisfaction even more. We have consolidated all of our service areas across all of our sites. Now customers worldwide have a central contact for all issues in the form of a Service Account Manager who coordinates the back-office teams. The individual Optima Pharma sites continue growing together as "OneTeam".

IMPORTANT FOR YOU

- OneTeam: new worldwide service organization at Optima Pharma
- Cross-location core teams for customer support, maintenance support, competence team, qualification & validation, and business development/processes
- Benefits to the customer include: a central contact with clear responsibility, higher satisfaction levels, unified services and quality standards, faster response times, and improved planning of spare part packages and external operations
- Benefits for Optima staff include: professional and personal growth coming from specialization and exchange of knowledge, standardized tools, and shared expertise, a stronger team spirit, and a reduced workload for specialist departments

> Our customers will clearly have the sense that we are one team and are working hand in hand on a product.
>
> Holger Burgermeister, Service Director at Optima Pharma

Harmonizing the service areas results in coordinated replacement and worn parts recommendations, standardized service descriptions, and offers from a dedicated contact.

2022 was a highly successful year for Optima Pharma. The integrated turnkey process, CSPE (Comprehensive Scientific Process Engineering), cuts the time to production start-up for filling lines. It has had a very positive take-up in the marketplace. Worldwide, the number of machines in operation has continued to grow. The service presence has also grown, with the new service hub opening in Raleigh, North Carolina, as one example. Even more than before, Optima Pharma is perceived by customers as a strategic partner for total systems that include technologies for filling and closing, for isolators, and freeze-drying. Hence work has focused on the service portfolio over the last year. What came out of this was a thoughtfully designed, target-group-specific program called "Lifetime Production Readiness."

Core teams across sites and a single point of contact

Holger Burgermeister, Service Director at Optima Pharma, explains, "The next step in our overall strategy is the collective, coordinated ongoing development of the service areas." That is why throughout 2023, Optima Pharma is now creating core teams for the following service areas: Customer Care, Maintenance Support, Competence Team, Qualification and Validation, and Business Development/Processes. These teams work in close collaboration across locations and with foreign subsidiaries. Optima Pharma's filling and closing technologies are created at its headquarters in Schwäbisch Hall, decontamination technologies and isolators originate in Radolfzell, and freeze-drying technology comes from Gladenbach-Mornshausen. One central Service Account Manager is in place to coordinate the customer's requests on all line items with these teams. Burgermeister says, "This is a response to our customers' desire to have a leading point of contact and leads to increased satisfaction."

The cross-location service strategy provides the turnkey concept with an even broader scope. The new service strategy accompanies increased internationalization. Burgermeister points out, "This is a significant advantage for our customers. Optima Pharma mainly has its own personnel in the markets." This means that service staff often work directly on site on the customer's premises or out of an Optima Service Hub and are in close contact with customers. Holger Burgermeister is responsible for the cross-location area of "Business Development/Processes" and supports the development of the global service structure.

Five Service Areas, five Managers

Customer support is centralized through Manuel Müller, Group Leader of Customer Support at Optima Pharma. His area covers project management, project planning, and worldwide customer support. "The reorganization aims to provide customers with a target-group oriented, coordinated service portfolio for filling machines, isolators and freeze-dryers, one that meets their high expectations of lifetime production readiness," says Manuel Müller regarding the restructuring of the service areas. "In the future, customer requests will be projected and processed in line with defined standards for the entire turnkey line. For quotations and order processing, we work as OneTeam, aiming to deliver real added value to our customers," says Müller.

↑
Now qualification documents for pharmaceutical lines come from a single source.

Our customer service is now being structured worldwide in line with this philosophy so that both the needs of local one-off projects and global turnkey projects are met.

“Our leading points of contact are operating globally, so they are usually in the same time zone, making them much more available to our clients,” says Müller. “Our staff’s greater availability ensures that our customer’s requirements can be coordinated more quickly and locally, but without sacrificing the link to the technical departments based in Germany.” To this end, service employees receive unified training via cross-location qualification programs, ensuring the same standard of training worldwide.

Matthias Staus, Group Leader of Service at Optima Pharma, heads up Maintenance Support. This service area schedules preventive and status-based maintenance work at customers’ sites. When asked about the benefits of the new service strategy, the answer is clear: “We are able to offer our customers proactive spare part and maintenance strategies across multiple sites,” says Matthias Staus. This standardization results in coordinated recommendations for replacement and worn parts for the entire plant, uniform performance descriptions, and a single quotation from a single point of contact. Service calls for the different line components can be better coordinated. “Our team is coming even closer together, and colleagues can benefit from the expertise and experience of their team members,” says Staus confidently.

Ronny Wiske, Group Leader of Life Cycle Services at Optima Pharma, will be responsible in the future for the Competence Team area across all locations. This department focuses on support services for the systems and troubleshooting. “In the event of malfunctions at the entire plant, customers can expect that troubleshooting will be easy, documented, and coordinated.

Our team is positioned to analyze and resolve complex, cross-product incidents jointly. To this end, unified procedures are followed, both in the choice of remote tools and methodology. The reorganization has enabled us to successfully use synergies and lessons learned for further installations in the field and in our new projects,” says Wiske. “By standardizing our tools and processes in Germany, with the organization in place overseas, and by having experts on the ground, we are learning together and becoming even more effective in handling all of our customer’s needs,” Wiske adds.

Andreas Milich, the Radolfzell-based Service Director, is responsible for qualification and validation across all sites. The same principle holds true in his area: One team, one approach, one qualified system for the customer. “When it comes to qualification and validation, we are continuing to embrace the CSPE 2.0 approach and are bringing the expertise of all our sites together even more effectively,” Milich explains. All the qualification documents come from a single source, and in-depth internal coordination means that extensive parts of the qualification process can be handled seamlessly during continuous plant operation. Also, customers benefit from this coordinated approach using resources like calibration materials. “This makes the CSPE 2.0 an all-around trouble-free package in terms of qualification and validation, too,” says Milich. Employees receive intensive training to prepare them for the new organization.

> We are able to offer our customers proactive spare part and maintenance strategies.
>
> Matthias Staus, Group Leader of Service at Optima Pharma

←
With our service account managers working all around the world, they have particularly close relationships with customers, and it’s clear that service response times can be significantly shorter.

CSPE for **perfect drug processing**

Time is of the essence. Especially when installing a new turnkey vial filling and closing line with an isolator in the immediate vicinity of a current pharmaceutical production area. CSPE ensured precise production start with minimized effect on the customer's ongoing manufacturing operations. The installed system also features comprehensive product saving functions.

The preliminary cycle development has already been carried out in the CSPE center at Optima Pharma.

IMPORTANT FOR YOU

- New turnkey filling system with isolator for vials for an international pharmaceutical company
- Comprehensive product saving functions for filling and closing are integrated
- Overhead cameras provide retrospective security, for example after interventions via the isolator gloves
- With the CSPE process, the system design is extensively optimized virtually in advance
- Adaptations of the system to the building could be flexibly implemented in several project phases with CSPE
- Thanks to CSPE, the on-site work phase at the customer was reduced by around two months

→ The CSPE process saved an estimated two months of time for this project, according to internal estimates.

It is very beneficial for pharmaceutical companies to minimize the time from installation to Site Acceptance Test (SAT). To accomplish this objective for a global pharmaceutical customer, Optima used the Comprehensive Scientific Process Engineering (CSPE) method – system integration at the highest level.

"CSPE starts early in the design and engineering phase. Ultimately, the approach addresses potential risks early on in the CSPE centers at Optima Pharma – solving any potential difficulties before delivery", says Armin Weber, Director Project Engineering at Optima Pharma.

Complete line fully integrated

High quality, sensitive and expensive pharmaceuticals are produced using scarce raw materials. Numerous system functions maximize the output of usable drugs from a given quantity of liquids per batch - optimizing the product yield.

This new line consists of a washing machine for vial cleaning, a sterilization tunnel, a filling and closing machine under an isolator, and a tray loader. The system design took place parallel to the building modifications, incorporating changes to account for limitations of the existing building. The installation area reverted to a shell state, but the ceiling height, supporting pillars and various ventilation ducts remained. Optima adapted the isolator technology to fit the building's existing ventilation, relocating elements of the isolator ventilation technology to the technical area above.

Work in progress: remaining flexible

Even in this phase, the advantages of the CSPE process were apparent. The project team coordinated the entire filling and closing line, as well as the isolator structure, meaning the new interfaces could be tested virtually and quickly.

The CSPE services during the design phase also included airflow simulations, creating an ideal, low-turbulence laminar flow over the entire isolator area. The filling nozzle geometry, in combination with the containers, was also simulated and optimized. The first parameter settings for clean and high-performance filling functions were developed. Later, the entire automation and safety circuits were tested live in the CSPE center.

Maximizing product yield

High product yield – an essential project objective – requires a high-precision filling system. In addition, specific functions are crucial. For example, when the system is started-up, a certain amount of time is required before the filling system can achieve consistent filling weights. To use the product to its maximum during priming, containers are first filled on a load cell until the target weight is reached. When complete fill accuracy is achieved, the filling system automatically switches to standard operation.

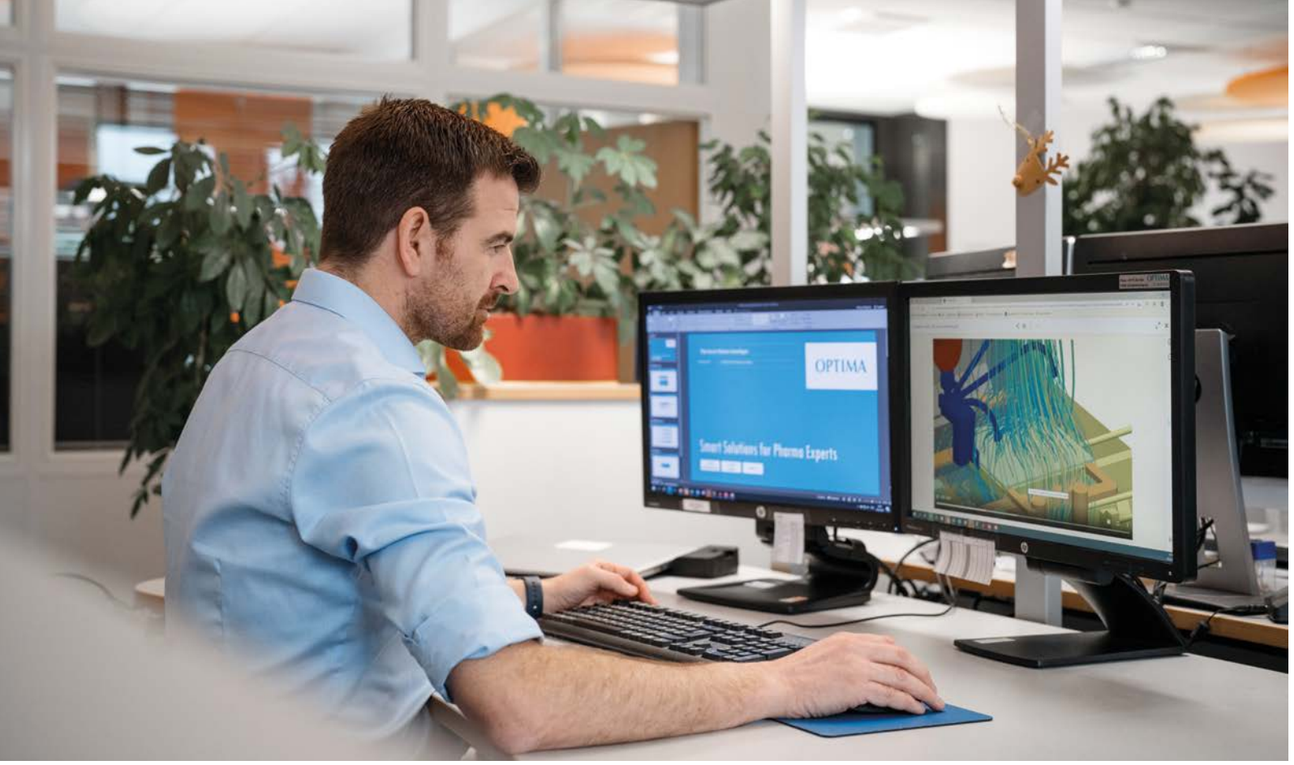
Even at full capacity, the filling weight of each individual container is checked. If deviations occur, the system immediately stops the regular operation process to refill missing product. Towards the end of a batch, this function can also be used to fill the "last drop" of the product without risk. Only the last container, without enough product, will be rejected. With these features, filling accuracy per batch is 50 to 100 times higher than conventional filling systems.

Other functions support the high product yield: If the first attempt to place and insert a stopper fails, the system stops regular operation and repeats the process - called re-stoppering. The stopper "pop-up effect" that might occur with larger fill volumes – an overpressure in the container after closing that might loosen a stopper – is no problem for the Optima system. To prevent this issue, the stopper placement is manipulated during the press-on process, allowing air to escape from the container. The cap-roundness-control checks the crimp caps with a camera for roundness in the sorting bowl. The Optima system only allows well-tested, round caps to be used, preventing unnecessary rejects.

↑ In the first step, the vials are cleaned in a washing machine.

↑ After the sterilization tunnel, there is a transition to the isolator-protected filling area.

↑ Up to 5,000 vials are processed per hour. Product saving functions make optimal use of the available quantity of drugs.



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Various simulations are part of the CPSE process, including the laminar flow and the filling behavior.

Recorded processes provide security

The integrated overview cameras from Optima's Intelligent Production Assistance Services (IPAS) portfolio "save" individual drugs or entire batches by continuously recording system processes. This is beneficial, for example, during manual intervention through the glove ports in case of a system failure. Any non-conformities can be clarified by consulting internal records and decisions can be made and accurately documented.
The line achieves an output of up to 5,000 vials per hour (70 ml vial format). For quick format changes, Optima has installed a transport rake that handles the entire range from 70 ml to 500 ml without format parts.

The mechanical format change over, which can be completed with a servo motor, takes about 30 minutes before the line is ready for use again.
In May 2021, the line was designed and extensively tested with an isolator in the CSPE center. Among other things, the tightness of the isolator and the function of all interfaces were tested here. As part of the integrated Factory Acceptance Test (iFAT), Optima carried out numerous qualification tests that would otherwise only take place at the customer site. Based on these tests, the pharmaceutical company later succeeded in significantly accelerating its own tests by leveraging values from the iFAT.

> The system technology will greatly increase our efficiency in the area of application that is already certain.
>
> Customer testimonial (international pharmaceutical company)

Two months saved

The same applies to the pre-cycle development for the isolator. Optima now offers this as an additional CSPE service. Using biological and chemical indicators, the first values were developed in Optima's in-house laboratory and temperature distribution studies were carried out. Together, this resulted in a very good basis for the final cycle development at the customer. Matthias Naser (Chief Operation Officer), who played a key role in the project, estimates that CSPE services saved around two months of time. These are two valuable months in which the employees of the pharmaceutical company were able to pursue their actual tasks.

The project took place during the peak of the COVID-19 crisis with strict travel restrictions. As a result, the customer's project participants were ultimately only on site at the iFAT in Schwäbisch Hall and with a reduced team. With online training courses, future operators began training with the system even before the iFAT. At the iFAT, only a small number of Optima employees were present in the assembly hall of the CSPE center, the rest of the Optima team participated remotely. This allowed all customer employees, who came to see the system to be onsite.

Precision up to the installation site

Bringing in the various parts of the system once again required full attention and a detailed move-in concept. The new system could be transported to its place of installation in parts, in stages and with millimeter clearances to an open outer wall and a platform specially built for this project. The SAT followed immediately in October 2021, because the isolator and filling and sealing machine were already a well-established team.

The customer is very satisfied with the course of the project and the system technology: "An almost smooth course of events under difficult conditions is something that cannot be taken for granted. And the system technology will greatly increase our efficiency in the application area – this is already clear today."

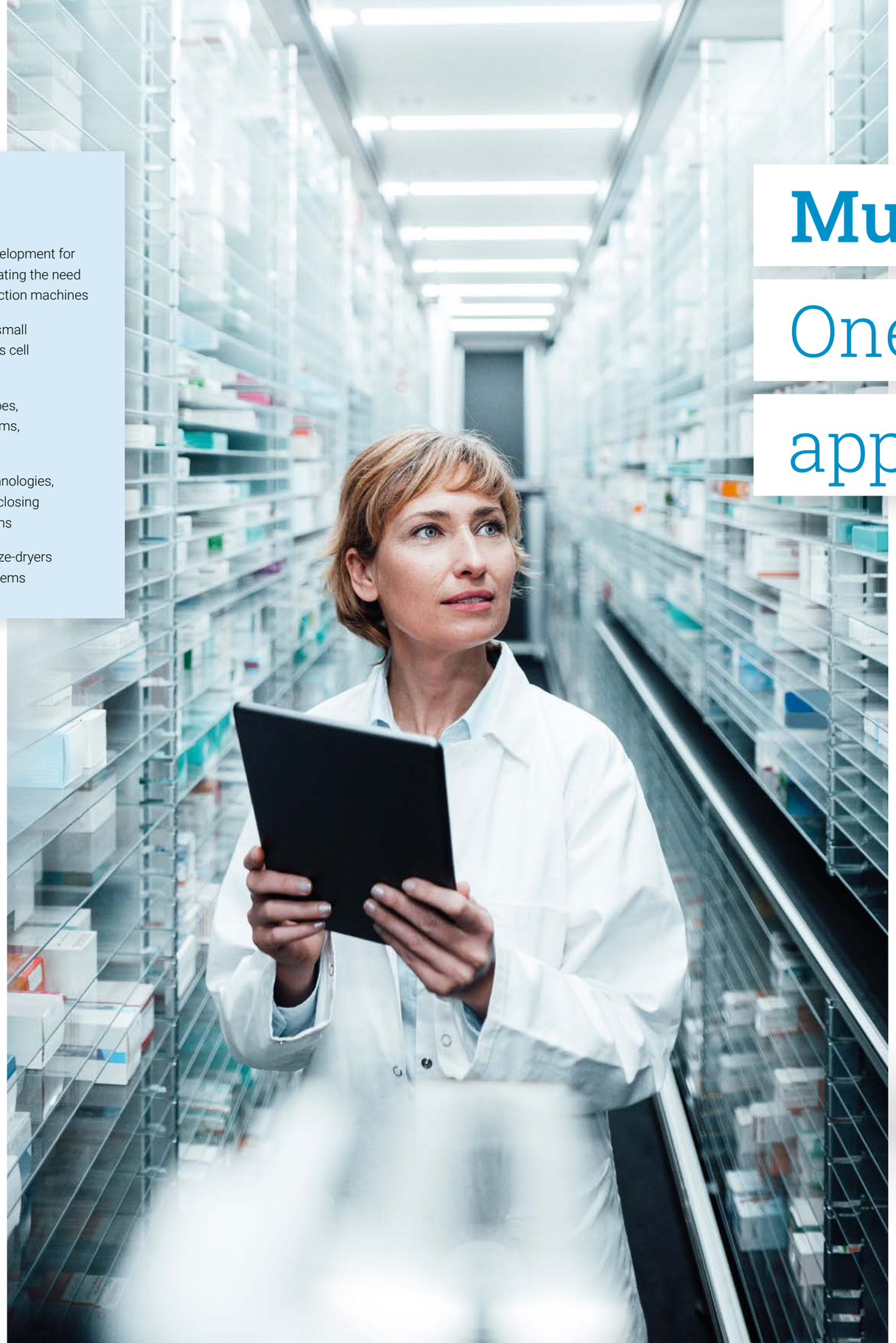
←
According to the customer, the new system for dosing and sealing expensive, sensitive medicines will greatly increase efficiency in the area of application.

Fully installed and and operational – the conclusion of the customer is clear. ↓

→
Customization dominated when designing and installing the machines in the existing building.

IMPORTANT FOR YOU

- MultiUse LAB: Perfect parameter development for MultiUse production systems, eliminating the need for additional development for production machines
- Flawless commercial processing of small batches of high-quality drugs, such as cell and gene therapies, under isolator
- Highly flexible: Different container types, functions, product paths, filling systems, formats and installation locations
- All product saving functions and technologies, like sensor filling, vacuum filling and closing are identical to the production systems
- Suitable isolator technology and freeze-dryers with loading systems as turnkey systems



MultiUse LAB:

One machine, two application areas

The MulitUse LAB handles small batches of high-quality drugs in a sterile process. It offers development parameter settings for production equipment – without additional development for the production machines.

↑ The MultiUse LAB fully covers two application scenarios: Producing small batches of high-quality pharmaceuticals and parameter development for high output equipment. Development tasks are completed for production systems.

The latest addition to the MultiUse portfolio has it all. The MultiUse LAB is a particularly compact machine – and yet its integrated functions correspond exactly to those in higher performance ranges. With the MultiUse LAB, the production system settings can be set-up perfectly from the beginning.

With its special design, the MultiUse LAB is equally suitable for the commercial processing of particularly expensive and complex drugs in very small batches. The field of applications of the machine with an isolator also include the clinical phases.

System settings to go

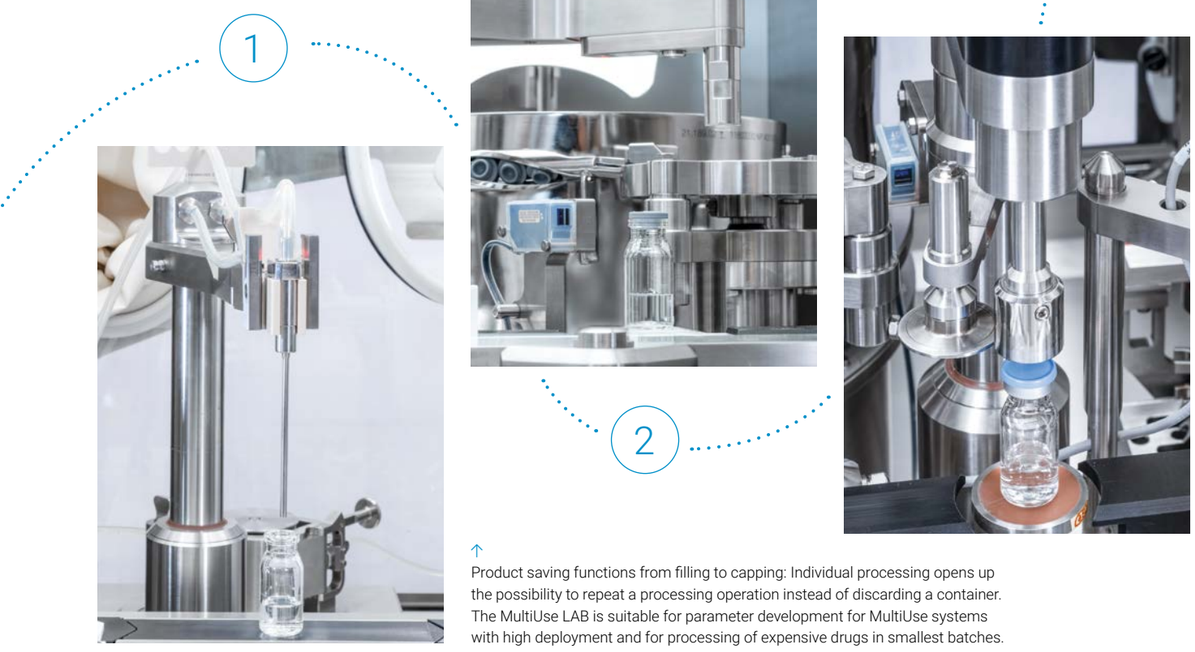
Let's first look at the development of the settings: The MultiUse LAB relieves existing MultiUse systems from recipe development tasks for which they were not originally intended. Determining new settings for a new drug or a new type of container can cause downtime for a production line, which could mean massive production interruption and revenue loss. Costs also arise when high-output MultiUse systems are used for the development of settings in which multiple containers and materials are used. The use of a MultiUse LAB is a much more efficient option.

If system settings are to be set for laboratory use, a number of technical requirements must first be met. Technical equivalence is one of them: Like the other machines in the portfolio, the MultiUse LAB can handle three different container types - vials, pre-filled syringes and cartridges. Like the high-output MultiUse systems, the MultiUse LAB has all product saving functions, from sensors to vacuum filling and closing of the containers to ensure technical equivalence.

Technically identical

In order for the settings to be scaled-up successfully on a production line, not only the function scope has to be identical, but also the respective design. Therefore, Optima has transferred most functions from the large MultiUse systems to the LAB version. For example, the design of the drives, the software and process-relevant mechanical parts, like insertion rod are unchanged from the production machines.

The same applies to processing functions, such as filling, stoppering and crimping, all of which are carried out the same as in the production systems. For the individual stations and functions



↑
Product saving functions from filling to capping: Individual processing opens up the possibility to repeat a processing operation instead of discarding a container. The MultiUse LAB is suitable for parameter development for MultiUse systems with high deployment and for processing of expensive drugs in smallest batches.

↑
The OPTIMA MultiUse LAB is designed on processing RTU containers.

to correspond to the high-output machinery, the containers are processed individually and fully automatically. Product-saving functions have to be designed one-to-one, for example re-dosing, so they can be transferred from the MultiUse LAB into the larger systems.

Parameter settings – a service

For best parameter settings, high-speed cameras can be integrated into the MultiUse LAB to observe crucial processes. Additional sensors like pressure monitoring for the crimping process can be installed. With the extensive information - visual insights and measurement data - the parameter setting is much more targeted than on high-output production lines.

With the MultiUse LAB, the first CDMOs will even offer parameter-setting development as an external service for pharmaceutical companies. Likewise, pharmaceutical companies that invest in a MultiUse LAB benefit from the precise scaling and transfer of the system settings to their larger lines.

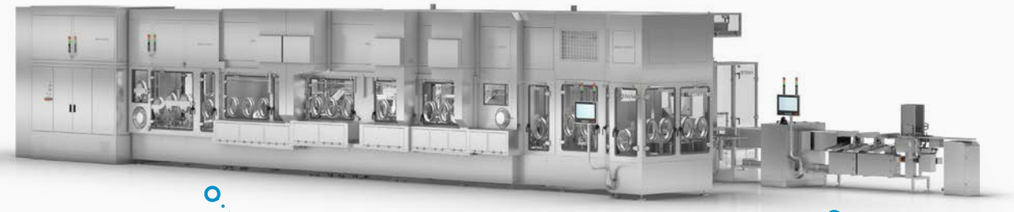
Everything for production: Cell and gene therapies

The MultiUse LAB is a complete production machine for high-quality drugs in small batches. For example, drugs from personalized medicine, cell and gene therapies, but also start-ups are among the target markets for the new machine type. The LAB version is designed for a reduced output.
For expensive drugs, users benefit from the integrated product saving functions. With particularly small batches, the product yield can be further maximized by switching to single-head dosing. With the flexible combination-filling module from Optima, the common pump systems can be integrated into the system quickly. The appropriate filling system depends on the product properties.

Sterile, gentle transport

The MultiUse LAB with isolator offers a fully automated transport and handling process from de-nesting to re-nesting under aseptic conditions. The containers are removed from the nest

From plants with
low output to a flexible
high performance plant



Identical processes and functions from laboratories to high-performance. The highest product yield and flexibility, variable processing paths and turnkey implementation including isolators and freeze-drying systems - all combined in the unique MultiUse machine concept. The MultiUse LAB completes Optima's portfolio of turnkey filling machines for batches of any size and container type.

and transported between stations with an automatic handling system – hands-on work on the container is eliminated. After individual processing, the RTU containers are placed back into a nest. There is no glass-to-glass contact at any point, which is an important criterion in commercial processing, especially in the case of sensitive packaging like cryogenic packaging.

The handling system matches the low performance range and offers cost advantages compared to the transport systems of the production lines. To modify the container type only the format parts need to be exchanged – not the modules. No additional rebuild work is required. A welcome advantage: no modules have to be stored. Everything remains in the "3-in-1" machine for vials, pre-filled syringes and cartridges.

Use in research & development

Depending on the drug type, it is conceivable that production batches will grow. There is already a qualified production process that can be transferred to a larger MultiUse system. Re-qualification or validation is now much easier because the processes are identical, apart from the transport.

The clinical phase is also an application area for the MultiUse LAB, when pharmaceutical liquids with APIs (Active Pharmaceutical Ingredients) are to be filled and closed as part of research and development. Pharmaceutical companies and universities reap benefits from the MultiUse LAB version. The implementation of media fills and stability tests of future drugs are additional areas of application from the laboratory area.

Isolator and freeze-dryer

The isolator of the MultiUse LAB corresponds to INTISO technology. Even on a small scale, the Optima turnkey approach and Comprehensive Scientific Process Engineering (CSPE) are effective, because the isolator is already extensively synchronized with the MultiUse LAB in its design. The air handling system of the isolator is fully integrated, and there is no separate HVAC unit, therefore, no connection to the technical area is required. With integrated cooling, the heat load is not released into the clean room. In addition, the H_2O_2 used for decontamination is catalytically neutralized after the decontamination process is complete and can be discharged into the installation room as exhaust air. This isolator design saves time and costs during commissioning.

For commercial use, but also for research and development, the connection to a freeze-drying process is often important. The first MultiUse LAB commissioned is a turnkey project and will be connected to an Optima freeze-dryer featuring row-by-row loading. New types of freeze-dryers are currently in the design and implementation phase at Optima. This equipment is specially designed for the development of freeze-drying recipes, for laboratories and for the production of particularly small commercial batches (see p. 32).

Fits everywhere

The MultiUse LAB needs very little space. Optima's isolator technology contributes to the small footprint. In addition, the machine can be broken down for transport and is designed to fit in standard freight elevators, making it easier to bring into existing facilities.
Conclusion: The MultiUse LAB has been thought through to the detail – both for development of recipe setting for systems with higher outputs and for the production of small batches of very high-quality pharmaceuticals.

MORE ABOUT THIS TOPIC

Highly flexible: MultiUse systems from OPTIMA

The MultiUse machine series is unique. Each MultiUse system can process three container types: Vials, pre-filled syringes and cartridges - without any module change. In order to maximize product yield, comprehensive product saving functions are integrated into MultiUse systems. Different product paths can also be installed in one system, for example for freeze-dried products, for RTU and bulk containers. The isolator and freeze-drying technology are designed and implemented turnkey in the OPTIMA CSPE process (Comprehensive Scientific Process Engineering). The MultiUse portfolio includes all performance areas up to high-performance systems with an output of up to 24,000 objects/h. The new MultiUse LAB is ideal for the development of recipe parameter settings for production systems, as well as for the commercial manufacturing of high-quality drugs in small batches and the clinical phases.

↑ Like every MultiUse machine, the LAB version is a 3-in-1 machine: vials, pre-filled syringes and cartridges are processed without module changes.

IMPORTANT FOR YOU

- New automation solutions meet current GMP requirements and help pharmaceutical manufacturers counteract the shortage of skilled workers
- Optima Pharma plans the minimization of glove ports, even for systems with high output
- Existing and future automations including: Inline environmental monitoring with germ analysis, inline stopper correction in pick-and-place infeed, product path handling, container infeed with automated RTP ports, rescue solutions
- The implementation of robot control technology, which includes artificial intelligence, has unlocked new possibilities, and the first function has successfully been executed

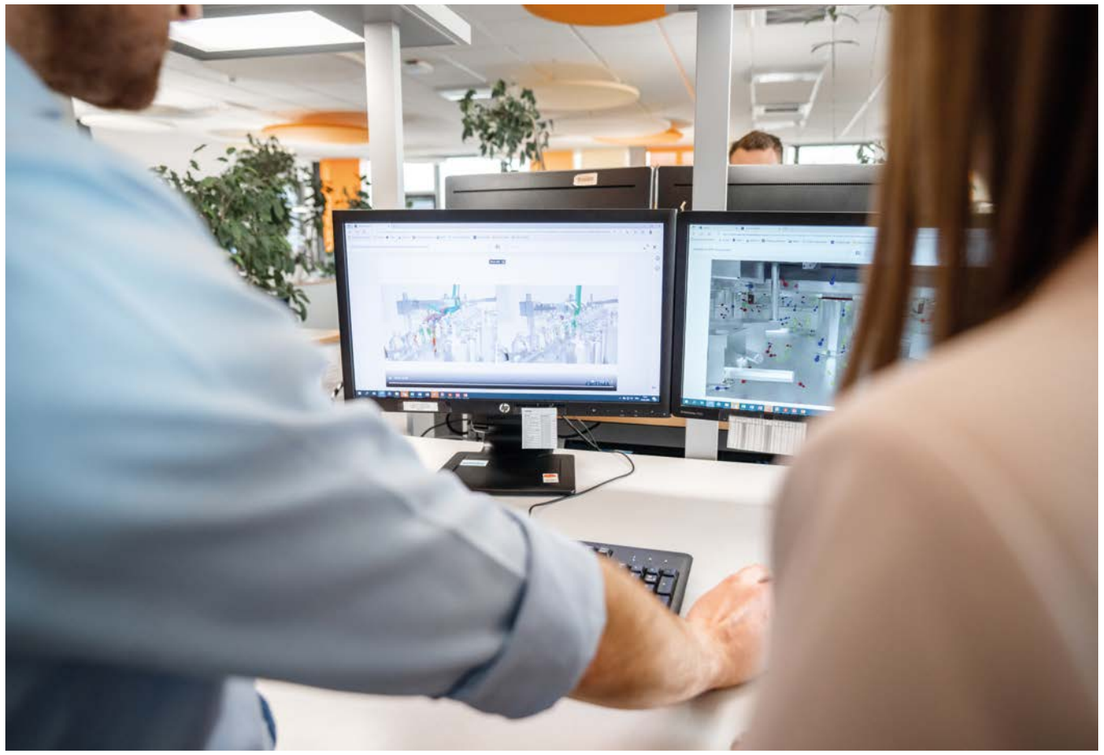
AI-automated into the GMP future

Less manual intervention, more automation: Annex 1, which has been mandatory since August 2022, promotes the pursuit of increased pharmaceutical safety. What impact can new automation solutions have? Will these solutions have a positive effect on the ongoing shortage of skilled workers?

New challenges lead to new solutions – often through a phase of incremental improvements until the benefits clearly outweigh any potential drawbacks. The introduction of isolator technology is one example; initially several hour-long decontamination cycles were opposed to the first reproducible decontamination results.
A new approach to isolator systems has emerged that eliminates the need for glove ports and opens up new possibilities. While manual intervention can have both benefits and drawbacks, those who have the chance to manually retrieve a costly drug batch will likely opt for GMP-compliant glove ports. However, there is no guarantee of consistent intervention and the gloves themselves pose a pharmaceutical risk, which is addressed through established methods.

Glove ports: Less is more

The idea of an isolator without glove ports is fascinating. GMP-compliant operation via glove ports can be trained, but ultimately people cannot be “programmed”. Even the slightest mistake, such as handling a decontaminated but not steam-sterilized glove over a stopper sorting bowl, could compromise the “first air principle” as outlined in Annex 1 for product contact parts.
This creates a demand for automation innovations that minimize potential pharmaceutical risks while reducing the number of needed personnel to counteract the shortage of skilled workers.



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Simulations support the design department to implement the current GMP Annex 1 requirements, in particular the "First Air Principle", optimizing the filling and closing systems. The laminar flow is precisely reproduced.

Improving reproducibility and solving labor shortages

It is certain that no single technology can be used to implement additional pharmaceutical processes automation. Differentiated technical solutions will be necessary for various sections of the system.
Optima Pharma understands the importance of ensuring that high output systems have access to these functions. This has significant advantages, since the vast majority of aseptic liquid drugs for patient care will be produced using such systems. Therefore, it is a priority for Optima Pharma to minimize, not eliminate, the number of glove ports.
Regulatory reference: With new technical functions, Optima Pharma wants to offer users, who know their aseptic processes and the potential contamination risks, to develop an appropriate production strategy or production rationale, as described in Annex 1.

New functions – also for high performance systems

Optima Pharma is using pilot projects to put the first new functions into practical use. The priority in developing new automation solutions is to minimize glove ports on production systems wherever possible – especially for medium and high output filling and closing systems.

> In order to reduce glove ports, Optima Pharma uses robots controlled by artificial intelligence.

Optima Pharma also envisions the benefits of introducing glove port minimization technology in systems for personalized medicine, including systems with a lower output. While keeping individual glove ports for product recovery may be necessary for processing expensive drugs, the benefits of glove ports should be weighed against their drawbacks. If safer and more efficient alternatives exist, glove ports should be avoided.

A glimpse of what's to come

Optima Pharma achieves the minimization of glove port with new functions and technologies. A glimpse of what's to come from Optima: For example, Petri dishes are still placed over glove ports to record a potential germ load in the isolator-protected area. This process can be risky and laborious, as machine operators must manually remove the dishes from the isolator through the glove ports for incubation and evaluation at regular time intervals.
In contrast, a new system targets the automatic detection of germ occurrence in the isolator in real time. This method analyzes a large volume of air per minute, guiding air through an isokinetic funnel, and detecting and documenting potentially present germs using laser light and biofluorescence particle counting, while counting non-living particles parallel and analogous. This means there is potential in the near future to (almost) automate environmental monitoring of aseptic processes - avoiding glove ports, which are otherwise necessary for the production isolator or upstream for handling Petri dishes.
Optima Pharma has installed this new system at various pharmaceutical companies, parallel to the "traditional" germ collection system using Petri dishes. Data is currently being generated that will allow comparisons and lead to independent findings with regard to the precision and reliability of the measurement results of the new system.

Thinking ahead: artificial intelligence

In order to reduce glove ports, Optima Pharma uses robots controlled by artificial intelligence. This system is already proven to correct misaligned stoppers in the infeed to the pick-and-place transfer station that would cause an error message. Controlled by cameras, the system recognizes whether and where stoppers are incorrectly positioned. If intervention is required, it is done inline, i.e. in the continuous high-speed process with a robot, equipped with a steam-sterilizable tool complying to high technical and pharmaceutical standards.

←
Strategically, isolator systems with fewer glove ports make sense for medium and high-performance outputs. Shown: AI-controlled robotic solutions for inline troubleshooting of an incorrectly placed stopper.

The performance or movement speed of the intervening robot must be synchronized with the process speed of medium and high-performance filling and closing systems – which would not be feasible with a “conventional” technical approach. Conventionally controlled robot movements would simply be too slow to intervene with a running process in real time without interrupting or risking errors. First, the robot movements must comply with pharmaceutical GMP requirements. This means that moving parts, in this case the robot arm or head, must not be located or move over the stopper. Here, too, the “First Air Principle” applies according to GMP guidelines, meaning that the HEPA-filtered air must first flow over the object to be processed without any deflection as it will later come into direct contact with the product. Second, the robot must not run the risk of touching any other system components.

Automation of high-tech and pharmaceutical requirements

How do you reconcile these complex requirements? The solution lies in the artificial intelligence that Optima Pharma incorporates into the process control. Virtual planning using a digital twin that runs ahead of the real process, mapping out the exact processes that the real system will undergo. This provides a look into the future, and the opportunity to simulate various scenarios to identify potential problems before they arise - without the risk of negative consequences. This prevents pharmaceutical integrity from being violated by robot intervention or collisions in the real system. Critical robot movements and processes would be recognized in advance in the digital twin.

The robot technology, which is initially too slow for medium and high outputs, is harmonized with the use of artificial intelligence, interaction with the comparatively faster processes of the filling and closing system - without duplicating robot stations. This additional automation function avoids the need for glove ports in this area. Here again, Optima Pharma is looking at systems in the field that are already equipped with this new technology.
An automatic feeding system for sterilized stoppers or other container components is another option to avoid glove ports. If the stoppers are fed into the system conventionally in bags and docked to the RTP ports, operators have to manually operate the inside of the RTP port, using glove ports to transfer the stoppers into the system. With a new transfer solution, this process can be automated and glove ports completely avoided directly at the system. Optima Pharma has already equipped several machines with this system.

New technologies in use

There are already several options to reduce the number of glove openings in isolator-protected systems – explicitly in systems with medium and high output.

← Manual interference with glove ports must be carried out in compliance with GMP guidelines, e.g. by camera recordings.

↑ The evaluation of system data obtained by sensors, like force and torque sensors, provides a proactive approach – leading to fewer unexpected system downtimes and improving overall process reliability.

Another possibility are rescue ports. Rescue ports are only installed at locations without regular hands-on work through glove ports. These fallback locations serve as reinsurance, to intervene manually in the event of a fault and to “save” a batch in a GMP-compliant and documented manner through glove ports. As a result, except for situations where manual intervention is necessary, the potential disadvantages and complex decontamination process of glove ports are largely eliminated.

Technology diversity will increase

The development of machines designed with a reduced number of glove ports, including systems with low, medium and high outputs, has picked up speed. These systems meet today’s GMP requirements – and reduce operator intervention as much as possible to counteract the shortage of skilled workers. These systems do not rely on any singular new technology – more exciting innovations in system automation are to come!

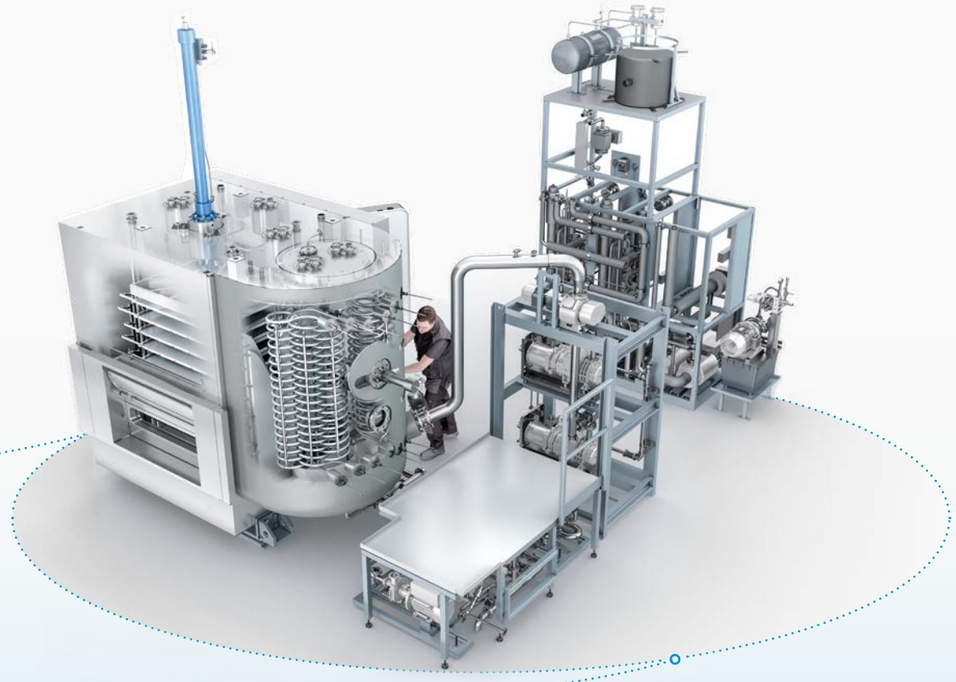
IMPORTANT FOR YOU

- New laboratory freeze-dryer LYO-SCALE from Optima: Perfect for parameter development for freeze-drying recipes as well as for drug formulation
- The system depicts Optima production freeze-drying systems “true to scale” in the geometries
- The LYO-SCALE contains identical parts for all sensors, components and the software
- The precise scaling of the parameters from the laboratory to production systems is possible
- Development of sterilizable versions, as well as with redundancies for the production of small and also very high-quality drug batches

LYO-SCALE: **Precision for parameters**

The new OPTIMA LYO-SCALE laboratory freeze-dryer is made for perfect scale-up of recipe parameters that can be applied to larger systems. This article shows the special functions of the new system and the reasoning behind it.

Freeze-drying: the rational way to production



Scale up

From the laboratory to production: The new OPTIMA LYO-SCALE has all the prerequisites for developing precise parameters for freeze-drying processes in production plants.

Freezing and drying – by definition, these are the two physical processes that work together to achieve freeze-drying. The development of recipe parameters for a stable process include extensive laboratory work, especially because every drug formulation is unique in its freeze-drying behavior.
Such behavior can be seen, for example, in the specific ice crystal formation of a drug during freezing. This also applies to sublimation (skipping the liquid state of aggregation) and applying a vacuum (evacuation): What are the optimal temperature and pressure conditions so that vapor can escape easily through the ice crystal structure in the vial?

Formulation first

To freeze-dry a drug and create a high-quality lyophilisate the formulation must be developed in the laboratory. Therefore, the active ingredient (API – Active Pharmaceutical Ingredient) is refined into a product that can be transported and stored. In this process, pharmaceutical water and additional substances like skeleton-forming agents are added, which influence the crystallization during freeze-drying. If a formulation, which meets the quality requirements for a lyophilisate and thus the requirements for a successful freeze-drying process, has been found and defined, the "scale-up" follows. During scale-up, the process parameters of laboratory freeze-dryers are transferred on a commercial scale freeze-dryer.

Now, the system specifications come into play. These have a major impact on the final freeze-drying recipe for a medical product. Ideally, the process parameters from the lab-scale freeze-dryer can be transmitted and applied in full to the production freeze-dryer or only a few parameters should require minor adjustments. Indeed, the scale-up of parameters from the laboratory to production also depends on various system properties, which are discussed below.

Efficiency and precision

It is easily explained why recipe development is carried-out with laboratory freeze-dryers. Initially, recipe development is an equation with several unknowns. Production systems would have a long period of downtime if this development work had to be completed with a production system. The energy consumption would also be disproportionate, even if only one shelf of a production system was loaded, since the entire system is cooled, heated and evacuated during each freeze-drying process.
The systems themselves must also be considered. If freeze-drying processes were to be developed on a production system with only a small amount of product, the values would in all likelihood have to be adapted to the production scale again, which would be a time-consuming process. Because the existing amount of liquid in relation to the mass of stainless steel that has to be cooled and heated, and other properties would have an influence on the results that would be difficult to calculate, i.e. the generated recipe. So, what are the requirements for a laboratory freeze-dryer to scale a recipe into production effectively and efficiently? Optima accepted the challenge: The freeze-drying experts provide exciting answers with the new LYO-SCALE laboratory freeze-dryer.

Proportions are crucial

To fulfill the parameter development mission, geometric equality ratios are a central prerequisite. Laboratory freeze-dryers should ideally depict the production processes on a smaller scale. All Optima freeze-dryers already show this "proportionality" in the production area. With the new OPTIMA LYO-SCALE, this principle is now extended to laboratory systems.
This initially concerns the surface dimensions of the shelves and the surrounding chamber. The size ratios should be identical in the laboratory and production freeze-dryer. This includes shelf thickness measurements in order to achieve the same ratio of heat transfer coefficients from steel to glass.
In addition, the size of the valve between the drying chamber and the condenser, as well as the size of the cold surface of the condenser must be considered. For example, a shelf surface of 40 m² that is loaded with 10 ml vials corresponds to a quantity of about 75,000 vials per load. This creates a steam volume flow of 128,500 m³/h, which flows through the steam passage - the valve between the drying chamber and the condenser. This volume flow must pass through a correctly sized valve (whereby further physical restrictions must be observed when calculating this flow

Additional versions of the OPTIMA LYO-SCALE are in development, including a sterilizable version with redundancies. This means that drugs in clinical phases and small batches of very high-quality pharmaceuticals can also be freeze-dried.

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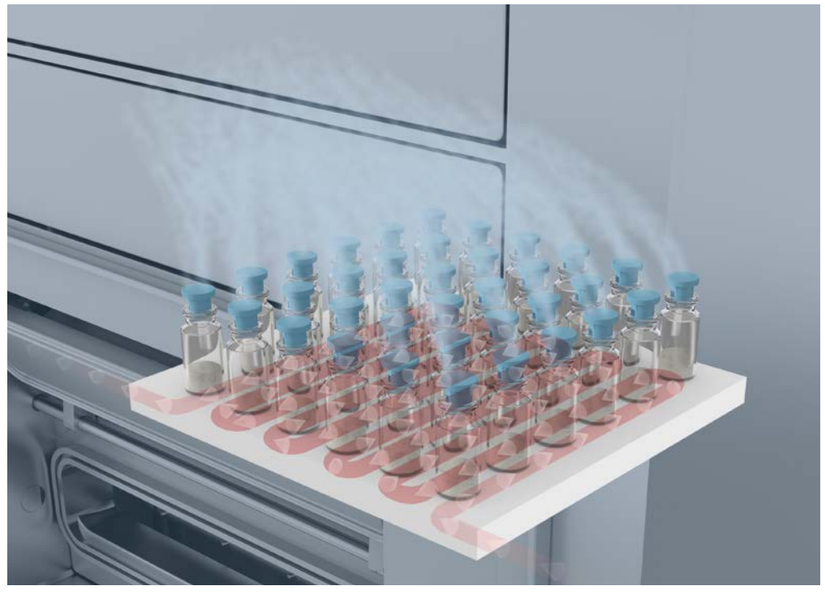
The same structure, for example of the setting plates in laboratory and production freeze-dryers up to coordinated setting plate thicknesses contribute to the precise scaling of freeze-drying recipes.



channel). Additionally, the vapor passing through must meet a specifically designed condenser cold surface size. The design of the surface size is in turn strongly dependent on the capacity of the cooling system.
If all of the above-mentioned criteria are identical in the laboratory and production systems, the optimal conditions for a precise process parameter scaling from the laboratory to production system are given.

The importance of equipment features

Both freezing and drying are equally critical to achieving high quality freeze-drying results. The goal is a homogeneous freeze-drying cake in the container with minimized, defined residual moisture. This is achieved by controlling the temperature curves and pressure (negative pressure or positive pressure). In the course of recipe development, it is also determined whether it is better to thaw in stages or continuously, with rapidly or slowly increasing temperature, when and how much pressure is applied, and how to evacuate. Various sensors measure all of these parameters in both laboratory and production freeze-drying systems.
The similarity principle between laboratory and production systems should also apply to components like sensors. Temperature and pressure sensors, but also control devices from identical manufacturers, will lead to a more precise scaling of parameters from the laboratory to the production system. Wherever possible, Optima uses identical parts and components in laboratory and production systems. If it is not feasible, the identical functional principle is achieved through similar components.
The Optima operating software of the HMIs is the same for the laboratory and production freeze-dryers. With known recipe structures and operating concepts that are already understood by the employees, the probability of errors decreases significantly. In addition, the identical software ensures optimal transferability between the system types.

> The scale-up of parameters from the laboratory to production also depends on various system properties.

Directly to the production system

Optima is known in the industry as an expert for production system manufacturing – particularly for pharmaceutical freeze-drying systems. It is an advantage to know and understand the special requirements of large production systems in order to be able to transfer them to and in laboratory systems.

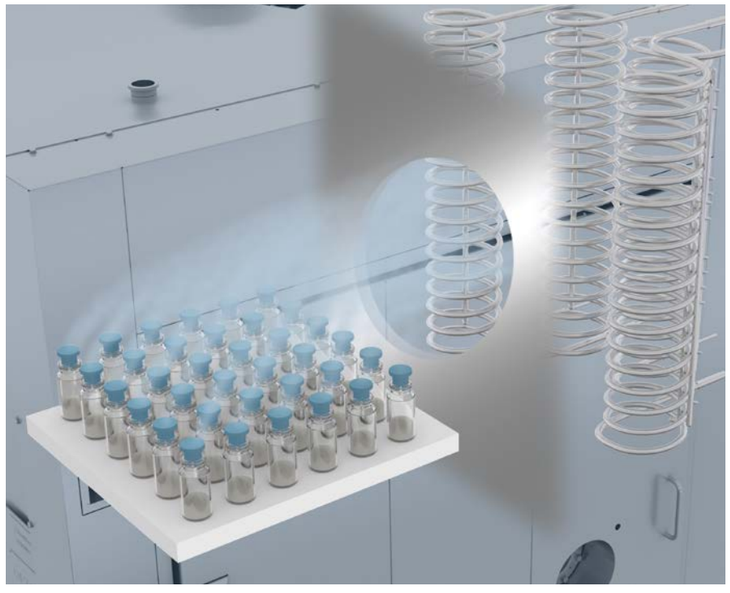
The OPTIMA LYO-SCALE is now being launched with identical software and practically identical mechanical and process engineering conditions to achieve the best results in parameter development. For the LYO-SCALE user, this means that the parameter transfer from the laboratory to the production line will result in a freeze-drying process that produces a lyophilisate of the same high quality as in the laboratory. This reduces the readjustments required during the product transfer and reduces downtime of the production machine.

For recipe parameters and diagnostic products

The first LYO-SCALE is currently being set up in Gladenbach/Mornshausen, Optima's lyophilization technology center in Germany. This laboratory freeze-drying system will be connected to an OPTIMA MultiUse LAB filling and closing system and is a turnkey project (see also p. 20). The possible batch sizes of the freeze-dryer range from 200 to 4,000 objects, depending on the container sizes and the number of loaded shelves. This LYO-SCALE system is intended for a CDMO for recipe development of freeze-drying processes, as well as for the development of drug formulations as an additional service offering to customers. The second LYO-SCALE commissioned to date will also be used by a research-based pharmaceutical company for the production of individual, very small product batches and for internal scale-ups.
Drug studies could also be carried out with the LYO-SCALE at any time prior to the clinical phases. This type also has applications for the freeze-drying of diagnostic products. A sterilizable version of the OPTIMA LYO-SCALE laboratory freeze-dryer is also in development. In the future, this will make it possible to freeze-dry pharmaceuticals in approval procedures for clinical phases 1 to 3, as well as small commercial batches of very high-quality pharmaceuticals, for example cell and gene therapies, in a very efficient manner.

Sterilizable version and redundancy

Optima's laboratory freeze-dryer portfolio includes additional LYO-SCALE versions. These will initially differ in terms of the installation area and the redundancy of process-critical components. For example, the production of very expensive pharmaceuticals requires – even with small batches – maximum process security with partially redundant components. In turn, this would cause unnecessary costs for systems that are used purely for parameter development. Therefore, the perfectly suitable OPTIMA LYO-SCALE laboratory and production system can be configured for every requirement.



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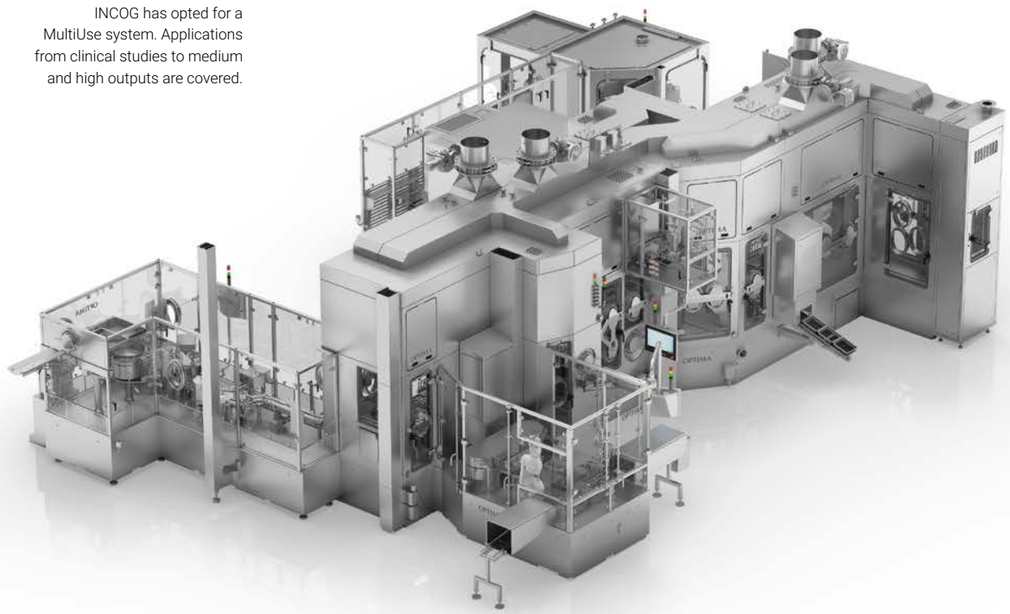
Freeze-drying systems consist of components that are precisely matched to one another. Liquid quantities, valve size, cold surfaces and other factors are decisive. Laboratory and production systems should have conditions that are as identical as possible.

Pole Position
for CDMO INCOG

INCOG BioPharma Services is a new standard of CDMO (Contract Development and Manufacturing Organization), whose management team has decades of experience in the pharmaceutical industry and the CDMO sector. To begin, the company opted for a highly flexible turnkey MultiUse system with an isolator from Optima Pharma.

IMPORTANT FOR YOU

- Highly flexible turnkey MultiUse system with an isolator for the new CDMO company INCOG in the USA
- Paths for nested and bulk vials, pre-filled syringes and cartridges
- A filling line for clinical phases and small batches, as well as commercial production for medium and large batches
- CSPE: Turnkey project with fully functional machine start-up in the CSPE center, VHP cycle development and integrated FAT. Easy installation at INCOG with a largely reduced overall project duration
- Close partnership between the international project teams



INCOG has opted for a MultiUse system. Applications from clinical studies to medium and high outputs are covered.

High flexibility – probably the most important feature for an isolated filling and capping line for a newly founded CDMO. The INCOG founders, including Cory Lewis and Tedd Green, worked for many years in managerial positions in pharmaceutical companies and managed well-known CDMOs to growth and success. According to Lewis, the INCOG team had already commissioned more than six Optima systems during their time at other CDMOs.
From the beginning of the project, the requirements for the new MultiUse system were clearly defined: The machine configuration had to cover production capabilities ranging from clinical studies to commercial production of medium and large batch sizes. Vials, pre-filled syringes, cartridges, RTU, and bulk containers must be processed. November 2020 was the project start for the turnkey system at Optima Pharma.

This is how diversity works

Two processing paths were set up for vials so that the system could handle very small batch sizes of approximately 500 containers, as well as large batch sizes. Bulk vials are less expensive but more time-consuming and expensive to process since they require washing (washing machine) and sterilizing (sterilization tunnel). This is adequate for larger batch sizes but not for smaller batch quantities. For smaller batch sizes, pre-sterilized RTU containers are the more economical choice. In addition, there is no glass-to-glass contact during the vial processing. The system offers filling with peristaltic pumps or a time/pressure system, including CIP/SIP cleaning and sterilization functions.
Therefore, INCOG is strategically well-prepared to handle different batch sizes and diverse container and drug types from the beginning. The system reaches outputs of up to 9,000 vials and up to 7,200 pre-filled syringes per hour.

Safety and greater product yield

"The company's objective is to offer customers not just good but outstanding services," says Cory Lewis. A closer look reveals an in-depth connection with the system technology. With the MultiUse system, INCOG has 100% in-line quality control. In terms of patient safety, this is a fundamental requirement. However, the unique feature of the MultiUse system is to correct deviations immediately. Containers that do not meet the specifications are not simply ejected but reprocessed in-line.

For example, the weight-dosing function of the Optima filling machine is designed to have the correct filling volume from the first container. To ensure that no containers are rejected during the priming of the product path, the containers are filled directly on the load cells until the target weight is reached. The redosing function can also be used to correct under-filled containers in the regular filling mode. The stoppering station has the same function, and if a stopper is not picked-up, the system will return to pick the stopper again and ensure the container is closed.

INCOG thus produces significantly more commercial product from the amount of liquid processed compared to systems without these product-saving features. These features of the MultiUse become even more critical for costly pharmaceutical products. In addition, even with large batches of less expensive drugs, the overall result is a profitable effect.

Optional freeze-drying path

INCOG also benefits from the system's modular design if a freeze-drying process has to be added later. INCOG chose a separate capping machine, connected downstream, that offers the opportunity to return the freeze-dried product to the line and close it easily. Syringe and cartridge processing or liquid filling in vials could then take place on a parallel path during freeze-drying.
A recently introduced innovation by Optima provides INCOG the opportunity to meet high machine outputs with the MultiUse.
To individually process the objects, an XTS oval conveyor transports the objects to the infeed at the beginning of the process.
Background: Individual processing is a prerequisite for all product-saving functions, including 100% in-process control.

The machine is prepared for the addition of a freeze-drying system as an additional product path.

←
The pre-sterilized and nested RTU containers are prepared for further processing. A robot peels off the Tyvek and then removes the lid liner.

→
Vials are crimped. This station is located downstream so that INCOG can add a freeze-drying process later.

Innovation with oval conveyors

The oval conveyor is a module for vials, pre-filled syringes, and cartridges. Both vials, after sterilization, and all RTU containers are removed from the nest and safely transported to the individual stations, corresponding to the highly flexible MultiUse concept. Thereby, the oval conveyor ensures high performance across all container types.
Another oval conveyor at the end of the line returns the pre-filled syringes and cartridges to the nest. This oval conveyor closes potential gaps (the product-saving functions already minimize gaps) created by any rejects that would lead to empty spaces in the nest. This is prevented by transferring the containers from the isolator-protected area to individually controllable shuttles of the oval conveyor. If necessary, the arrangement of the shuttles is configured to allow each shuttle to take over an object. Potential gaps between the shuttles are closed on the transport route in the oval conveyor. On the opposite side, a robotic arm takes over a complete row of containers and puts them back into the nest.
All vials are placed in trays after crimping. Apart from the crimping path, the containers are processed without glass-to-glass contact.

In good shape with CSPE: Processes and technology

INCOG benefited from Comprehensive Scientific Process Engineering (CSPE) during the design and implementation phases. An approach that Cory Lewis describes as "a simplified, improved installation and maturity phase." These included, among others, simulations of the laminar airflow for bulk vials and RTU containers and their respective product paths. For example, the simulation for the sterilization tunnel was also included for bulk vials.

The H_2O_2 distribution in the isolator-protected area, as the first phase of the VHP cycle development, was also part of the simulation. The injection nozzles in the customized isolator were virtually placed and tested to achieve complete coverage with H_2O_2 and a homogeneous H_2O_2 distribution. Subsequently, parameter settings, like the injection rate and time, were optimized in a more detailed model, providing an excellent basis for cycle development using chemical indicators.
The isolator, which includes the very efficient DECOpulse® decontamination system, was set up and ready for operation with the MultiUse system in the CSPE center at Optima Pharma. The software was integrated, and the tightness of the isolator was tested, as well as the signals and all functions, including the CIP/SIP processes. Based on the simulations, the laboratory-based cycle development with chemical indicators was followed at Optima Pharma in the CSPE center. An effective, timesaving decontamination cycle has been fully defined

Extensively tested: iFAT

In February 2022, Sascha Winter's team at Optima completed a smooth integrated Factory Acceptance Test (iFAT). The complete system was tested, and various customer requests were implemented, like adjusting the monitoring zones.

The CSPE pre-installation and testing effectively reduced the installation time at INCOG onsite in Fishers (Indiana, USA). After completing the SAT in October 2022 and the IQ and OQ, INCOG could go straight to the PQ and the media fills. Over the course of the project, the CSPE process saved an estimated three to four months. Altogether, the success of the project is a reflection of the close partnership between the project teams from INCOG, Optima Pharma (Schwäbisch Hall, Germany), and Optima Machinery Corporation (Green Bay, USA) – a considerable benefit for turnkey projects.

What's next?

In December 2022, just 23 months after the groundbreaking of the building in Fishers, Indiana, INCOG achieved GMP-compliant aseptic filling and closing processes for parenteral products. Media fills for a first format were successfully completed, and a commercial Process Performance Qualification (PPQ) started. In March 2023, INCOG announced the start of its first commercial production. With current and past experiences in mind, the INCOG team already decided to work with Optima Pharma on their next project. In January 2023, the kick-off meeting for another turnkey system took place. The highly flexible MultiUse system is supplemented by an Optima H6-10 high-performance syringe filling and closing machine.

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As part of the preliminary cycle development at Optima Pharma, indicators were used to identify best-case and worst-case locations in the isolator-protected area.

What was INCOG's experience during this project?

The o-com editors interviewed Cory Lewis, CEO and founder of INCOG.

Mr. Lewis, why did you choose a MultiUse Filler from Optima? What do you expect from the machine in terms of the challenges INCOG faces?

With our services, INCOG strives to position itself as a leading CDMO (Customer Driven Manufacturing Organization) in the market. Our filling line very well supports our customer-driven manufacturing organization approach, as its design allows both small and large batch sizes, clinical studies, and commercial campaigns to be processed, and this, in turn, with different format sizes and container types, such as pre-filled syringes, vials, and cartridges. The variety of process possibilities supported by the flexible MultiUse Filler allows us to shorten the time to clinical applications. At the same time, we can scale up to commercial use and provide lifecycle management across different container designs.

Optima has implemented CSPE (Comprehensive Scientific Process Engineering) as a turnkey provider to shorten the customer's installation phase and support the qualification process. What is your impression of this offer?

Our capacities were ready for use more quickly with the CSPE process. We got there in less than six months, from installing the filling and closing line to the media fills. As implemented at the Optima site, the turnkey solution has resulted in a simplified, improved installation and maturity phase of the project from the moment it arrived on site. Excellent service, thank you!

What were the most important reasons for choosing Optima as the filling and capping line supplier?

There were several reasons. First of all, the industry experience and Optima's proven expertise. Then the scope of services is integrated into the filling and closing line. Also important to us was the easy access and availability of the service and support team after the installation of the line for ongoing operations in our company. Last, we can look back on a broad partnership between a CDMO and Optima, which we had already achieved before. This shows the partnership approach, in contrast to a customer/supplier relationship.

Do you already have an impression of how the new system is running?

The system works very well when processing pre-filled syringes or vials. The functionality of the filling and closing line, the integrated robotics, and the integration of the isolator in the line all allow us to take customer requests with great confidence.

What is the next step before you start production?

Our MultiUse filling line is already in production, and we are continuing to complete qualification activities to ramp up future customer production. We have media fills for the 1mL – 3mL syringe, 2R-10R vials, and 3mL cartridge formats and are completing a commercial PPQ (Process Performance Qualification) batch for one of our commercial customers. We anticipate an FDA regulatory inspection of our facility in early 2024 to begin commercial manufacturing. We are excited to continue to expand our customer base with both clinical and commercial customers because of the flexibility of the MultiUse filling line.

How satisfied are you with the project so far?

I am extremely satisfied for the reasons mentioned above. Ultimately, Optima met all of our needs on time, on budget – and, more importantly, with successful media fills. Ensuring sterility is the central key performance indicator for success.

Cory Lewis, CEO and founder of INCOG

Turnkey and a closed loop in China

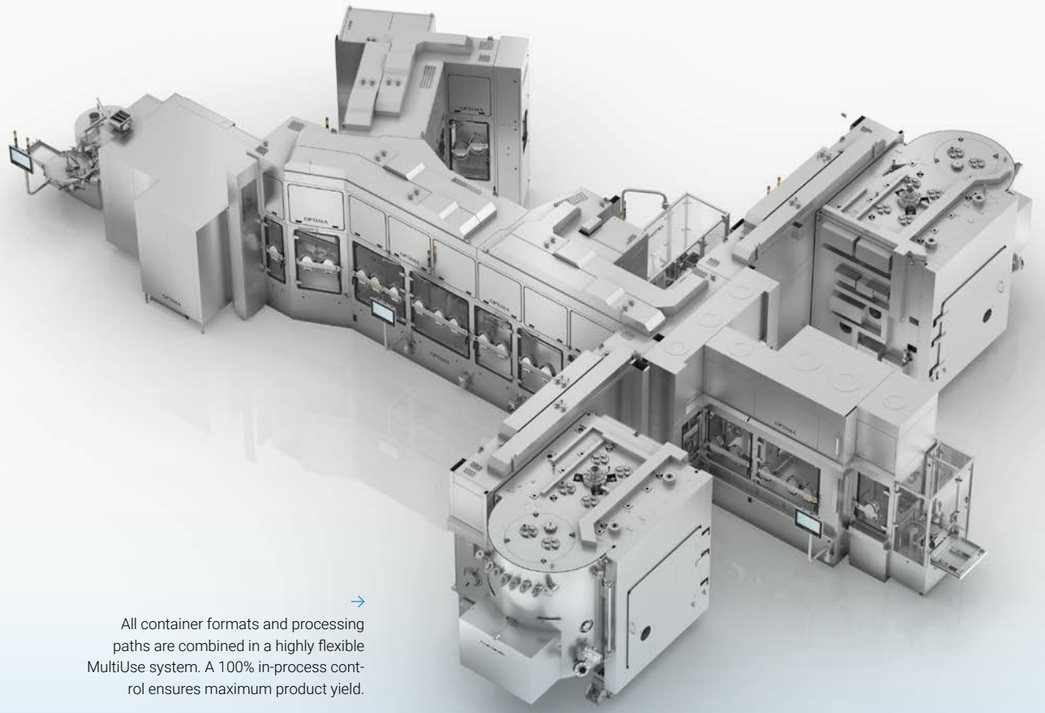
IMPORTANT FOR YOU

- Highly flexible MultiUse system with isolator technology and two freeze-dryers for a CDMO in China: Vials (RTU and bulk), pre-filled syringes and cartridges, highly active ingredients, additional one-digit R&D MultiUse system with isolator
- Despite strict lockdowns, first in Germany and then in China, all potential for project progress was explored and used
- High level of commitment and close cooperation between all involved parties, including the CDMO
- Sophisticated on-site procedures: from bringing the system into a “closed loop” to working in different time blocks and two work shifts
- International turnkey project in close coordination between Optima Pharma in Germany and Optima Shanghai: global project management combined with expert know-how and local competence

“Closed loop” is not a new technical feature. In fact, it was the only option to advance a complex turnkey project at an international CDMO in China when the Covid-19 pandemic forced a hard lockdown. This project crossed many borders.

Before the crimping process, a camera checks the exact position of the stoppers.

A robot takes containers from the nest and places them in the transport rake.



All container formats and processing paths are combined in a highly flexible MultiUse system. A 100% in-process control ensures maximum product yield.

Ready-to-use path: Tubs with pre-filled syringes or cartridges are unpacked automatically.

In November 2020, Optima Pharma received the order for a complex project in China. However, the project had to be carried out under difficult circumstances due to the outbreak of the COVID-19 pandemic. The complex project consisted of a turnkey MultiUse system with isolator and two freeze-dryers with an output of 6,000 containers/h, as well as a MultiUse R&D system with isolator.

Challenging for everyone involved

During the pandemic, different countries had their own regulations in place to control the spread of the virus. Hendrik Hempel, Director Pharma at Optima Shanghai has been living in China for several years. He explains that life in China was relatively normal at first, as long as there were no registered infections nearby. While entry restrictions were imposed on foreigners, restaurants were still open within the designated "bubble". In contrast, Germany implemented measures such as remote work and lockdowns to combat the virus.
In the second half of 2022, the delivery of Optima's system components coincided with the rise of the Omicron virus variant. In Germany, most of the regulations were lifted, unlike China, where the government enforced a zero-Covid policy with a hard lockdown.
The question now was how could Optima possibly install two lines in China, especially with one being a very complex system, under such circumstances?
First, the single-lane R&D MultiUse system was sent up-front, since Optima Shanghai was proficient to completely set up, wire and prepare the R&D MultiUse system with an isolator for commissioning independently.

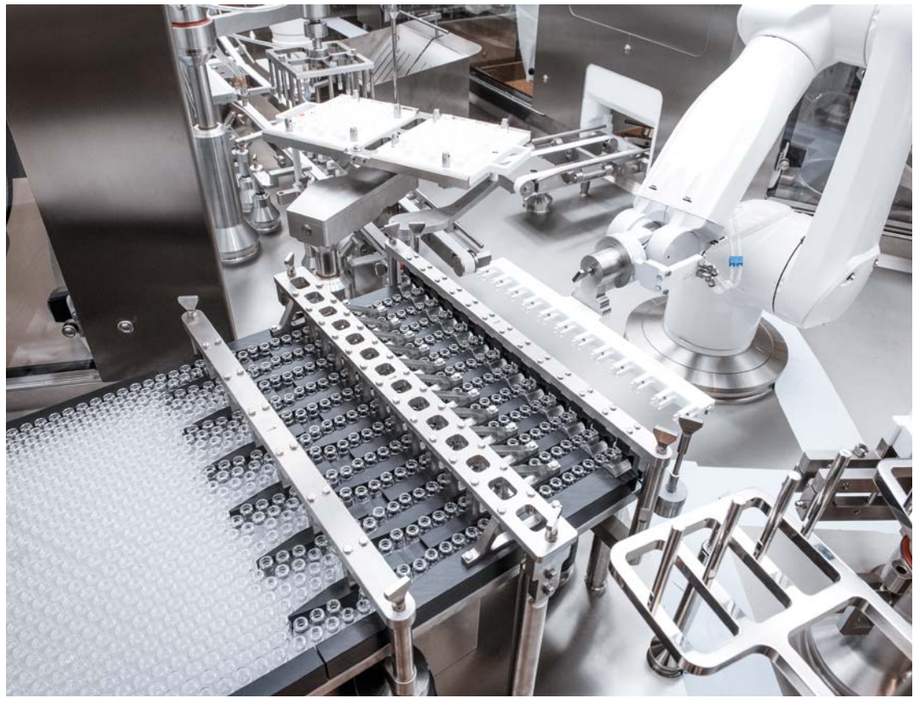
Everything comes to a halt – or is it?

What about the larger part of the project, the four-lane MultiUse system with an output of 6,000 containers/h, isolators and two freeze-dryers? Time constraints on the customer side led to challenges on Optima's side due to the new Covid regulations. With the sure prospect of ten or more days in quarantine, travel to China became virtually impossible. However, without the support of the German specialists, the installation of the complex line would be virtually impossible. The CDMO submitted an application for a "closed loop", which essentially created an extended quarantine zone within the customer's facility for the German/Chinese Optima crew to work safely.
This also allowed the Optima's German experts to work on site, which helped expedite the project. Entry of the specialists into the country was carefully planned to avoid overlapping times and minimize quarantine phases. After a negative Covid test, free movement was permitted in the separated zones including the hotel, the company premises and the shuttle bus between the hotel and the customer. Cody Ma (Optima Shanghai), who was the responsible site manager and the interface to the customer, found out that this closed-loop regulation was strictly enforced when he brought the first German colleagues from the airport to the hotel and he had to quarantine with them.

A sophisticated organization shows the way

Due to the closed-loop regulations, the installation area turned into a narrow one-way street. The question "When will each part of the line be brought in?" was crucial. A single mistake would have meant taking

After the sterilization tunnel, bulk vials are separated for filling and closing and transported to the next station. →



The system has two freeze-dryers: The isolators of the loading and unloading units are designed to process highly active substances. ↓

steps backward and complicated logistics. The team now worked in two-shifts to get back close to the original timeframe again. This involved meticulously planning. While the first shift was setting-up the filling line, the second shift worked on the isolator and had exclusively access to the filling machine to work on the isolator integration, reports Cody Ma. Special tools and testing devices always had to be available on time and at the correct location.
Optima's on-site employees demonstrated remarkable commitment, which the customer appreciated. However, the region was hit by a large wave of infections when strict Covid regulations were unexpectedly lifted at the beginning of this year, affecting the customer's site as well. Meanwhile work is now back to normal on site without any restrictions.

Cooperation with the customer and across borders

Specific organizational processes were and are essential for the success of this international project. This means Optima Pharma Germany assumes responsibility of the project management, in close cooperation with Optima Shanghai, as well as the Optima isolator and freeze-drying experts. Project discussions with the Chinese CDMO are held between Optima Pharma Germany and Optima Shanghai, reports Hendrik Hempel. Optima Shanghai in turn reports to the German project management on the on-site progress.
According to Cody Ma, there is also close international cooperation at the customer's site. They use virtual reality to send instructions and explanations across geographic borders from Germany to the customer's site in China. The deployment of the ten German employees during the closed-loop phase was also closely coordinated between Optima Shanghai and Optima Pharma in Schwäbisch Hall, ensuring a smooth and efficient process.

After the German colleagues arrived on site, they immediately set-up the one-lane R&D MultiUse system. A process engineer from Optima Shanghai supported the completion of cycle development. Cycle validation began at the end of July 2023, followed by the customer's media fills. The large MultiUse line is also progressing well - various formats are already tested or completed. The CDMO's employees are available to support the commissioning if necessary, such as for media connections.

Another culture

It's interesting to learn about the experiences of German employees working with their Chinese counterparts at Optima Shanghai. One of the challenges the German employees faced was figuring out how to pay for things while in China, since a payment app is necessary. Fortunately, with the help of locals, they were able to install the app and make purchases. Cody Ma also contributed to the project with his cultural know-how. For example, the Chinese co-workers are used to a "faster-faster" pace of work, while for German colleagues a step-by-step approach has priority.

Several major turnkey projects in China including filling machines, isolators and freeze-drying systems are already on the order books. Optima Pharma looks forward to these new projects with great confidence due to the organizational background and the great cooperation between the Chinese and German employees illustrated by this recent project.

MORE ABOUT THIS TOPIC

Highly flexible MultiUse system with isolator and two freeze-dryers in China

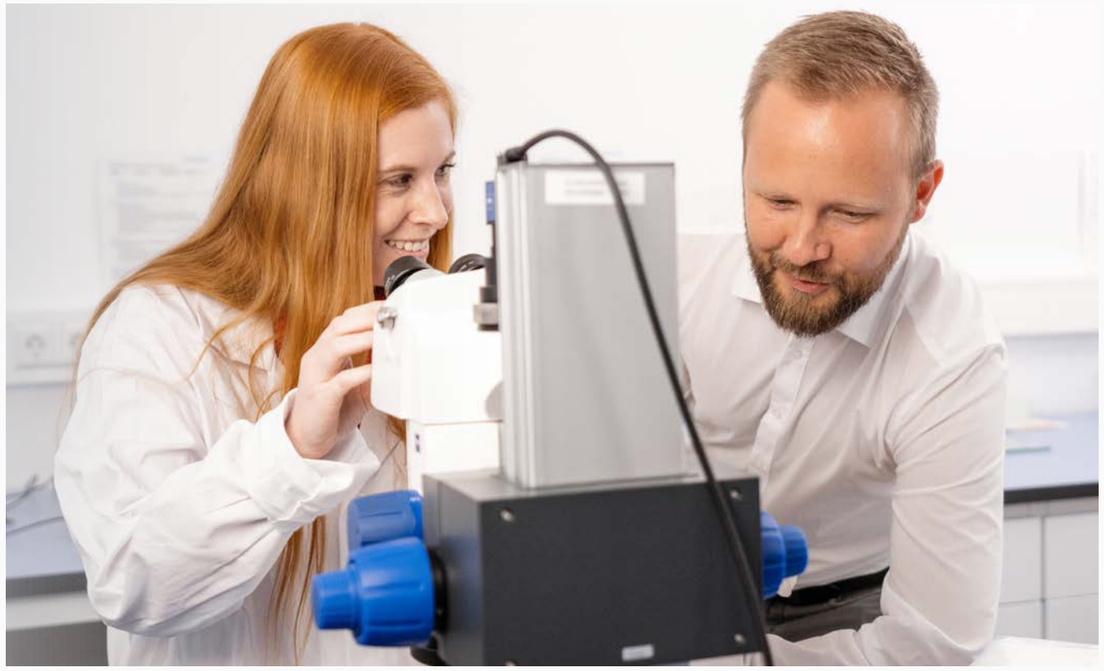
The Chinese CDMO market is very competitive. The decision for a certain filling and capping line with an isolator and freeze-drying system requires careful consideration of price structure, quality, product yield and on-site service. In addition, the system's configuration is very important, as it can influence the productivity and efficiency, as well as the market positioning of a CDMO.
The multinational CDMO has opted for a highly flexible MultiUse system from Optima for the Chinese market. This system will process vials (bulk and ready-to-use), pre-filled syringes and cartridges, each with a wide range of format sizes.
The turnkey system has a 100% in-process control for all container types, up to a maximum output of 6,000 objects per hour with four-digits. CDMO customers can be sure with functions like priming, post-dosing and re-stoppering, that there is almost no product loss. Almost 100% of the existing drug is converted into salable product. For CDMO customers dealing with high-priced and valuable pharmaceuticals, these system functions can quickly prove to be profitable. Pharmaceuticals with highly-active ingredients can be processed with a special isolator design and an external washing machine.
The CDMO also benefits from the quick change-over time of format parts. The short decontamination cycles of the Optima isolator allows the system to be ready for production quickly. The T-shaped set-up of the freeze-dryers provides the potential for increased system uptime. If pharmaceuticals are in the freeze-dryers, vials, pre-filled syringes and cartridges can still be filled and closed during the freeze-drying process, which can sometimes take several days. The second freeze-dryer can also be actively used at the same time.
The vials closure is completed on the downstream crimping machine. The product paths of the two freeze-dryers are separated at a crucial point, so vials can be transported to the crimping machine after the stopper is placed. The stopper placement station, with a connected renester, is located before the transition to the loading station of the freeze-dryer. Prefilled syringes and cartridges leave the MultiUse system on this path. This extensive turnkey MultiUse system at the CDMO is supplemented by a single-lane MultiUse machine with an isolator, which is used for R&D purposes.

Interview

with Dr. Stefan König

Dr. Stefan König has been a member of the Optima Group management board since the beginning of 2021.

“**OPTIMA** has evolved from **machine manufacturer** to **solution provider**”



Working together with customers and partners, Optima is developing sustainable packaging solutions – from the initial idea through to production.

What does sustainability mean for Optima?

We understand sustainability as long-term, partnership-based and resource-conserving management. Our goal is to safeguard the world for future generations. Sustainable production, filling and packaging along the entire value chain – this is what our core sustainability strategy “We care for tomorrow” stands for. That’s how we wish to excel across the board in the areas of the environment, social affairs and corporate governance. Our strategy is based on three pillars.

- Circular packaging:
  In cooperation with our customers, we develop straightforward packaging solutions that enable a functioning circular economy.
- Corporate sustainability:
  Optima is committed to ecological, fair, and successful long-term business practices.
- Sustainable technology:
  We design machines and systems to operate as resource-efficiently as possible while taking the entire life cycle into account.

How have the demands of the market changed in recent years?

In the past, product packaging usually consisted of a non-recyclable material mix with the focus on cost minimization. Sustainability aspects were not considered. The task of machine manufacturers was clearly defined: Please design a packaging system for this product with this packaging.

Today, we use many new products, including concentrates and dry products. These require new packaging with a holistic sustainable design, and often portion packaging. New alternative materials are being used, which require other sealing processes, for example. Optima has evolved from machine manufacturer to solution provider. Today, the requirement is: This is my product, please assist me in developing sustainable packaging and transferring the concept to a fully automatic high-performance packaging machine (engineering-to-order). We accompany and guide our customers from the initial idea to successful production. This includes, for example, consultation on packaging. The focus is on aspects such as the style and type of packaging, the materials used for packaging, the product protection and the legislation applicable in the country. In addition, our service portfolio includes the manufacture of samples (simple mock-ups or samples for test markets). We also conduct barrier tests and shelf life tests together with our partners. Small semi-automatic systems are then scaled to fully automatic turnkey systems.

How long have you noticed a growing interest in sustainability topics?

For around four years now, we have noticed a greater demand for sustainable packaging solutions. Our customers have been inquiring about sustainable packaging solutions for around two years now. The demand today is for an overall sustainable concept tailored to the company (at Optima: Corporate Sustainability) and product (at Optima: Circular Packaging and Sustainable Technology).

Which specific wishes and demands does Optima receive?

Alongside the changing market requirements already described, the systems need to be as flexible as possible when it comes to packaging materials. The currently changing legislation in Europe (packaging directive) is a game changer. Here, we expect to see new packaging requirements. This is why our customers want to change their systems over to alternative materials very quickly.

Which trends are you seeing in Germany and other countries in this context?

In addition to the required flexibility in terms of packaging materials, using paper as a packaging material is a very clear trend. Two reasons are apparent: The recycling possibilities for paper are the most well developed in the world, and end consumers consider it the most sustainable packaging material. If you compare Germany with the rest of the world, we are one to two years ahead when it comes to plastics recycling.

How will packaging machines, filling and production systems continue to change with regard to sustainability aspects?

For us, it is particularly important to meet the demand for maximum flexibility in terms of packaging material. Machines will have to be checked for alternatives in the future in terms of the materials used. Manufacturing processes must be weighed up against each other regarding sustainability aspects. Different technologies for performing specific functions need to be compared. This will ensure that we continue to reduce the product carbon footprint holistically in the manufacture and usage phase.

Which specific sustainability goals has Optima set?

By consistently using renewable energy sources, Optima has already been able to reduce greenhouse gas emissions by 40 percent. With an extensive package of measures, we will reduce our climate footprint by an additional 25 percent by 2030. The company is also systematically working on advancing emission reduction goals using the approach of the Science Based Targets Initiative (SBTi).

With regard to regulatory measures: how do you see the development here?

We welcome suitable regulatory measures that continue to drive forward the topic of sustainability in a positive way. This means that projects, which have not been implemented recently for cost reasons, could be realized with a positive effect for the environment.

With the new travel set "Trific" the cooperation partners Optima, Holmen Iggesund, Yangi® and FutureLab & Partners are revolutionizing the value chain for personal hygiene travel sets. ↓

↑ Optima offers a new sustainable can portfolio with different shapes and closure solutions. The highlights include aluminum-free barrier solutions and a completely fiber-based lid with hinge function.

Taking into account the entire packaging industry as well as the consumer goods industry: Do you get the impression that everyone involved is pulling together or are there areas making compliance with sustainability criteria difficult?

We are setting a good example here. For years now, we have relied very successfully on cooperations across the entire value chain, for example with three partner companies from Sweden, in order to develop the sustainable packaging concept "Trific". As a technology partner, Optima has supported the development of a sustainable travel set for daily personal hygiene from renewable, fiber-based raw materials. The project aims to motivate brands to switch to sustainable packaging.

Key benefits of OPTIMA pharma's turnkey expertise

Key Facts

Fastest time-to-market
of customer-tailored processing lines

Fast production start
with comprehensive simulations and VHP-cycle development

Integrated solution
of filling line, isolator and freeze-dryer from one partner

Entire life cycle
with turnkey approach – from conception to production

Highest safety
due to fully tested line at Optima CSPE-Center

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