SARTORIUS

Customer Case Study

From Concept to Compliance: How Boehringer Ingelheim, Syntegon, and Sartorius Delivered Innovation in Final Filling

Customer Profile

Company Name:
Boehringer Ingelheim

Company Type:
Large biopharma and CDMO

Industry:
Health care

Company Profile:
www.boehringer-ingelheim.com

Customer Challenge

Boehringer Ingelheim set out to install its first single-use final filling system at its Ingelheim site, where it would be largely used for handling clinical trial materials, and market launch. The setup needed to support frequent product changes and a wide range of fill volumes, requiring both high flexibility and regulatory robustness. A key challenge was the newly updated EU GMP Annex 1 guidelines, specifically section 8.80:

> [...] Due to the potential additional risks of a sterile filtration process, as comparedwith other sterilization processes, an additional filtration through a sterile sterilizing-grade filter, as close to the point of fill as possible, should be considered as part of an overall contamination control strategy.

The novelty of using single-use technology in this regulated GMP environment added pressure to find a technically sound and compliant solution. Boehringer Ingelheim needed partners capable of interpreting regulatory language, proposing alternatives, and co-developing equipment and consumables.

SYNTEGON

Boehringer Ingelheim

Background Information

Boehringer Ingelheim was working with Syntegon as the supplier for the fill-finish line, and the filling line had been designed with an integrated isolator to support the handling of highly potent products. The isolator-based architecture aligned with Boehringer Ingelheim's operator protection strategy and included provisions for in-isolator pre-use post-sterilization integrity testing (PUPSIT), in line with their initial interpretation of Annex 1. At that stage, however, the single-use assembly—particularly filter assembly components for PUPSIT and filtration—had not yet been defined.

Sartorius was brought in as the single-use partner and, during joint technical discussions and a full-scale mock-up exercise using a model of the system at Syntegon's site in Crailsheim, it became clear that placing the PUPSIT components inside the isolator would create significant operational constraints. These included limited installation access, the need for glove port manipulation, and reliance on rapid transfer ports for large assemblies. These factors introduced unnecessary complexity and increased contamination risk.

The isolator design was originally selected to support operator safety, particularly given the facility's use of highly potent compounds. However, the project team recognized that a closed restricted access barrier system (RABS), positioned in front of the isolator, could offer equivalent protection while simplifying handling and installation. This re-evaluation allowed the team to explore a modified configuration that preserved both compliance and process efficiency.
The decision to reposition the PUPSIT function outside the isolator was ultimately informed by practical risk assessment, equipment usability, and alignment with regulatory intent.

Project Key Indicators

Keywords:
PUPSIT, Single-use final filling, RABS, EU GMP Annex 1

Process Steps:
Final filtration and filling

Success Criteria:
Regulatory compliance, operator ease-of-use, aligned consumable and equipment design

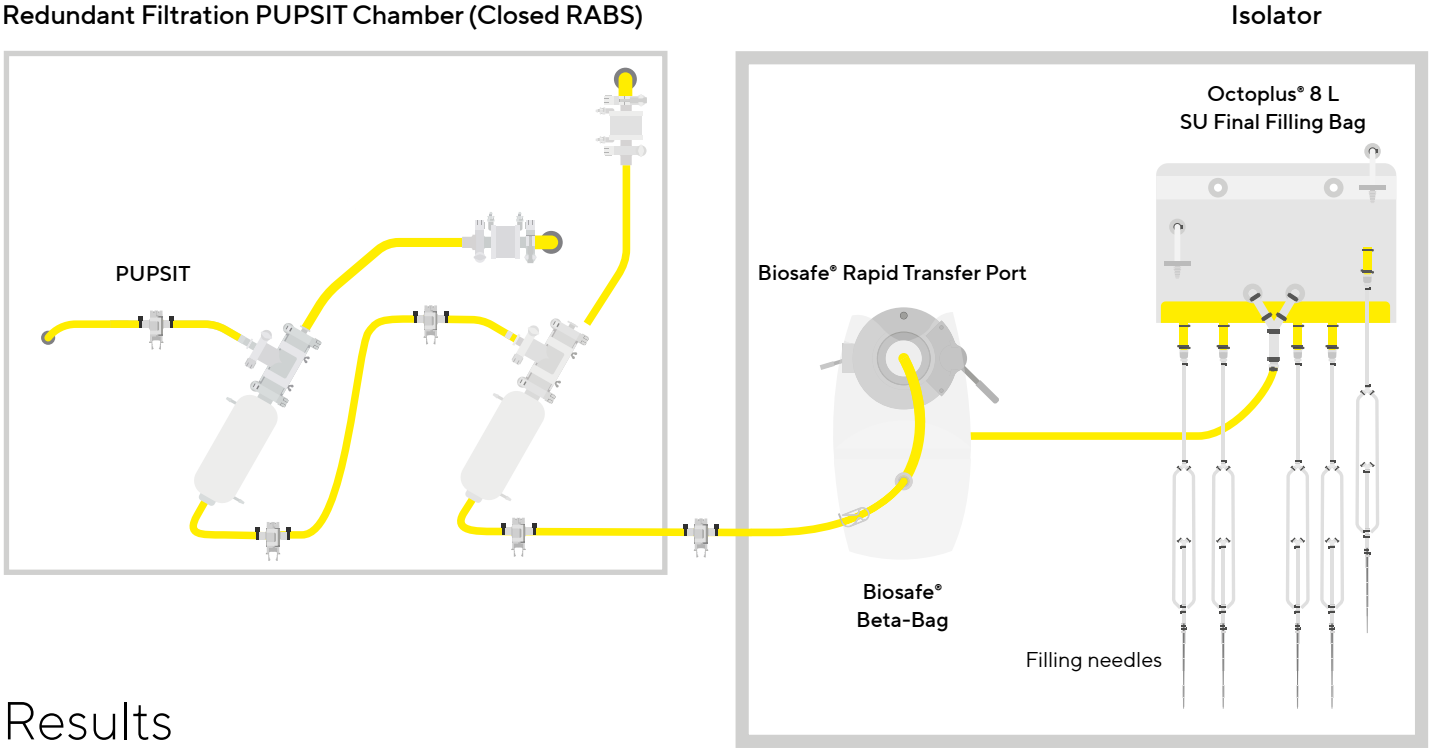
Provided Solutions:
- Octoplus®
- Filter Transfer Set for PUPSIT
- Biosafe rapid transfer port
- SU final filling bag , executed at Syntegon's site in Crailsheim
- Automated filter test rack in a cRABS (Syntegon)

Provided Solution

- Sartorius convened a joint workshop with Boehringer Ingelheim and Syntegon to evaluate Annex 1 compliance and the integration feasibility of single-use assemblies.
- A customized Octoplus® Final Filling Assembly and PUPSIT transfer set were co-developed specifically for this application. These assemblies were customized in close collaboration with Syntegon to ensure compatibility with the filling equipment. Early involvement allowed Sartorius to contribute to machine design optimization in a way that supported the reliable production, sterilization, and integration of the consumables (Figure 1).
- To mitigate risks, Boehringer Ingelheim opted for a redundant filter setup. If the primary filter, located nearest to the filling needle, fails the post-use integrity test, a successful test of the secondary filter can save the batch. Both sterilizing-grade filters (primary and secondary) must undergo PUPSIT. This requirement complicates the filter transfer set, making it more challenging to bring it into and place it in an isolator.
- Additionally, for enhanced risk mitigation, Boehringer Ingelheim ordered a redundant configuration for the vent filters, which are used for filling, venting, and the pre-use integrity test. This redundancy is particularly beneficial since these filters cannot be pre-tested in situ.

- Syntegon designed an automated filter test rack that requires no manual intervention during the testing process
- Through sustained collaboration, the project team identified a more practical configuration for operators with disconnectable small sets for flexibility and optimized disassembly and disposal via endless liner (HSE purpose). Rather than installing the PUPSIT assembly inside the isolator, a revised layout has been positioned within a closed RABS connected to the isolator. This compromise—reached through technical dialogue between all three partners—achieved regulatory compliance while enabling efficient handling and standardized single-use design for both the PUPSIT kit and final filling bag.
- Sartorius provided detailed single-use component specifications and defined process steps to support Syntegon's automation design and adaptation of the filling line, including integration of the isolator system and closed RABS architecture. By combining Sartorius' expertise in single-use systems with Syntegon's capabilities in fill-finish automation, the project team was able to streamline integration and accelerate progress toward a shared customer objective.

Figure 1: *Schematic of the Octoplus® and PUPSIT Setup*



Results

- Delivered a functional, operator-friendly single-use final filling system tailored for clinical production and market launch.
- Selected a closed RABS setup as the more suitable solution, offering an optimal balance between regulatory compliance, operator accessibility, and contamination control.
- Maintained full compliance with EU GMP Annex 1 while simplifying installation and reducing operational burden.
- Ensured reproducibility and compatibility through early alignment between consumable design and equipment interface.
- Implemented a fully automated filter test rack where no human intervention is required to perform the PUPSIT.
- Enabled a sustainable, scalable approach now being applied at a second Boehringer Ingelheim site.

Conclusion

This project demonstrated the value of early collaboration in navigating complex regulatory and operational requirements. By working in close alignment, Boehringer Ingelheim, Syntegon, and Sartorius established a solution that balances compliance with practical usability. The result is a reliable, operator-friendly system that reduces setup complexity and builds confidence in ongoing implementation, offering peace of mind in a critical step of drug product manufacturing.

At a Glance

Achieved
~50%
time savings

100% **regulatory compliance with PUPSIT**

Risk mitigation
achieved through redundant sterilizing filters and air filters

Entirely single-use flow path:
No steaming, no cleaning

Before

Filters inside the isolator
- High risk of product contamination
- Difficult to automate
- Production constraints and supply chain issues

After

Automated filter test rack in a seperate closed RABS in front of the isolator
- No risk of isolator contamination (and thus product contamination) due to complex handlings
- Automated operation, including PUPSIT
- Standard PUPSIT consumable designs
- Easier to install

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