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Case Study

RoSS.FILL Automated filling

032020

THE SITUATION

It has been standard procedure to fill drug substances into primary packages manually. Now, sophisticated **innovations of automated filling have entered the market**. However, many companies hesitate to adopt these innovations for their own, as there exists ignorance about the advantages, financial aspects and cost-value-ratio.

Among these was one biopharmaceutical company from the Netherlands who wanted to know in detail and **instructed Single Use Support to compare costs and further advantages/disadvantages of manual handling versus automated filling** of bulk drug substance according to their requirements.

The biopharmaceutical company had filled their drug substance into single use bags manually and aspired to fill their bags in an automated manner, depending on the outcome of the comparison.

THE ANALYSIS AND DATA

The Dutch biopharmaceutical company provided us with information that reflected their current situation. This data has been compared with performance data of the platform for automated filling: RoSS.FILL.



The total drug substance volume to be filled every year was **4,800 liters**. One batch consisted of 200 liters, which resulted in 24 batches per year.

The value of the BDS per batch (200l) is defined with approx. **500,000 €**.

With manual filling it is required to employ 3 people to fill the bags for 2 days, whereas with automated filling, only one instructed staff is required for a filling of 200 liters in one to two hours. It is not only filling itself which leads to such a **long and cost-intense labor force when filling manually**, but also the documentation, validation and the introduction of SOPs. With automated filling these compliance requirements are redundant, since there is a GMP compliant software control unit integrated in RoSS.FILL that takes care of a seamless and proper documentation according to GDP.

Closed systems in handling with bulk drug substance are not only recommended by the FDA, but also lead to cost savings due to the smaller risk of product loss - in both, risk of contamination and the use of residual BDS volume in the tubings.

	Automated filling	Manual filling
Risk of contamination	Very low	low to medium
Scalability	High (10ml – 300l)	Low
Control/predictability	Yes (barcode scan)	Medium
Loss due to residual filling	Very Low (Towards 0%)	Low (1-2%)
In-plant labor hours required	2 hours (1 pax for max 2 hours per batch)	54 hours (3 pax for 18 hours per batch)
Documentation/validation according to GMP	GMP compliant software control unit integrated in RoSS.FILL	Manual documentation, validation, SOP required

TCO – Total costs of ownership

The total cost of ownership (TCO) displays the overall expenditures of implementing a new technology and is being summarized by CAPEX and OPEX.

CAPEX (capital expenditure):

With manual filling, there is only filling equipment, containers and sterile manifolds/tubings required. With automated filling, there are upfront expenditures that comprise of one filling unit, one RoSS.FILL and sterile manifolds/tubings.

OPEX (operational expenditure):

For filling manually, there are ongoing costs with regards to labor hours, documentation, validation, the creation of SOPs and higher risk of product loss incl. risk of contamination and residual BDS. Automated Filling requires running costs of far fewer labor hours, and less risk of product loss

Automated filling vs. Manual filling beyond costs

Automated filling of bulk drug substance is the only way to **ensure sterility, to eradicate risks of human errors, and to achieve an efficient filling capacity within a short time.**

This becomes more and more apparent with rising volumes. Higher volumes do not come along with an increased need of staff. On the contrary, as they are supported by automated filling, only one person is required to fill up to 200 liters of bulk per run. The volume per bag is being tracked by means of **integrated weighing cells** to avoid overfilling. RoSS.FILL makes sure that the bags are filled **fast, but also safely and accurately**.

Optionally, **bulk filtration** can be implemented with automated filling. Modular manifold designs allow flexibility in carrying out filling and filtering or multiple bags at the same time.

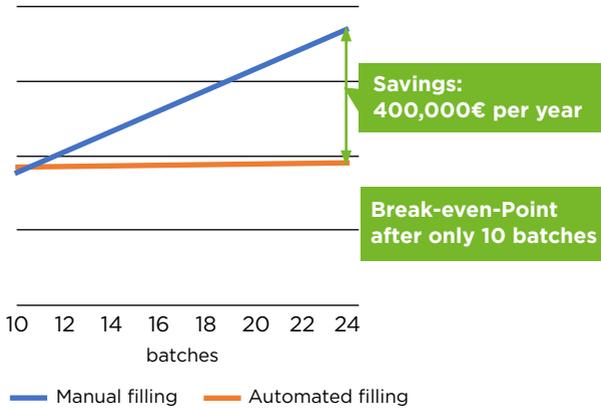
Also, in terms of documentation everything will be done automatically. For each bag filled, a **label** with information regarding weight and including the batch identification number is being printed. This safeguards the correct allocation of information per bag through barcodes.



RoSS.FILL with Bag Filling Rack (left) and Bottle Filling Rack (right)

THE RESULT

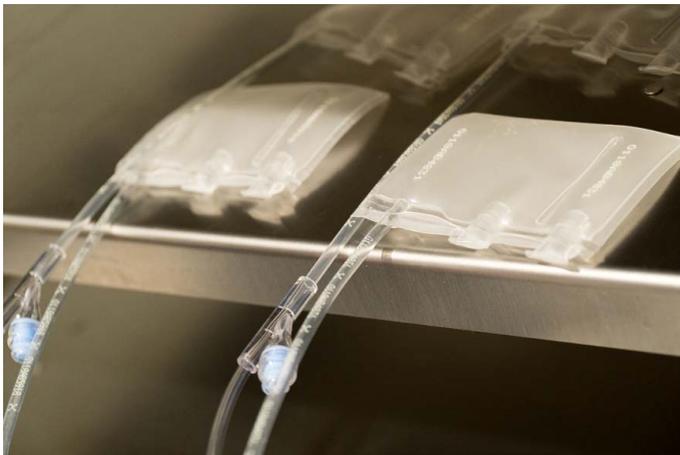
TOC Comparison Manual vs Automated Filling



After one year the initial costs for automated filling paid off, given the real-life assumptions provided. **Even though there is bigger CAPEX upfront, automated filling pays off very soon.** Our comparison shows that the costs that are required in the beginning are amortized after the 11th batch by reason of the massive amount of OPEX with manual filling. **After 12 months and 24 filled batches, the cost savings amount up to 400,000 Euro.**

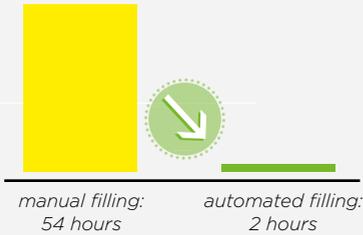
The case study examined the occurrences of a company with a mid-size volume. **For a company producing larger volumes of drug substance or filling multiple quantities of single use bags, the cost savings rise even further.**

In case of filling multiple, smaller single use bags (0.1l to 5l) the higher amount of product loss due to residual drug substance in the tubings come to play a higher role. In case of filling larger amounts of volume, on the other hand, more labor hours are required with a higher risk of human errors and product risk by reason of contamination.



Regardless of costs, **the advantages for automated filling prevail** which, in the end, **convinced the biopharmaceutical company to switch** to the next level of automated drug substance handling, with RoSS.FILL:

In-plant labor hours required



- High filling range
 - Bags: 10ml to 500l
 - Bottles: 30ml to 20l
- Very high weight accuracy due to individual weighing cells
- More sterility granted
- Less product loss
- Less labor force required
- Compatibility and flexibility for all sizes and manufacturers of single use bags
- GMP compliant validation granted and GDP
- High speed of filling
- Independence of consumables and primary packaging; can be sourced from a wide range of suppliers
- Works with any bag size of any bag supplier
- Very low footprint
- Racks are customizable
- Automation flexibility concept: works with any MES
- Consumable independent
- Bulk filtration included
- Modular manifold design

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