

## Full Throttle For Vaccine Filling

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**When the pharmaceutical industry started research in spring 2020 on vaccines to fight COVID-19, the issue of manufacturing and packaging capacities arose almost at the same time. For Thermo Fisher Scientific, it meant upgrading its contract development and manufacturing business to support production of therapies and vaccines. Requests for suppliers like Optima to provide new sterile fill finish lines with isolators were scheduled to start immediately as emergency drug approvals were granted. New ultra-high speed fill/finish lines from Optima enabled by new technology vials from Corning now offer the possibility to further increase filling capacities within a very short period as is discussed in this joint in-depth evaluation.**

The COVID-19 pandemic is placing particular demands on vaccine producers and equipment manufacturers. The pressure on pharmaceutical companies, contract manufacturers, and mechanical engineering firms to increase vaccine filling capacities as quickly as possible is mounting again in light of the accelerating mutations of the coronavirus. The Optima Group's Pharma Division, based in Schwaebisch Hall, Germany has been at the forefront ever since the pandemic began, supporting pharmaceutical companies and contract manufacturers worldwide with equipment solutions for the safe filling of high-value pharmaceutical drugs such as vaccines.

### Important contribution to overcoming the pandemic

Since the outbreak of the pandemic, Optima Pharma has been making great efforts to adapt existing filling systems for vaccine filling and to build new filling systems with isolators as quickly as possible. "Our employees have been extremely challenged and are delivering top performance worldwide," says Juergen Rothbauer, Managing Director of OPTIMA pharma GmbH.

One example for a successful collaboration during the pandemic is with Thermo Fisher, headquartered in Waltham, Massachusetts. The company's Pharma Services business provides contract development and manufacturing services, which includes sterile fill operations for COVID-19 vaccines and other critical care medications for pharma companies globally. As a strategic partner with the necessary technological know-how, and end to end drug substance and drug product development and manufacturing capabilities, Optima is helping the company increase capacity for vaccine filling at several of its sites as quickly as possible.



Figure 1. The vaccine is dosed multi-digit into the vials. (Optima)

"Against the background of this historic task, it goes without saying that we are making every effort to ensure that the worldwide vaccine production can be increased as quickly as possible," adds Rothbauer. "We are confident that we will bring these projects to a speedy conclusion and thus make an important contribution to overcoming the pandemic," says Rothbauer.

### A record time from dispatch to starting production

Optima Pharma makes every effort to keep delivery times as tight as possible: "This is about nothing less than saving lives by expanding global vaccine filling. In this light, we have pulled out all the stops to expedite

the completion and delivery of the filling lines for Thermo Fisher,” Rothbauer reports. Besides the employees’ high level of commitment, a whole package of measures contributed to the extremely rapid starts of production. These include the CSPE approach (Comprehensive Scientific Process Engineering), rapid modifications to machines that were already under construction, and the simultaneous development of vaccines and filling lines. The digitalization of engineering as part of CSPE has been a time saver. High levels of precision were already achieved in the 3D models and simulations, and this was carried over into installation, with high efficiency/high quality lines being created right from the start.

A significant amount of time was also saved by assembling the isolator and the entire filling line together in the CSPE Center at Optima in Schwaebisch Hall before delivery as well as extensive testing of the complex technology. Optima’s experts remained available to be contacted by Thermo Fisher around the clock. On-site installations were carried out by a large crew of Optima staff using careful hygiene techniques. The U.S. government’s easing of regulatory requirements such as expedited domestic entry permit procedures as part of the U.S. COVID response, formerly known as Operation Warp Speed, also helped complete the projects as quickly as possible. Delivery times were also significantly reduced with the help of smart logistics concepts.

### Pathways to higher filling capacity

In addition to fast project processes, selecting the right primary packaging materials offers great potential for increasing filling capacities. As is the case for filling lines, the global demand for primary packaging materials has risen in response to the COVID-19 pandemic. Global supply chain leaders have identified vials as a supply chain vulnerability for both COVID-19 and non-COVID-19 products<sup>1</sup>.

Recent US Food and Drug Administration guidance highlights this concern and helps to address it by outlining pathways to facilitate vial and stopper changes<sup>2</sup>. FDA points to Comparability Protocols (CPs) as well-suited for glass vial changes (such as shifts to Corning’s Valor® Glass), as CPs can support vial changes broadly including across multiple products that use the same container (e.g., group supplements, transBLAs). In recent guidance, manufacturers are encouraged to contact the FDA to discuss specific cases that might warrant modified post-approval reporting categories and other risk-based approaches.

For a long time, desired speeds were at a static level in the filling process of liquid medications. The demands of industry have now changed. “New drug formats and current pandemic surge capacity requirements have mandated that we at Thermo Fisher find a better way,” Stephen Closs, VP, PSG Technical Operations at Thermo Fisher explains.

It is core to the Thermo Fisher values of Integrity, Intensity, Innovation, and Involvement that we look at and champion new capabilities such as the ultra-high speed fill/finish lines made available from companies like Optima that can use and take advantage of improved quality and operational output gained with Corning glass. “As a world leader in serving science, this allows us to stay true to our mission of enabling our customers to make the world healthier, cleaner, and safer,” stresses Closs.



Figure 2. Valor Glass vials (Corning)

### Line efficiency increase of up to 50 %

“Corning has tested its coated vial technology on numerous customer lines and has repeatedly demonstrated that line efficiency is improved by 20 to 50 percent relative to conventional vials”, says Brendan Mosher, General Manager at Corning. Corning, headquartered in Corning, NY, and employing more than 50,000 worldwide, is one of the leading innovators in materials science, with a 169-year track record of life-changing inventions. The improvement in efficiency is largely attributed to the benefits of the low friction coating applied to Corning’s Valor® vials, which reduces the likelihood of events such as glass breakage, jams, and tip overs that can lead to significant downtime and loss of throughput.

This was also confirmed in a recent collaboration between Thermo Fisher, Corning, and Optima Pharma. Corning Valor Glass was tested at Optima Pharma, Germany to evaluate two situations. On the one hand, retrofitting of existing Optima filling lines to reach higher speeds by use of Corning Valor Glass vials. On the other hand, building new lines that operate at even higher speeds without compromising established quality features such as 100 % in-process controls or product saving technologies such as re-dosing, re-stoppering and re-capping functions.

In order to test the limits of Valor Glass vials, worst-case conditions beyond existing in-field situations were simulated. The results were superior and confirmed the analyses already carried out by Corning.

### Improved production reliability and product quality

During the testing of Valor® Glass vials, no breakage occurred at any time, even though worst-case conditions were provoked, Tobias Dombrowski, Project Engineering Manager at Optima Pharma, reports. “The low friction of the vials surface combined with its very high strength are excellent properties”, he says. Regarding the challenging situations for vial filling under the highest speeds, this results in an avoidance of negative cosmetic effects to the vial, breakage of the vial, static charge and less wear of the machinery equipment such as guidings and star wheels. Due to fewer interventions and a better processability in comparison with traditional borosilicate glass, line efficiency is increased.

### Increase of line output by 70%.

“Simply substituting Valor vials for conventional vials under typical operating conditions can provide an immediate operational benefit,” Mosher explains. This is illustrated by the difference between points 1 and 2 in Figure 3. “We have also observed that line efficiency tends to rapidly decrease when using conventional vials because of increased downtime,” he adds. In contrast, the improved flow behavior, damage resistance, and other characteristics of Valor vials enable efficient operation at speeds up to 750 vials per minute as shown by point 3 on Figure 3.

To apply these findings to Thermo Fisher, the joint team of experts from Corning, Thermo Fisher and Optima Pharma undertook more in-depth evaluation and further developed the concept onto a project to boost Thermo Fisher sterile fill/finish production with highest speed and quality.

As not only investment costs, but also operating costs are very relevant for pharmaceutical companies, the estimation of required cleanroom and isolator space proved to be a major consideration during this project. While raising the speed by almost 70 % from 450 vials to 750 vials per minute, space requirements increased by only 25 % without compromising accessibility of the line. The results expected by Corning could be achieved in the in-depth investigations as shown in Figure 4.

Luca Andretta, Sr. Director within the Pharma Services Technical Operations team at Thermo Fisher said this about his observations during technical assessments: “With Corning glass evaluation and trials we have seen improved quality through reduced risks of glass defects usually seen in normal operation due to Corning’s low coefficient of friction coating, higher yields as a result of reduced AVI rejects, all of which can allow us to operate our fill/finish lines at higher speeds, resulting in improved overall line outputs.” According to Andretta, the quality of primary packaging makes a significant impact on filling line performance and ability to operate with highest efficiencies and improve the quality of the product they deliver to their customers. “In our experience with Corning glass options, we have concluded that substantial operational and quality improvements may be achieved, with minor qualification and regulatory impact,” Andretta explains<sup>2</sup>.

### New vials as a retrofit option

Existing sterile fill/finish lines at Thermo Fisher plants were analyzed and requirements for retrofitting were defined. Downtime due to retrofitting had to be kept at the lowest level possible. An extension of complete stations or machine parts is not justifiable and causes further consequences, such as a revalidation of the isolator’s decontamination cycle. With minimal well thought interventions in the existing machine design, performance increases of 10 to 20 % can be achieved, depending on the current system. “The combination of a higher efficiency of up to 50 % at increased operating speeds ultimately provides a step change improvement in pharmaceutical manufacturing capacity,” Mosher summarizes.

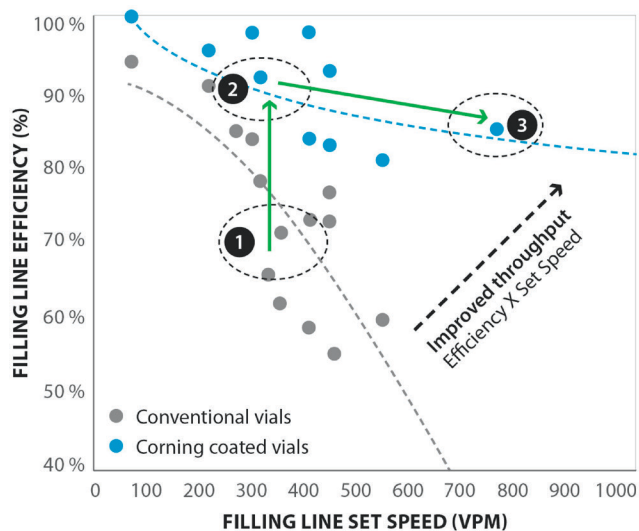


Figure 3. Filling line efficiency tends to rapidly decline with increasing line operating speed when using conventional vials. Corning Valor® vials maintain high line efficiency relative to conventional vials, even as line set speed is significantly increased. (Corning)

Speed at 2R	Relative speed	Space requirement
450 vpm	Standard line	Standard line
600 vpm	33 % faster	20 % larger
750 vpm	67 % faster	25 % larger

Figure 4. Increase of vial output per minute and space requirements using Corning Valor® vials on an Optima filling line. (Optima)

## Primary packaging and high speed filling solutions as game changers

“In a time when the pharmaceutical industry and our customers need us to ramp up sterile fill/finish capacity to meet the growing needs of patients both for COVID-19 pandemic and emergency healthcare medications, as well as many live-saving mRNA and other treatments, we see the increased quality, output, and capacity potential of using Corning Valor® vials in combination with ultra-high speed fill/finish solutions by Optima as a game changer in our ability to serve patients in need of these products,” Closs emphasizes.

In conclusion, rapid vaccine filling not only requires individual solutions, but needs close cooperation between vaccine developers, contract development and manufacturing organizations, equipment manufacturers and primary packaging manufacturers. This allows for rapid capacity expansion, increase in line output and availability as well as improved yields, better product quality and more production reliability, all critical factors in mitigating the challenges posed by the COVID-19 pandemic.

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## References

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