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Unlocking Pharmaceutical Fill/Finish Manufacturing with an Innovative Glass Packaging Solution

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Examining supply chain risk for pandemic preparedness

The 21st century has witnessed multiple epidemic and pandemic infectious diseases including those caused by the SARS, H1N1 influenza, Ebola, and SARS-CoV-2 viruses. While the consequences of these events have been wide-ranging and varied, one constant is the ripple effects sent through the entire pharmaceutical value chain, including drug development and testing, manufacturing, and distribution.

Significant attention understandably has been placed on approaches for accelerating the development and subsequent testing of vaccines and therapies including through evaluation of novel and repurposed products. Various solutions are being explored to reduce bottlenecks in this phase, many of which focus on increased regulatory flexibility. For example, the FDA's Center for Biologics Evaluation and Research (CBER) is taking action to expedite clinical trials for SARS-CoV-2 vaccines and other therapeutic biological products to reduce time-to-market[1]. However, these emergency policies do not address all global shortages in API manufacturing capacity, fill/finish capacity, and the supply of pharmaceutical grade primary packaging. Manufacturing facilities needed to produce vaccines from biological sources can typically take ~5 years to construct at a cost that is at least three times greater than non-biological facilities[2]. The non-profit sector has stepped up to help de-risk some of the significant capital expenditures needed to bring such manufacturing facilities online. The Bill and Melinda Gates Foundation has committed to building new factories for seven vaccines while acknowledging that a majority of the drug candidates will ultimately not be used[3]. In addition, the Coalition for Epidemic Preparedness Innovations (CEPI) is making targeted investments in both vaccine development and enhancing global manufacturing capacity to support the delivery of billions of doses worldwide[4].

The distribution of drugs to the end-user is already a complex, multi-step process, particularly at an international scale. A number of distribution problems arise during widespread disease outbreaks. For example, a recent survey found that the average cost of shipping has increased by 224% due to travel restrictions[5]. The requirements for transporting drugs to maintain safety and efficacy can further hinder distribution. Many of the vaccines that are needed to fight pandemic diseases are temperature-sensitive and must therefore be refrigerated or frozen. The need for a robust cold chain is amplified during a pandemic[6]. Developing regions of the world that are often at the greatest risk also tend to present the greatest challenges to maintaining cold chain distribution – e.g., extreme environmental conditions, unstable or fully absent access to electricity, and complicated logistics due to weakened healthcare systems.
There is no panacea that will immediately enable the rapid deployment of vaccines and other medicines during a global health crisis. However, the remainder of this article will focus on a combination of innovative technologies that can substantially reduce the fill/finish manufacturing bottleneck – that is, ultra-high-speed filling lines that are enabled by next-generation pharmaceutical glass packaging.

Current pharmaceutical filling line utilization can be limited by glass packaging

There are many factors that limit the speed and efficiency of pharmaceutical filling machines, including the type of glass vial being processed. Traditionally, filling machines have been deliberately engineered with output constraints due to the physical interactions between the machine and conventional borosilicate glass vials. Stress and friction generation on turn tables, tracks and trays, particularly at junctions between intermittent and continuous motion, lead to glass breakage and human line interventions, which risks greater contamination of sterile environments.

Decades of experience with borosilicate glass have allowed design engineers to develop machines that can fill vials at ultra-high speeds of up to 750 per minute with certain contingencies. For instance, to achieve line speeds of over 500 per minute, borosilicate glass is typically siliconized on the outside upstream of the depyrogenation tunnel (to reduce glass-to-glass contact friction) and electrostatic eliminators are installed around the filler infeed turntable (to diminish attractive interactions). Without a combination of such contingencies, ultra-high speeds could not be attained, and line efficiency would likely be impacted compromising the commercial viability of the approach.

Unlocking pharmaceutical fill/finish manufacturing with an innovative glass packaging solution

New vial technology is now allowing filling machine engineers to explore new frontiers without the constraints mentioned above. A new packaging option, Valor® Glass, is chemically strengthened and has a low coefficient of friction outer coating which has proven to significantly improve manufacturing throughput. Conventional borosilicate vials typically operate in the range of 60-70% efficiency at up to 450 vials per minute. Valor vials, in comparison, have been shown to achieve over 80% efficiency at maximum filling speeds up to 750 vials per minute[7]. Furthermore, processing Valor vials does not require the use of siliconization prior to filling, reducing complexity and risk of contamination. Valor technology improves vial flow and reduces breakage helping to enable previously unattainable levels of productivity in pharma filling manufacturing. On existing and new assets, Valor Glass can enable a boost in capacity and accelerate the scale up of new filling line equipment. These technologies are particularly essential during demand surges created by a pandemic like SARS-CoV-2.

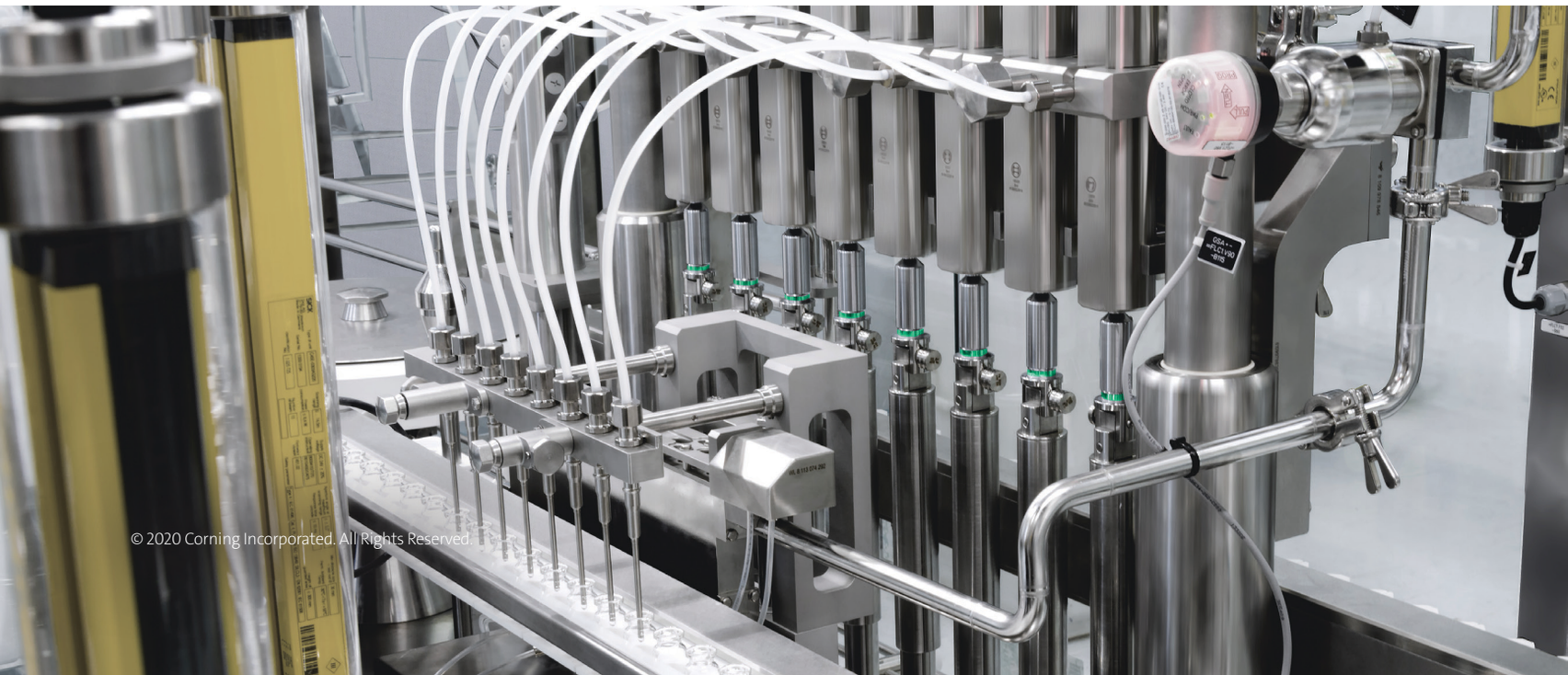
Filling machines, of course, do not function on their own. They are part of a larger final fill solution that typically includes a washer, depyrogenation tunnel, capper, one or more tray loaders, and the fill suite environment. In order to fully recognize the optimizations enabled by Valor Glass, the complete fill/finish line must be evaluated. Equipment manufacturers are exploring opportunities to exceed traditional speeds and efficiency with designs specifically tailored to Valor Glass' capabilities. Syntegon, a leading equipment manufacturer with over 150 years of packaging expertise, is taking the initiative by applying these designs to existing lines in the field to quickly allow for higher speeds and efficiencies to be realized when using this new packaging technology.

Corning and Syntegon are working together to support the implementation of new capacity

Millions of Valor vials have been tested on numerous Syntegon commercial filling lines in the USA and have shown compatibility and in certain circumstances superior operational performance compared to conventional borosilicate. Valor vials from 2mL to 30mL in ISO and custom formats are commercially available for clinical trials, stability testing, and line trial runs. To meet increasing demand, Corning has installed additional capacity that could ramp up to support 1B+ additional doses per year. Syntegon, for its part, has standardized its most popular pharmaceutical vial filling and closing machines into complete high and ultra-high-speed line solutions, with lead times as short as 7 months. Together, Syntegon and Corning are pushing the boundaries for the rapid implementation of additional fill/finish manufacturing capacity.

The future of pharmaceutical fill/finish productivity demands the adoption of new technology

Before the SARS-CoV-2 pandemic, the global sterile injectable drugs market was valued at approximately USD 370 billion in 2017 (over 40B annual doses globally) and expected to generate around USD 780 billion by 2024, at a CAGR of around 11% between 2018 and 2024[8]. Now, the race for effective COVID-19 therapies and vaccines has rallied over 100 research groups and billions of dollars in global funding to identify safe and effective products. Several promising candidates are moving into human trials. Such additional demand may lead to over 1B+ additional doses which will create pressure on the existing supply chain and impacting fill/finish as well. The likely surge in demand is placing pressure on pharmaceutical manufacturers to produce at unprecedented rates. Pharmaceutical companies and contract manufacturers have started to invest heavily in cutting-edge aseptic fill/finish technologies to increase production



capacity and overall equipment effectiveness. Still, the fill/finish industry is expecting a gap between demand and supply. With little fill/finish capacity to spare, pharmaceutical manufacturers will have to rely on allocating existing capacity and building new capacity to meet SARS-CoV-2 global medical countermeasures. The former solution may lead to shortages of other life-saving medications while the latter option will require time and money to ramp capacity.

Ultimately, a forward-thinking approach that takes into account much needed equipment modernization combined with next generation packaging capabilities will be the key to unlocking ultra-high-speed capacity preparedness. Closing the gap in the midst of the pandemic will require government and industry coming together to support the implementation of additional capacity in a way that fully leverages the latest technological advancements in packaging and manufacturing technologies. For example, the U.S. Biomedical Advanced Research and Development Authority (BARDA) has selected Corning's Valor® Glass as part of the United States Government's Operation Warp Speed Initiative – a program to facilitate, at an unprecedented pace, the development, manufacturing and distribution of COVID-19 countermeasures[9]. These commitments in addition to advancements in ultra-high-speed filling technology that Syntegon has pioneered can improve fill/finish productivity to increase capacity and speed to market, both key to ending this global pandemic.

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