

## Parenteral Packaging: 2021

**Parenteral packaging of the future will include more automated lines, ready-to-fill packaging formats, and supply-chain transparency.**



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Over the next five years, parenteral packaging will experience changes: more pre-filled and ready-to-use containers, more efficient filling/closing operations, more automation, more stringent quality requirements, and a more transparent supply chain, as well as fewer counterfeit products, fewer quality problems, and less human intervention in the fill/finish process.

"A much larger share of production will be executed in smaller batch sizes driven by the requirement for specialty medication," predicts Christian Treitel, director of Pharma Business Development, Bosch Packaging Technology, a manufacturer of packaging machines for pharmaceutical products. As a result, he says, "the [number] of presterilized vials and cartridges in the market are expected to grow significantly and offer increased flexibility. We will also see the emergence of new and [currently] unknown pack styles combined with drug-delivery devices, which will be tailored to various patient groups."

Driving forces for these changes include "the availability of new biotechnology products, patient comfort requirements, and [the development of] new therapies requiring specific features, such as pre-filled syringes, single-use vials, and IV premixed bags," notes Frédéric Kahn, global vice-president Key Account Management at Gerresheimer, a supplier of glass and plastic packaging.

Increasingly, material choices will involve newer polymers such as cyclic olefin copolymer (COC) and hybrid constructions. Gerresheimer's MultiShell vials, for example, deliver high barrier properties, clarity, and break resistance using a triple-layer structure that sandwiches a layer of polyamide between COC layers. Another new technology is the COC/glass container offered by Wheaton. According to Wayne Brinster, president and CEO of Wheaton, "This breakthrough will allow us to provide products that have the best of both worlds: the lightweight, break-resistant properties of plastic, with the barrier qualities and inert inner surface of pure glass .... There are applications where having both materials in one product has long been needed." Benefits of a glass interior include the elimination of extractables and leachables that could contaminate contents, plus a surface with lower vapour transmission and higher resistance to solvents. The plastic exterior protects the glass from cracking and breakage (1).

### Vial filling

The trend toward ready-to-use containers is likely to drive changes in the production and filling of

small-volume vials, currently the most common packaging format for parenteral products. Aseptic Technologies, for example, has introduced the Crystal Closed Vial and customized filling line. Already in use worldwide, the vial is aseptically molded and closed under ISO-5 conditions, irradiated, and delivered to the filling site. Vials sizes include 1, 2, 6, 10, 20, and 50 mL. The design maintains closure integrity at low temperatures, making the package well suited to cryogenic storage conditions (2).

The Crystal Filling line can be manual or fully automated and consists of three steps: filling through the thermoplastic elastomer stopper, laser resealing of the stopper, and snap-fit capping. The streamlined filling process requires less cleanroom space and eliminates the need for water for injection, vial and stopper washing, vial and stopper sterilization, stoppering, and capping by crimping (2).

### Material choices will involve newer polymers such as COC and hybrid constructions.

Filling line options include the Crystal M1 manual filling station for batches of less than 1500 1-mL vials; the Crystal L1 Robot line; and the Crystal PX filling line. The single-robot L1 line, rated at 10 vials per minute, handles nests of closed vials and can be configured for ready-to-fill glass vials and syringes. The faster PX line delivers a maximum output of 180 vials per minute, can be equipped with up to eight pumps, offers 100% in-process control, and occupies a footprint of 16 m<sup>2</sup> (2).

### More automation

"As biologics mature in the drug development pipeline, we see an increase in complex manufacturing requirements," says Kahn. In addition, he says, as markets and customers become more demanding, ready-to-use formats will experience growth. "Therefore," he predicts, "parenteral packaging equipment/lines will become more automated and integrated, including ever more sophisticated quality control systems."

"Quality requirements for glass containers are likely to be tightened further and include specifications regarding the particle load, lower rate of cracks or cosmetic defects, and smaller dimensional tolerances," says Kahn. "Prefillable syringes are associated with specific requirements such as

low hold-up volumes and reduced tungsten or siliconization levels. A recent Parenteral Drug Association Congress revealed that risk-based approaches to quality control are an important tool and should be implemented with competence."

Treitel agrees that demand for automation and integration will rise. He says, "Price pressure due to generics and biosimilars will press large-scale parenteral manufacturing to become more efficient."

Automation technologies include robotics, machine vision, servo-motors and drives, and an ever-increasing array of sensors. Robots can perform many material handling functions on parenteral packaging lines. "The incorporation of robotics into various functions will continue to evolve, specifically as it pertains to material handling within fill/finish and downstream packaging applications," predicts Randy Fraatz, business development manager for MG America, the US subsidiary of MG2 of Bologna, Italy, a supplier of processing and packaging equipment.

With the evolution of collaborative robots that can work safely alongside human operators, Kahn predicts utilization will continue to rise and "further improve quality and safety especially in manipulation of high toxicity parenteral drugs fill and finish."

Product quality also will be supported by isolator integrations. Fraatz believes the transition to isolators will continue. He predicts adoption of isolators "will lead to operational changes and some paradigm shifting for those organizations that are not familiar with isolator technology, but still need to remain competitive and demonstrate risk-reduced packaging processes for industry acceptance."

"As the physical mechanics and materials change for both sterile and non-sterile parenteral applications, such as the use of robotics ... or advancements in machinery design for single-use filling systems, it is important to recognize the changes in software programming and electronic controls that will be necessary for efficient machine operation. Packaging machinery will continue to change in ways that rely on software

automation designs that can manage the command and control required as the data input/output progressively increases," Fraatz concludes.

### Product security

Expanded systems integration, serialization, and supply chain connectivity will enhance productivity and support counterfeit prevention. "Connected industry' solutions will offer full transparency of the production and supply chain, thus

The Gerresheimer Gx RTF (ready-to-fill) syringes arrive washed, siliconized, preassembled, and sterilized.



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providing for significantly improved quality and efficiency,” says Treitel.

Anticounterfeiting technologies will continue to play an important role in product security. “Initiatives like decoration–identification–differentiation systems offer a range of possibilities including non-human-readable ultraviolet ink,” reports Kahn.

“There is definitely a growing trend to multi-functional labeling solutions that enhance end user safety and comfort,” adds Gene Dul, president of Schreiner MediPharm US, a developer of specialty labels for healthcare and pharmaceutical products. He predicts, “Buzz words like ‘patient centricity’ and ‘digitalization’ will play an important role when designing customized label solutions that contribute to user experience.

“Smart labels with integrated near-field communication (NFC) or radio frequency identification technology will become more and more important to equip injection devices with interactive functionalities. This will allow for easy check of product authenticity, expiry date, or product recalls via a smartphone, and the patient may access important information or videos on drug or injection device use. In addition, NFC applications can support patient compliance by app downloads that allow recording and tracking of patient compliance behaviour, or enable reminder options for regular drug use.”

Another developing technology, printed electronics, applies sensors, antennas, and other devices to flexible substrates and could help deliver NFC, RFID [radio frequency identification], and other technologies to support serialization and anticounterfeiting efforts.

### New terminology

By 2021, another parenteral packaging change may involve terminology. In the 22 Oct. 2015 *Federal Register*, the US Food and Drug Administration (FDA) published a draft guidance that revises definitions for “single-dose container” and “multiple-dose container,” and it replaces the term “single-use container” with “single-patient-use container.” The guidance defines the terms as follows (3):

*Single-dose container—“A single-dose container is a container of a sterile medication for parenteral administration (injection or infusion) that is not required to meet the antimicrobial effectiveness testing requirements. A single-dose container is designed for use with a single patient as a single injection/infusion. When space permits, a single-dose container is labeled as such and should include on the label appropriate discard statements. Examples of single-dose containers are vials, ampules, and prefilled syringes.”*

### Robots can perform many material handling functions on parenteral packaging lines.

*Multiple-dose container—“A multiple-dose container is a container of a sterile medication for parenteral administration (injection or infusion) that has met antimicrobial effectiveness testing requirements, or is excluded from such testing requirements by FDA regulation. A multiple-dose container is intended to contain more than one dose of the drug product. When space permits, a multiple-dose container is labeled as such. Multiple-dose containers are generally expected to contain 30 mL or less of medication. The beyond-use date for an opened or entered (e.g., needle-punctured) multiple-dose container is 28 days, unless otherwise specified by the manufacturer in the label. An example of a multiple-dose container is a vial.”*

*Single-patient-use container—“A single-patient-use container is a container of a sterile medication for parenteral administration (injection or infusion) that is intended to be used mul-*

*iple times for a single patient. When space permits, a single-patient-use container is labeled as such and should include on the label appropriate discard statements. Examples of single-patient-use containers are patient-controlled analgesia cartridges and certain pens for injection.”*

A primary goal of the changes is to reduce bacterial and viral infection outbreaks caused by misuse of single-dose containers and confusion about single-use containers, such as insulin pens, that contain multiple doses, but are intended for use by only one patient. FDA recommends labeling changes be made within two years of the publication of the final version of this guidance. If finalized in its current form, the guidance would apply to new drug applications, abbreviated new drug applications, biologics license applications, premarket approval applications, and premarket notifications under section 510(k) of the US Federal Food, Drug, and Cosmetic Act (3).

### References

1. Wheaton, “WHEATON to Commercialize Breakthrough Technology Providing Plastic Components with Pure Glass Interiors,” News Release, 27 July 2015.
2. Aseptic Technologies, “Filling Solutions,” Internal Presentation, September 2015.
3. FDA, “Selection of the Appropriate Package Type Terms and Recommendations for Labeling Injectable Medical Products Packaged in Multiple-Dose, Single-Dose, and Single-Patient-Use Containers for Human Use,” *Federal Register*, 22 Oct. 2015. **PTE**

### We'll be seeing more...

- presterilized containers
- new pack styles
- new container materials
- ready-to-use containers
- automation and robotics
- system integration
- anticounterfeiting technology
- multi-functional labels