INCREASING FLEXIBILITY IN PHARMACEUTICAL PACKAGING

The importance of integrated Ready-to-Use vials and packaging systems for aseptic fill/finish

SGD PHARMA

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Abstract

Highly complex biologics and other specialty drugs are representing an increasing proportion of the pharmaceutical market, and their pivotal role in this market has been challenging glass primary packaging producers year after year. Together with this, trends such as more personalized treatments in place of blockbuster drugs, increasing regulatory quality and compliance requirements, and a move towards more self-medication, are changing the way drugs are administered and therefore manufactured. Pharmaceutical companies are requested to be flexible, to reduce time-to-market, increasing quality and reducing costs. To meet the needs of the market and address these challenges, primary packaging design is moving towards Ready-to-Use (RTU) components as a preferred solution.

Glass continues to be the most widely used type of primary container for parenteral drug products, offering excellent barrier properties, chemical resistance, and regulatory acceptance. RTU primary packaging configuration is now key to addressing the changing needs of the pharma industry. Starting from syringes and then extending the technology to tubular vials and cartridges, RTU glass containers are now tackling the challenges Pharma Companies face in keeping pace with the market, increasing flexibility, reducing time-to-market and total cost of ownership (TCO), and preserving safety and quality standards of the system.

Based on the proven success of other RTU glass primary packaging solutions, RTU molded glass vials are offering a new choice to pharmaceutical industries in the aseptic manufacturing processes and technologies. Molded glass brings its own improved chemical durability and greater mechanical strength, combined with proven industrial platforms for RTU primary packaging as well as state-of-the art packaging systems, such as Trays and Nest & Tubs.

Introduction

Parenteral drugs – sterile drug products that are presented in the form of solution, suspension, emulsion, or reconstituted lyophilized powder, suitable for administration by injection – are an increasingly important segment of the pharmaceutical industry. Parenteral dosage forms are often preferred due to their direct absorption directly at the site of delivery, compared with an oral route via the stomach that can lead to irregular absorption and often a slower onset of action. Parenteral drug delivery is typically associated with biological drugs (although this route can be used for small molecule drug products, particularly where solubility is a challenge)[1] and in 2018, parenteral drugs accounted for 32% (by volume) of the global drug market[2]. Growth of the parenteral market has therefore been attributed to the increase in development of biologics and complex active pharmaceutical ingredients (APIs), which in turn is being driven by the rising prevalence of chronic illnesses across the globe, such as cancer, cardiovascular diseases, and diabetes.

Pharma and Biotech Companies are also incentivized to develop biologics because these drugs often target unmet medical needs or orphan diseases. However, these innovative, niche product areas require greater flexibility regarding volumes and components. As a result of the focus on parenteral drug development, the parenteral packaging sector is expected to experience considerable growth at a compound annual growth rate (CAGR) of 11.14% by the end of 2024[3]. At the same time, there is an increasing pressure on regulatory aspects to better control the contamination risk of aseptic fill-finish operations.

The increased demand for personalized medicines and biological drugs, and the consequent need for flexibility in manufacturing capacity, has led to a growing requirement for Ready-to-Use (RTU) packaging systems.

Such systems reduce significant investment or operational demands, leaving Pharma Companies with more time and resources to focus on drug development and core added value operations.

As well as the considerable growth of biotech therapies, other drivers of the industry's movement towards RTU packaging components are:

- **The need to reduce total cost of ownership (TCO):** Pharma running costs will continue to escalate, with typical investment of over US$2 billion required to progress from a laboratory idea to successful commercialization[4]. Traditional filling lines require space and high running costs, so many are seeking new solutions.
- **The pressure to increase efficiency, lower drug prices, and to minimize patient risk:** Society and government demands for lower cost and increased access will put pressure on Pharma Companies worldwide. A patient-first and right-first-time mindset, and the need to deliver higher yield and on-time release, add to this pressure.
- **The requirement for flexible and fast reactions to industry needs:** Need to frequently change primary packaging (according to emerging markets and personalized medicine) and need for a smaller batch filling.
- **Increasing regulatory and quality compliance:** Pharma Companies are seeking ways to keep up with the fast-evolving global regulatory environment and externalize responsibility.

In RTU systems, packaging is washed, depyrogenated and sterilized by the packaging supplier so that the only step left in the process in-house is to fill and finish the container, which eliminates a significant part of the operational constraints. While RTU solutions for small-volume containers are now widely recognized and adopted by industry and smaller labs, the option for larger volume containers (defined as those above 20ml) remains a crucial need in the market[5].

Over the last decade or so, glass vial geometry and composition have been fine-tuned to the needs of Pharma Companies manufacturing biologics and complex drug products. Molded glass represents an important share of the global injectable glass vials market (approx. 40%), and offers high chemical and mechanical resistance. Molded glass vials offer a complementary solution for Pharma Companies using tubular vials, with solutions from 20–500ml currently available. With these advantages in mind and as RTU components are becoming the preferred choice for clinical trials, small batches, new biotech developments, and multi-product processing lines, RTU molded glass vials address the industry need for increased quality and flexibility in pharma manufacturing.

Application challenges

The manufacture of sterile drugs, such as parenteral dosage forms, requires an intensive process that can affect the stability of the drug's final form. The time and costs associated with completing an effective and compliant aseptic fill and finish process are another barrier to sterile drug manufacturing. Currently, RTU primarily addresses the needs of Pharma Companies for processing small volumes of higher added value products. For these Companies there are direct and indirect costs associated with traditional filling line models, and larger investment required due to the necessary maintenance and validation. The additional steps, such as washing and depyrogenation at the start of a traditional model, need a larger footprint and additional workforce, and introduce potential for rejection due to challenges during these stages, such as a high risk of glass particles due to vial breakage.

These challenges have driven parenteral packaging suppliers to broaden their RTU component offerings, from the introduction of RTU syringes in the 1990s to RTU tubular vials in 2010. The availability of these packaging solutions provided the link across the whole supply chain and gave Pharma Companies access to the technology needed to succeed in this market.

Why choose RTU?

RTU components address the needs of the parenteral market, by ensuring a completely sterile packaging solution ready to be filled, therefore minimizing time-consuming upfront steps required of Pharma Companies. Moving to an RTU platform reduces the time-to-market and minimizes the risk of stops and failures. Pharma Companies do not need to invest in sterilizing equipment and can therefore reduce TCO, which helps to address the increasing costs of bringing drugs to market.

RTU components allow Pharma Companies to focus their efforts on drug product development and processing by improving operational efficiency and sharing regulatory and compliance responsibility with the component suppliers. Pharmaceutical and parenteral packaging component manufacturers are continuously evolving in alignment with advancements in technology and increasing regulatory requirements, to ensure the quality and safety of injectable drug products for patients. With the increasing call for RTU components, the relationship between component suppliers and drug manufacturers is changing and as a result, suppliers are now adopting the responsibility for optimizing and validating all component preparation processes.

Pharma Companies externalizing their packaging can rely on suppliers to guarantee sterility, endotoxin reduction, and particle control, and to ensure compliance with regulatory standards. International Organization for Standardization (ISO) 21882:2019 specifies the characteristics of sterile and ready-for-filling empty glass vials for injectable preparations, including the minimum requirements of materials, packaging systems and analytical test methods.

Regional need is also driving interest in RTU solutions for aseptic filling. For example, due to the 2020 COVID-19 pandemic, some countries have decided to reduce imported drugs to promote local production. This is driving investment in new facilities for more sophisticated products, such as injectable drugs. For some of these companies, it is easier to focus on the filling process for capital expenditure (CAPEX) and operational expenditure (OPEX) reasons, but this is also often driven by a lack of available qualified resources to set up aseptic facilities. In this case, an RTU configuration is a sensible operational decision.

Extending RTU vials to molded glass

Since RTU first appeared on the market, the focus has primarily been on tubular vials up to 30ml. However, larger volumes are now emerging (50, 100 and 250ml vials) for different injectable applications, including oncological drugs, blood derivatives, and veterinary products, allowing Pharma Companies to gain flexibility in these segments. Developments in parenteral primary packaging have culminated in the recent introduction of RTU molded glass vials onto the market in 2019. There are many benefits of molded glass vials as novel RTU primary packaging solutions. The most prominent benefit is the improved chemical and mechanical properties, which provide Pharma Companies with the assurance of minimal breakages, and stability and safety of the drug product.

Mechanical resistance of tubular and molded glass vials can be measured in terms of the vertical load (the pressure exerted during the stoppering phase) and the radial load (the pressure exerted during the loading and the manipulation of the vials). As a result of improved mechanical performance, a drug producer will avoid issues with particles generated by glass breakages in a production line or worse, breakages inside a freeze dryer, avoiding loss of product or productivity impact during the manufacturing line.

Molded glass vials are ideally suited to both liquid and lyophilized drugs, and improve the safety and efficiency of the lyophilization (freeze-drying) process and effective product temperature during drying[7]. Therefore, the glass vial properties significantly impact the heat transfer from the source to the product, which requires homogeneous heat transfer for the whole batch. Vials are also susceptible to breakage during lyophilization, so the quality of the glass primary packaging is an important consideration. RTU molded glass vials, such as the EasyLyo range of sterile empty vials from SGD Pharma, are highly resistant to breakage and are therefore a good choice to ensure the success of the lyophilization process.

EasyLyo vials combine the mechanical strength and chemical durability of molded glass with the cosmetic quality associated with tubular vials. In contrast with the traditional molded glass manufacturing process that can affect inspectability of the vial, EasyLyo achieves uniform thickness that reduces the number of false rejections in automatic inspection lines, minimizing product loss and improving operational costs and ultimately ensuring patient safety.

Integrating RTU primary packaging and containment solutions

SGD Pharma is the first molded glass leader to align with Pharma and Biotech Companies' need for flexibility within the drug manufacturing line, by providing molded glass vials available with RTU containment solutions for aseptic filling lines. RTU containment solutions are designed to protect the vials during handling, distribution, and storage. This maintains the microbiological, physical, and cosmetic integrity of the vials over the designated shelf-life.

There is therefore a need for well-designed containment solutions that are compatible with fill/finish technology in use by the market. For manufacturers of parenteral drugs, containment solutions must also maintain sterility: RTU offerings provide this option without the need for washing and depyrogenation by the Pharma/Biotech Company or contract manufacturing organization (CMO), thus saving time and money and the need to manage in-house.

Drug manufacturers at various stages of the drug development pipeline, with different capabilities in filling (small batch to high quantities), can choose the ideal packaging configuration for their needs:

- Tray
  - Supports RTU molded and tubular glass vials on industrial lines based on conventional filling processes
  - Avoids glass-to-glass contact, eliminating scratches on the glass and reducing particle generation
  - Manual filling at laboratory scale
- Nest & Tub
  - Configuration to fill molded and tubular glass vials, cartridges, and syringes in a combi line set-up
  - Avoids glass-to-glass contact, eliminating scratches on the glass and reducing particle generation

Manufacturers of innovative new drugs can now benefit from the advanced performance of RTU molded glass vials, available in sterilized Stevanato Group's EZ-fill® Nest & Tub packaging configurations. SGD Pharma is the first global molded glass supplier in the world to provide this solution for the pharmaceutical industry, which offers the highest level of flexibility to Biotech companies and CMOs that use combi lines for fill/finish. This approach to aseptic filling not only affords manufacturers and CMOs a wider choice of primary packaging options for multi-sourcing, but reduces the number of machines required for multiple packaging formats. The end result is a fast and flexible integrated packaging solution for innovative drugs going through early-stage development, that allows Biotech Companies to react to changing market needs rapidly.

A collaborative solution

SGD Pharma and **Stevanato Group (SG)** began working as partner suppliers of complementary pharmaceutical packaging products in 2017. SGD Pharma's expertise in molded glass for pharmaceutical primary packaging, combined with Stevanato Group's leadership in Ready-to-Use (RTU) solutions for aseptic filling, provides Pharma Companies with an integrated, flexible solution for different sources of primary packaging.

The **Sterinity range** of sterile empty vials in molded glass (ISO and EasyLyo) from SGD Pharma is powered by the **Stevanato Group's EZ-fill®** packaging technology. This technology enables multiple filling line options for multiple primary packaging sources, and protects the physical and microbiological integrity of the vial.

Premium Vial Manufacturing by SGD Pharma

Type I molded glass vials are manufactured in a state-of-the-art facility located in France before 100% inspection with state-of-the-art visual and mechanical systems in an ISO 8 environment.

Washing

In the Stevanato Group's EZ-fill® area, containers are washed with water for injection & dried in an ISO 8 class clean room.

Depyrogenation

Vials are depyrogenated in a tunnel according to European and US pharmacopeias.

Secondary Packaging Loading

Containers are placed into Trays or Nest & Tubs in ISO 5 and ISO 7 class environments.

Tyvek® Sealing & Steribag Bagging

Sealed with a Tyvek® lid in an ISO 5 class clean room packed in steribags and placed into a box allowing for sterilization.

Sterilization

Sterilization is completed through EtO and a process validated according to ISO 11135.

Storage & Delivery

Ready-to-Use vials are stored at SGD Pharma facilities with 5 years shelf-life For Human Use (FHU).

Icons courtesy of Stevanato Group.

The development of Sterinity molded glass vials by SGD Pharma filled the gap in the market for a secondary source of compliant RTU Type I glass vials, to minimize the risk of supply chain disruptions. To address the changing needs of drug manufacturers, SGD Pharma continues to expand its offering of clear and amber molded glass vials and has introduced 20, 25 and 50ml EasyLyo vials in Stevanato Group's EZ-fill® Tray, 50 and 100ml ISO vials in Stevanato Group's EZ-fill® Tray, and 20ml EasyLyo vials in Stevanato Group's EZ-fill® Nest & Tub. These sterile empty vials are available globally ex-stock and are compatible with leading filling machines. The Drug Master File has been registered and the LOA is available upon request.

Conclusion

The parenteral primary packaging market has seen considerable growth in recent years, mainly owing to the rise in demand for biologics and complex drugs that require dedicated aseptic fill-finish operations. The COVID-19 pandemic has also placed a greater pressure on Pharma and Biotech Companies to innovate quicker - the result of which is demonstrated in the rapid development and regulatory approval of the first vaccines. Small-to-medium sized Biotech Companies have played a particularly important role in the pandemic thanks to their flexibility and adaptability.

Tubular glass vials represent the largest market share of the injectables glass vial markets, but the benefits of molded glass are becoming increasingly recognized and these components are on the rise as complementary RTU solutions.

Innovations, such as the recently introduced RTU molded glass vials, help to improve the safety and stability of biologics and specialty drugs, and provide Pharma Companies with the flexibility to react to the changing needs of the parenteral drug market and integrate second sources of packaging into the pipeline. Packaging systems that preserve the sterility and physical integrity of molded glass vials enhance this flexibility.

By externalizing the washing, depyrogentation and sterilization steps of fill-finish lines, drug manufacturers can reduce CAPEX, OPEX, and TCO, while handing over responsibility to packaging suppliers. The integrated RTU solution from SGD Pharma and Stevanato Group addresses the overall market demand for alternative primary packaging solutions that meet regulatory requirements in a dynamic industry.

SGD Pharma RTU molded glass vials, powered by Stevanato Group's EZ-fill®

SGD Pharma has incorporated **EasyLyo** molded glass vials into its Ready-to-Use (RTU) **Sterinity** range. Key features include:

- **Uniform wall thickness** for high mechanical resistance and better cosmetic aspect.
- **Optimized heel radius** for higher mechanical resistance.
- **Same external dimensions** as tubular vials (20ml and 25ml), eliminating need for major changes to filling line, and enabling same shelf configuration on freeze-dryer.
- **Flatter base and base mold marks** removed, to enhance heat transfer during lyophilization.
- **30% less mass** than industry standard, improving energy cost and footprint.

The novel workflow of EasyLyo powered by Stevanato Group's EZ-fill® simplifies RTU primary and secondary packaging for Pharma Companies looking to reduce costs and time-to-market for high value biological drugs.

To learn more about the Sterinity range of empty glass vials, please visit https://www.sgd-pharma.com/sterile-empty-vials-sterinity-sgd-pharma

For more information about the EasyLyo RTU molded glass vials, please visit https://www.sgd-pharma.com/easylyo-vials

To learn more about integrating molded glass into manufacturing processes, please watch our webinar https://bit.ly/webinar-sgdpharma

For more information on SG EZ-fill® solution, please visit https://pharma.stevanatogroup.com/glass-primary-packaging/products-platforms/ez-fill-platform/

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About SGD Pharma

Founded in 1896 in France and with a global footprint and a strong sales force, SGD Pharma is recognized worldwide as a key player that customers can rely on to support new product development, day-to-day delivery, quality or regulatory support. SGD Pharma benefits from a long know-how and a best-in-class manufacturing footprint. The company has a long-term investment plan to regularly leverage its manufacturing facilities and develop people competencies to be at the cutting edge of the technology. SGD Pharma commits to have the same standard in all its facilities. In 2020, all plants are certified according to ISO 15378 standard, pharma GMP's compliant and equipped with ISO 8 clean rooms. SGD Pharma is a producer of molded glass for pharmaceutical primary packaging, operating worldwide with five factories and a network of more than 90 partners and distributors. For more information, please visit www.sgd-pharma.com

About Stevanato Group

Founded in 1949, Stevanato Group is a leading global provider of drug containment, drug delivery and diagnostic solutions to the pharmaceutical, biotechnology and life sciences industries. The Group delivers an integrated, end-to-end portfolio of products, processes and services that address customer needs across the entire drug life cycle at each of the development, clinical and commercial stages. Stevanato Group's core capabilities in scientific research and development, its commitment to technical innovation and its engineering excellence are central to its ability to offer value added solutions to clients.

For more information, please visit www.stevanatogroup.com

Authors

Carole Grassi Mircich, Chief Innovation & Development Officer, SGD Pharma

Riccardo Prete, Product Manager Vials Platform - Stevanato Group

FRANCE

Headquarters & sales office
Tour CB16
17 place des Reflets
92097 Paris La Défense Cedex

Sucy-en-Brie plant
4 route de Bonneuil BP N°2
94371 Sucy-en-Brie
Tel : +33 (0)1 45 10 70 07

Saint-Quentin-Lamotte plant
1 rue des Terres à Flacons PEA
Bresle Maritime 80880 Saint-Quentin-lamotte
Tel : +33 (0)3 22 26 06 00

Société de Services Verriers (SSV)
5 rue du stade 76260 Saint Remy Boscrocourt
Tel : +33 (0)2 35 86 58 52

Embelia
14 place de la coupole
CS 40016
94227 Charenton-le-Pont Cedex
Tel : 01 53 66 68 68

GERMANY

Kipfenberg plant & sales office
Altmühlstraße 2 D85110
Kipfenberg
Tel : +49 (0) 84 65 / 171-0

ITALY

Milan sales office
Via Caldera 21, REGUS Business Center, Edificio F - 1° piano
20153 Milano
Tel : +39 02 30 35 76 87/88

SPAIN

Barcelona sales office
Gran via Carles III, 84 3e planta
Edificio Trade, Torre Sur 08028
BARCELONA
Tel : +34 93 496 57 54

UNITED STATES OF AMERICA (USA)

New York sales office
900 Third Avenue, 4th Floor NY
10022 New York
Tel : +1 212 223 7100

CHINA

Zhanjiang plant
No. 11 Shuanggang road, Chikan district 524039 Zhanjiang City
Guangdong
Tel : + 86 75 9327 8666

Guangzhou sales office
Room 3402, Pearl River Tower
15 Zhujiang West Road 510623
Guangzhou
Tel : +86 20 8516 8123

Shanghai sales office
Room 217, U-Cube center 841
Yan'an Middle Road Jing'an district
200040 Shanghai
Tel : +86 21 6289 3082

BRAZIL

São Paulo sales office
Av. Doutor Gastão Vidigal, 1132 - Sala 815B, São Paulo, Brazil
Tel : +55 11 2619-2514

INDIA

Vemula plant
Vemula, Moosapet (M)
Mahabubnagar Dist. Telangana - 509 380
Tel : +91 800 8888144

Hyderabad sales office
Office N° 115/1, Kapil towers, IT Park, Nanakramguda, Gachibowli
Hyderabad - 500032
Tel : +91 40 43578800

www.sgd-pharma.com