SCHOTT
glass made of ideas

THE FUTURE OF SMART FILL-AND-FINISH

In this article, Diana Löber, Global Product Manager Vials at SCHOTT, discusses new developments in digitised pharmaceutical manufacturing and the role SCHOTT's Smart Containers can play in traceability along the entire value chain.

The industry is constantly looking for solutions to enhance pharmaceutical processes such as fill-and-finish procedures. By taking advantage of the latest developments in machine vision and data science, the pharmaceutical industry can unlock a new era in digitised pharmaceutical manufacturing, which can ultimately lead to levels of automation that have never been possible before.

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In a recently introduced approach, known as SCHOTT Smart Containers, individual containers can now be laser-marked with a unique data matrix code at the earliest possible stage in the value chain. This allows for distinct, single-container-based unprecedented traceability throughout the fill-and-finish process and beyond. While the code itself represents a specific numeric or alphanumeric sequence, it is possible to add any relevant data to the code at various points of the fill-and-finish process via a parallel data management system. Each container could be traced, for example during infeed, depyrogenation and filling. Information such as date and time, exact temperature during depyrogenation, retention time in heating tunnel and weight before and after filling could be added to the data matrix code after each step.

Compared with currently available solutions, where this type of data can be collected but it is only possible to match it to an individual container unit after it has been singulated on the fill-and-finish line, this new Smart Containers approach sets itself apart. In addition, after processing using current systems, it is necessary to mark, for example, the cap to keep the data connected with the corresponding container throughout its lifetime. Such workarounds bring other disadvantages. With SCHOTT Smart Container, in each subsequent process step, real-time data can be retrieved and matched with the container. This creates the basis to support the elimination of mix-up risks, optimise lyophilisation processes, improve reject management and line clearance, and foster pinpoint accurate recalls.

> "Using a highly advanced laser to melt the data matrix code onto the container leads to low impact on the glass structure, maintaining the container's strength needed to run on filling lines."

Mrs Diana Löber
Global Product Manager Vials
T: +49 6131 664924
E: diana.loeber@schott.com

SCHOTT AG
Hattenbergstrasse 10
55122 Mainz
Germany

schott.com/smart-container

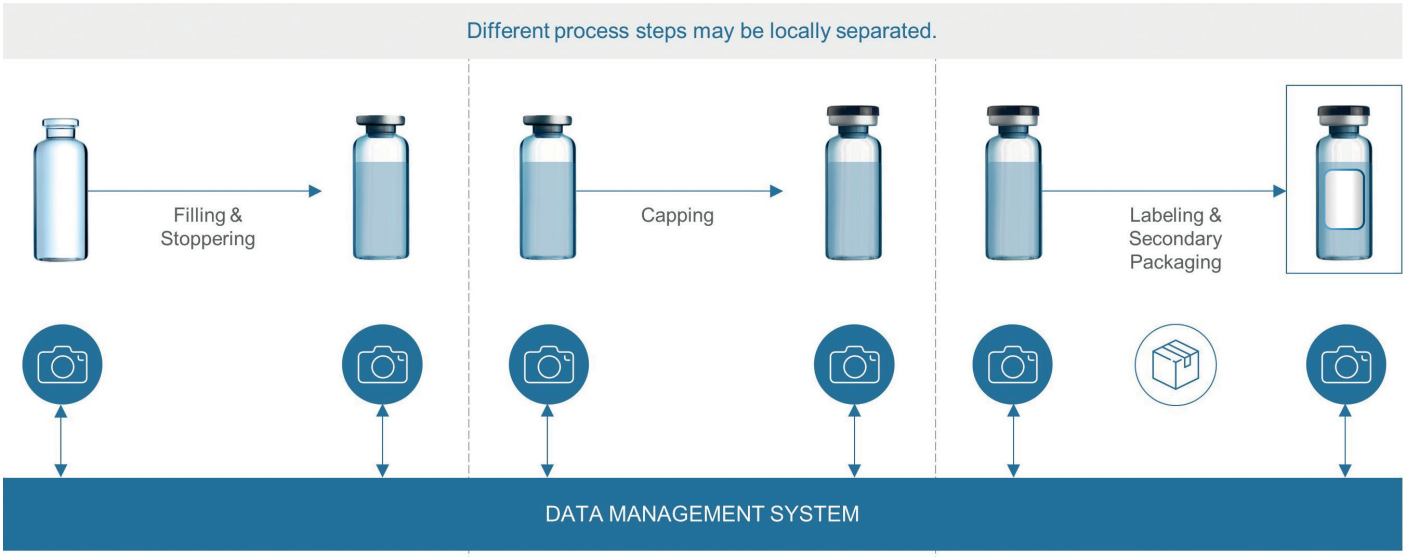

Figure 1: Reducing mix-ups.

THE LASER-MARKED CODE

The data matrix code is based on ISO/IEC 16022 and can be applied in a size of 2 x 2 mm or 1 x 1 mm containing a 14 x 14 dot data matrix. With 16 or 24 digits, the combinatoric possibilities can reach several sextillion possible individual unique numbers. Due to its size and transparency, the code is almost invisible in order to ensure unimpeded inspection by systems or the final user.

Using a highly advanced laser to melt the data matrix code onto the container leads to low impact on the glass structure, maintaining the container's strength needed to run on filling lines. Simultaneously, the code remains stable throughout the entire fill-and-finish process, including washing, autoclaving, and depyrogenation up to a temperature of 600°C. It also resists abrasion and avoids the risk of particle contamination, a key advantage over solutions that require additional substances to be able to apply a code.

For vials, the unique identifier is positioned at the bottom to enable easy readability when the cameras are installed under the fill-and-finish line itself. The positioning at the bottom eliminates the need to rotate the container or to install multiple cameras, as would be the case if the code were placed on the side of the vial.

APPLICATIONS AND ADVANTAGES OF CODED CONTAINERS

Reduced Risk of Mix-Ups

The larger a pharmaceutical company's portfolio of drugs, the greater the risk of mix-ups. This can occur, for example, when the same drug is filled in different concentrations at one filling site, or when numerous steps of the process are performed at various locations, e.g. the vials are kept in storage after filling and before being finally packaged.

Currently, this risk is addressed by methods such as the use of different capping colours. However, the approach is limited by the number of cap colours available and is prone to error. A unique identifier on each container itself, applied at the very beginning of processing, ensures that pharmaceutical companies can now match each container with the right content, cap, label and secondary packaging based on the article data stored in the system (Figure 1). Hence, the content of the container can be identified at any time in the filling process.

Container-Based Targeted Recalls

A recall of pharmaceuticals can cost double-digit million-euro amounts and pose significant risks to pharmaceutical companies. Yet above all, when a recall occurs, it can put human life in danger. Hence, there is industry-wide consensus that recalls need to be handled as quickly and effectively as possible.

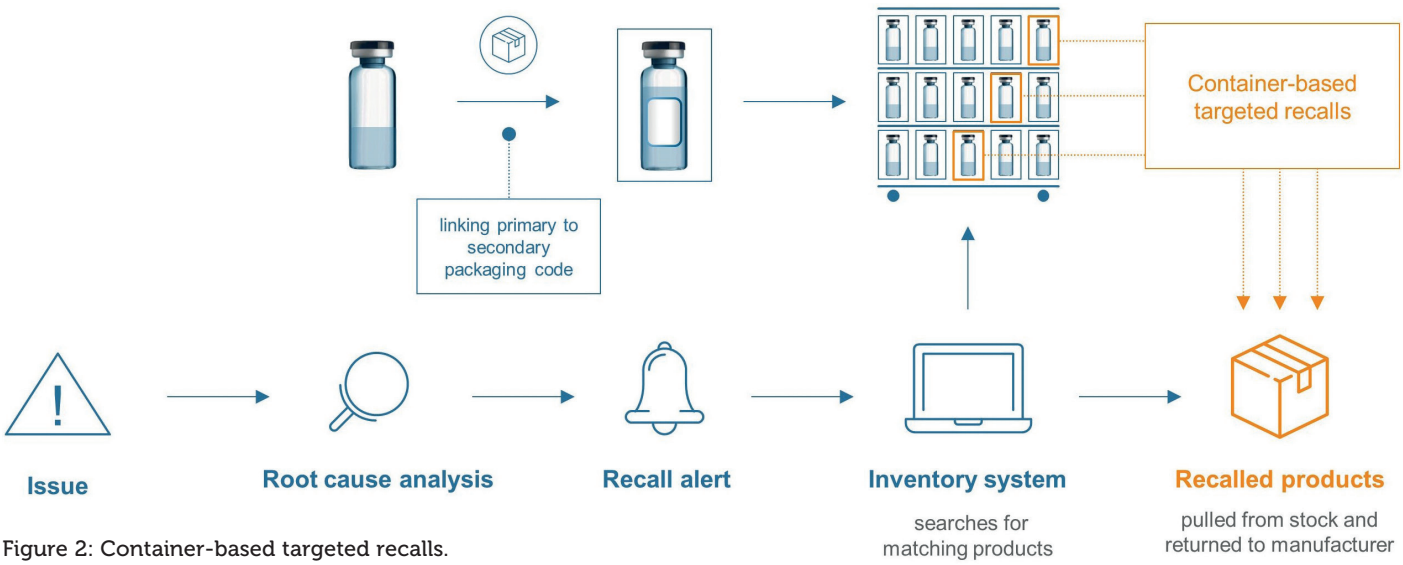

Figure 2: Container-based targeted recalls.

When each individual container is marked with a data matrix code, it can be digitally linked to the secondary packaging code to ensure product traceability at any stage of the supply chain. This can allow a container to be tracked right down to an individual pharmacy's or hospital's inventory management system. In cases when a limited assortment of batches is affected, the corresponding products can be tracked via the inventory system for secondary packaging (which is a regulatory obligation), and withdrawn from circulation (Figure 2), thus narrowing down the recall to save time and reduce costs.

Improved Reject Management and Line Clearance

After each batch production is completed, the fill-and-finish line must be "cleared" for the next batch, which means ensuring that it is free of any material related to the previous batch (e.g. vials, stoppers, caps). This line clearance procedure is mainly performed manually by the operating personnel and is highly time-intensive. However, it does not guarantee the complete removal of remains and subsequently poses a risk.

Currently available IT solutions are capable of generating data at both the beginning and at the end of the fill-and finish process. By doing so, stray containers can be identified. However, with traditional systems, the data cannot be linked to the individual container and it thus remains unclear at which stage of the process the container was lost.

The new approach, comprising laser-marked containers and cameras located at different positions on the filling line, allows each individual item to be tracked throughout the entire fill-and-finish process (Figure 3). In addition, the reason for rejection can be linked to each container in real time. Digitally tracked counts can simplify line clearance by locating the exact spot of any missing container. The increased transparency further supports the employment of corrective actions for smoother reject management and line clearance.

Lyophilisation Optimisation

In the near future, 50% of injectable drugs need to be lyophilised according to US FDA estimations.[1] For pharmaceutical companies this presents another challenge, as freeze-drying is a complex and time-consuming process. Numerous defects such as eutectic melting, cake cracking, collapse, or lifting, fogging, splashing, puffing, or "skin" formation can occur leading to unacceptable products.

It is apparent, that a stable, reliable, tightly controlled lyophilisation process is needed for commercial production. While sensors already exist that measure the temperature of the products in real time, which has the greatest potential impact on product quality, they are only used selectively and often neither the exact position nor the product quality of the vials around them can be tracked.

With sensor-tracked SCHOTT Smart Container vials, the exact position can be determined, as well as the position of surrounding vials. This then allows manufacturers and quality assurance teams to draw conclusions about the lyophilisation process and how to improve it in a timely manner.

THE FUTURE: SUPPLIER DATA ENABLES TRACEABILITY OF CONTAINER-RELATED TOPICS

While the Smart Containers concept already provides a number of advantages, it can be further enhanced in the future. For example, pharmaceutical manufacturers could receive containers that are pre-encoded with the exact information needed. This could include anything from production site, date, time as well as container-related data, e.g. article number, tubing used, quality levels, results of dimensional and cosmetic inspection.

Another option could be to aggregate the data on the label of each tray to simplify incoming inspections. Furthermore, if container-related issues during fill-and-finish occur, these could be linked to the container data received.

A SMALL CODE OFFERS HUGE POSSIBILITIES

In summary, SCHOTT Smart Containers help set the stage for Industry 4.0 in the pharmaceutical industry. The discrete, robust

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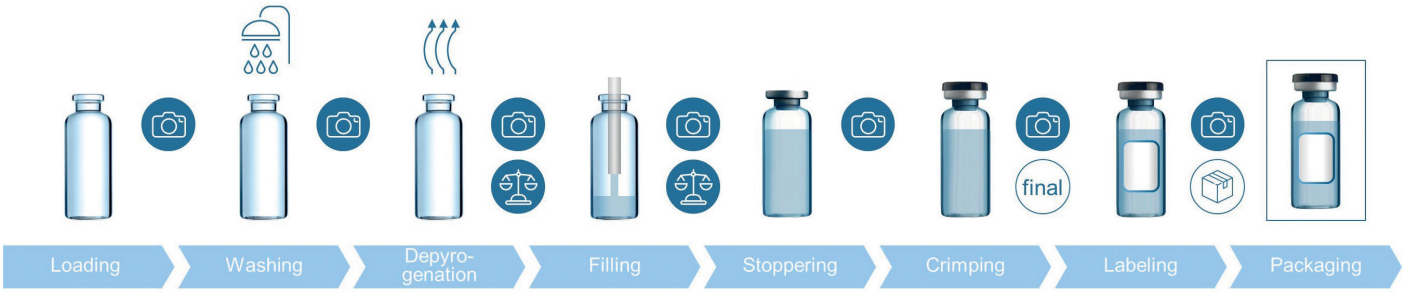

Figure 3: Laser-marked containers and cameras located at different positions on the filling line allow each individual item to be tracked throughout the fill-and-finish process.

and durable code solution that is inextricably linked to the container ensures traceability along the entire value chain. Usage on filling lines is simple and cost efficient, while it does not compromise production speed or create any additional risks. This offers vast possibilities to optimise fill-and-finish operations through improved data management on a single container basis while allowing the user to select what information to use based on the individual's needs.

ABOUT THE COMPANY

SCHOTT Pharmaceutical Systems helps people around the world protect, access and use the medicine they need as safely and conveniently as possible. As a market leader in primary packaging made of glass and polymer, SCHOTT safeguards and advances the integrity of injectable solutions and more. SCHOTT is a pioneer with unsurpassed quality, safety and reliability.

REFERENCES

1. *LaTorre-Snyder M, "Lyophilization: The basics. An overview of the lyophilization process as well as the advantages and disadvantages". Pharm Process, 2017, Vol 32(1), pp 1–2.*

ABOUT THE AUTHOR

Diana Löber started her career in the medical device industry before she came to SCHOTT in 2018. In her role as Product Manager for bulk vials, Mrs Löber is responsible for product strategy, including the identification of new market opportunities and the development and launch of innovative products.