Secondary Packaging

Creating Value with Product Life-Cycle Management

with Daniela Guttmann and Susanne Hall

Increasing regulatory requirements combined with the market pressure to develop patient-friendly drug-delivery systems make product life-cycle management (PLM) a decisive field for today's pharmaceutical and biotechnology companies. Their strategic service providers also are affected by those conditions. For example, as an internationally operating contract development and manufacturing organization (CDMO), Vetter reports an increasing number of life-cycle management projects with its customers in the past years.

Background

When incorporated into early planning, PLM can boost a product's chance for success by helping a company meet market requirements and save money. The biopharmaceutical industry is facing cost issues and is constantly under pressure to bring innovations to the market. PLM activities can help here.

Vetter's first webinar presenter is Daniela Guttmann (product and service manager), who opens with a refresher definition: "PLM is a systematic approach to managing materials that change as a product goes through design and development to its ultimate retirement or disposal," she explains. "A product is never finished; there is always something to improve on to change its functionality or make it easier to use."

The pharmaceutical industry uses PLM primarily for four reasons:

- Patient demand for user-friendly systems
- Increasing product safety requirements
- Economic pressure
- Constantly increasing regulatory requirements (serialization is a current hot topic in secondary packaging).

A Closer Look at Serialization: "*Serialization* is the application of a unique identifier to each package. **The packages' look and feel for patients has not changed much.** In practical terms, a two-dimensional (2-D) data matrix or linear code is applied and variable data inserted along with serialization numbers. This benefits the entire supply chain — and patients, too. They shall be protected from counterfeit drugs while improving transparency in a company's internal and external supply chain. That makes potential recalls easier and helps control inventory.

"For Vetter as a CDMO, serialization requires flexibility for implementing all kinds of possible regulatory and customer requirements. No global standard is yet available for implementation in terms of time lines, country requirements, methods of reporting, or product codes.

"The process aspects of serialization are multifaceted, and packaging changes lead to process changes. Implementing serialization requires addressing different technical questions. For example, how do we enable code readability with small packaging and different code-placement requirements? How do we enable serialization data to be protected and safe? And how do we adapt to emerging serialization technologies, such as radiofrequency identification (RFID) and other anticounterfeiting measures? We must consider not only about what is going on now, but also what will come in the future.

"The first big process change for many packagers in upgrading for serialization is related to information technology (IT) infrastructure. The challenge is to implement a solution that can meet all current regulatory requirements while being adaptable to your current systems. CDMOs also need to be flexible to enable different customer requirements. So in daily practice, generated reports also include commissioning and advanced shipping reports, aggregation reports, and handling reports for serialization. Service providers can generate either randomized or sequential serial numbers for their customers, then store the serialization data and even add more identification attributes.

"The second process change is manufacturing related. Decisions related to packaging lines depend on company strategy and what kinds of lines are in place, as well as what batch sizes are currently produced. Two options are applicable: mobile stations and line upgrades.

- The former includes a serialization station and an aggregation station in a stand-alone system — with reduced line speed. This is more suitable and flexible for smaller batch sizes but needs additional manpower, especially with manual packaging. A guideline: If a company is manually packing smaller batches and wants serialization now, then implement a mobile unit first.
- A packaging-line upgrade involves more time direct on the line for qualification and validation but less line-speed reduction because it's not an extra process step. This is more efficient for larger batches, and it requires no additional manpower. A guideline: If a company runs bigger batch sizes with more automation, then a line upgrade would be the adequate solution."

Challenges and Pathways

Susanne Hall is Vetter's team leader in secondary packaging. In the first part of her talk, she describes some technical challenges and operations of serialization. Then she highlights selected case studies of secondary packaging redesign activities.

"For readability," she begins, "space is needed for code printing on small packaging, with variable data and a 2-D

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data matrix code that includes all serialization information. Whether four or five rows are used, enough space is needed in the front top-left area. If there is not enough space, then printing on both sides can be considered. Maybe an uncoated section is needed for good printing quality, so that text will not blur and can be read by a camera. More space is needed for linear code, so this is one fact that needs to be considered before creating artwork. Packaging materials have their own manufacturing tolerances. When printing artwork on folding cartons, tolerances have to be considered for cutting the cartons themselves. Realizing a proper serialization process needs to make tampering obvious — in gluing the carton itself or through a tamper-evident label. That could take up space, that's why also the carton suppliers are often included into the discussion to offer other alternatives."

Safety and Convenience at the Center of All Activities: "With lyophilized vials, kit packaging is always helpful for patients. For example, a special syringe or adapter is included to provide for better handling and instruction.

"As for dual-chamber cartridges, which are already more convenient for patients than vials, they need to be assembled in pens. A pen could go into a kit along with a needle and an alcohol swab. It's very patient-friendly to have everything needed for administration in one package.

"To enable product integrity, applying a tamper-evident system is necessary. There are several options in the market (e.g., perforations or holograms). You can glue cartons together or use tamper-evident labels to protect against counterfeiting."

Case Study 1 — A Recent PLM Activity to Meet Regulatory Requirements: "Vetter supported one customer in launching a kit-packaged dual-chamber syringe internationally. The Japanese market had more stringent regulatory requirements regarding particles. So together with the customer, we had to design special blister packs for this market. A blister protects each enclosed pen against particles, and all go into the same box size, so the same machines for packaging could be used."

Case Studies 2 and 3 — Start Thinking Ahead with Your Goal in Mind: "To keep costs down, future needs have to be considered at the beginning of a project. For example, is just one filling volume needed?

"In one of our projects, the customer began with a filling volume of 0.8 mL for adults and later added 0.4-mL volumes for children. Thus a new blister tool for the smaller volume had to be designed. But Vetter was able to offer its customer a solution of making just one tool for both filling volumes sufficient. We saved the customer cost and storage area as well as tool maintenance and qualification.

"In another kit package project, there were blister trays and inserts of different sizes. The kit included paper inserts to prevent movement inside the kit, and assembly was manual. That took lot of time, and it was difficult for operators to assembly this kit, not to forget the low level of patient friendliness. So the challenge was to redesign the whole kit. All inserts were deleted, thus making it very easy for operators to assemble the kits. We redesigned the vial tray to match the blister size and redesigned the booklet to match the blisters as well, allowing for a smaller box. That saved pallet space. The results were more patient friendly and improve logistics for shipping fewer pallets to different countries. Of course users were also happy as their kits took up less space in the refrigerator."

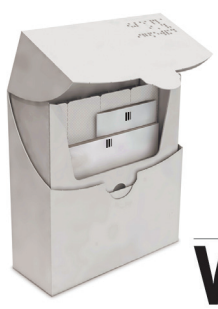
A Robust Process in Secondary Packaging: "Each new customer project starts with a complete intensive discussion about the packaging-relevant product parameters including target group, target markets, administration frequency. Then in the first step, package-material drawings and specifications are created to see what the options are. Prototype samples might be created that could include artwork if already existing. Later, we plan test runs to determine whether a kit is able to be efficiently assembled by our operators or lines. Together with the customer we create a process-development specification showing what the whole manufacturing process looks like. Parallel to development of a packaging process, we perform a risk analysis to verify and (if necessary) reduce potential risks for the product. Sometimes a further adaptation of that analysis is needed (e.g., based on test runs performed or added control systems)."

About Vetter and Its Secondary Packaging:

Vetter is a premier CDMO and global leader in the fill and finish of aseptically prefilled syringe systems, cartridges, and vials. Headquartered in Ravensburg, Germany, with facilities in Germany and the United States, the company provides state-of-the-art manufacturing, from early clinical development through commercial filling and packaging of parenteral drugs.

The company's offered drug delivery systems include vials, cartridges, syringes, tamper-evident closures such as V-OVS systems, and other versatile options for specialized manufacturing or compound requirements. Vetter's comprehensive menu of packaging services for commercial production includes assembly (e.g., of safety devices, pens, and autoinjectors); printing and labeling; blister packing and cartoning; serialization; shipping packaging and storage. All packaging options can be adapted to customer's specific needs. The company also offers specialized production technology for products with high cosmetic requirements. All packaging and filling operations comply with applicable CGMP guidelines for the US, Europe, and Japan.

Find more information online: www.vetter-pharma.com.



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