0. Summary

The last 30 years have witnessed continuous updates and innovation in the pharmaceutical packaging and drug-filling technology, especially in a sterile environment. The introduction of sterile ready-to-use syringes has been a very important breakthrough from the pharma operations’ perspective, since they allowed, de facto, the use of a new container (the pre-filled glass syringe) alongside more traditional, consolidated containers such as vials and ampoules.

The complexity of the syringe filling process, due to the absence of a container’s stable bottom and to the presence of far more components with respect to the common vials, determined a radical change in the role of the primary packaging suppliers. The main reason of this radical change is straightforward: a great deal of the process’ complexity, ie the syringes washing, the depyrogenation cycle (ie the cycle in an oven designed to eliminate agents of chemical or biological nature which, introduced into the body, cause the increase of body temperature) and the final sterilization (for syringes, typically with EtO – Ethylene Oxide) are transferred from the pharmaceutical company to the packaging manufacturer. Moreover, on the customer side, the filling process itself has been revolutionized, switching from a linear to a matrix-type filling, by exploiting the nest in which the syringes are kept in position during the transportation or the shipping.

From 2010 onward this revolution started to invest also vials and cartridges, which were first presented in a sterile format by OMPI, the only company able to process three different containers for pharmaceutical use in a ready-to-fill format. Nevertheless, this revolution lacked to address one issue: the introduction of the containers (within a steribag – the sealed box containing the sterile containers–) inside a clean room.

The most common sterilization methods, such as alcool, steam, a double layer of steribag, gamma rays or e-beam (a flow of electrons irradiating the external surface of the tray) are not always effective and/or extremely complex and expensive, and are used only in high-volume high-speed productions.

Another issue linked to sterile products is the following: an
increase in the materials used to preserve the sterility means an increase in the waste material that needs to be processed. In order to give some numbers, let it be known that the disposable packaging material for 160 syringes stored in one nest&tub amounts to two tyvek steribags, a polypropylene nest and tub, two tyvek sheets... It is easy to understand the amount of waste material needed for a whole pallet, that contains more than 200 nest&tubs.

The decontamination phase, moreover, has also an impact on the energy consumption.

Starting from these considerations, OMPI developed a new technology to transfer the sterile containers into the isolator. The starting point was the analysis of how the rubber components are inserted in the isolator: through special doors (Rapid transfer doors, RPT) that allow to connect the bag to the filling environment in a very easy way, without compromising the sterility of the environment and avoiding the decontamination of its content.

1. Project Objectives

The main goal of the EZ-Ecopack project is the development of a new packaging system capable of:

- Eliminating the decontamination phase – very expensive and impactful (energy consumption)
- Reducing the amount of packaging material while guaranteeing the sterility

The potential target customers of this project are both pharmaceutical companies and laboratories, regardless of the container type: EZ-Ecopack applies to all sterile containers in the market. This should also increase the use of flexible filling machines, capable of processing more than one type of containers, thus increasing flexibility and reducing process costs.

Waste disposal and in general the environmental impact are becoming a fundamental issue for all companies attentive to their social responsibility. Companies are looking for solutions capable of reducing the amount of waste material linked to the packaging, and a possibility to reduce the energetic consumption throughout the process.

The same standard packaging as for traditional «pallet» scheme for prefilled syringes

Ez-Ecopack:

- Same overall dimension of a traditional pallet
- Same space required than usual pallet in warehouse
- Less wastages and less costs
2. Method

A simple packaging yet revolutionary: a squared rapid transfer door (not round, as usual) and a unique bag instead of multiple bags, with separators inside to divide the layers of tubs with their content of sterile containers.

That is all we needed to avoid our customers a very complex and costly operation, the decontamination process.

OMPI started its analysis on the shape of the rapid transfer door. Round transfer doors, largely used to introduce sterile rubber components in a sterile environment without decontaminating them first, have dimensional and structural limits. But what happens if we “simply” change its shape?

A rectangular door, with round corners, proved to be the best interface to overcome the round door’s limits. As for the steribag, the almost forced solution was to design a unique bag, the same size of a pallet, capable of storing the same amount of tubs contained within a traditional pallet.

The akylux structure, already in place for the traditional packaging (and therefore not additional) was re-engineered to favour the safe housing of the steribag and its extraction, guaranteeing the safety and the protection from external agents.

The akylux box has an active role in safeguarding the steribag from cuts and losses of sterility during the transportation from the supplier’s facility to the customer and inside the warehousing facilities.

The Aseptic Transfer

Actual Method

Decontaminator

Rabs, Isolator (sterile area)

VHP, E-Beam, other

Primary Packaging need to be decontaminated before feeding inside a sterile area

Actual Rapid Transfer Port (RTP) doesn’t allow the transfer of Nest & Tub

EZ-Ecopack

A Lean Process

Steri Bigbag (sterile bag)

Rabs, Isolator (sterile area)

As for closures, no need of added decontamination process

New RTP allows the transfer of Nest & Tub inside a sterile area
3. Results

The first results demonstrate that by combining the sterile EZ-fill products with the EZ-Ecopack system the benefits obtainable by pharmaceutical companies, contract manufacturers but also laboratories and hospitals are huge.

Supplying a sterile container means eliminating the washing, depyrogenation and sterilization phases for the pharma company. Such operations need space, dedicated personnel, infrastructures… all of them costing the organization in terms of process and operating costs (in particular electricity and water for injection, WFI).

EZ-Ecopack increases the advantages for our customers because eliminates yet another delicate and costly operation, increasing the benefits for the user and in general for the environment.

4. Market and Business Opportunities

EZ-Ecopack was showcased in many trade fairs and exhibitions: it created a great interest among the industry insiders, particularly among the pharma’s heads of Operations, who immediately understood the advantages of this solution.

In particular, biotech companies see this solution as the “missing link” to introduce safely and without additional operations the sterile containers in a sterile environment.

Being a product that has a great impact on the routine of a highly-controlled and regulated industry, our implementation strategy is similar to the one applied from the pharmaceutical companies in the development of a new drug: start with a few customers, testing thoroughly the solution, in order to control for all possible risks, and then expand rapidly worldwide.

From our analysis and from our customers’ reactions we believe that also contract manufacturing organizations (CMOs) and biotech drug manufacturers will be interested in this solution: the former because of the flexibility they would earn by using a unique filling machine for three sterile products and by avoiding the acquisition of expensive decontamination machineries, whereas the latter can benefit from EZ-Ecopack’s scalability, that allows them to start with little quantities for the clinical trials and then eventually getting to large volumes in the industrial phase.
The Project Data

Project full title Sterile and Ready to fill Glass Containers with New Packaging and Connection Solutions
Project acronym EZ-ECOPACK
Contract no. ECO/11/303867/SI2.626374
Start date of the project 10/07/2012
Duration of the project 24 months
Contacts ez-ecopack.com

Partners

Ompi

Ompi is an Italian multinational company headquartered in Piombino Dese, Padua – Italy. It stands more than 60 years of history in the production of pharmaceutical glass primary packaging containers for injectable use. Its product portfolio comprises glass vials, ampoules, cartridges and syringes, both in bulk and in sterile (EZ-fill) format. Nuova Ompi is the core member of Stevanato Group, a multinational structure with manufacturing plants in Mexico, Republic and China employing over 1,500 people. Thanks to the synergy with the other group partners has a complete control over the entire production processes, from purchasing the finest raw materials up to after-sales assistance. It is the first worldwide producer of insulin cartridges for diabetics therapy.

Boursier

Established in 1980 in the heart of the Basque Country, Boursier developed from a company specialized in precision mechanics to a plastic injection moulds and products manufacturer. As a SME employing 55 people, 3 of them fully dedicated to the technical design and product development unit, Boursier has strategically chosen to integrate in its activities the whole production process, form the mould study and design to the after sale product care and maintenance services. The company flexibility and ability to respond to the specific requests of the customer has allowed to access quite different market sectors, varying from the medical and pharmaceutical industries, to geophysics and communications, with the common elements consisting in the elevated technological content and the expectation of high quality standards. These commitments are pursued through a constantly upgraded and diversified equipment, that consists in 22 injection presses (from 25 to 330 tonn) that can cover a broad range of products. Boursier is a ISO9001 certified company since 1997.

Areta

Areta was founded with private capital at the end of 1999, as a spin-off of cell biology laboratories of Lepetit Research Center. Areta works at all stages of development of biodrugs and products for innovative therapies, offering its services in the field of process optimization, manufacturing, aseptic filling, development of new analytical methods, quality control testing, batch release and stability studies, while also offering highly-qualified consultancy for quality and regulatory requirements. Areta offers its customers a GMP facility, authorized by AIFA, to produce and release biopharmaceuticals for clinical trials. In 2004, Areta has been authorized to produce cells for cell therapy, and in 2009 the authorization was extended to become truly multipurpose, enabling the company to manufacture different biodrug types (cells, proteins, immunological products, plasmids for DNA-based vaccines), as well as executive aseptic filling, final lyophilization and release of finished product. The facility and the acquired know-how allow Areta to simultaneously manage projects which are very different one from the other, both in terms of product categories and quantity of the finished product.