FLEXmag

Nov 2012 #04 The news magazine of the Technoflex Group

Focus

Terminal sterilization: crucial every time!

Design and innovation in boat ports

A new organization adapted to customer requirements

TECHNOFLEX

Editorial

Technoflex never forgets that the end users of its products are patients, and the safety of both patients and healthcare professionals remains a constant preoccupation. The last issue of Flexmag highlighted the importance of protection against particulate contamination, while this issue focuses on terminal sterilization methods. Even if customers are ultimately responsible for terminal sterilization, Technoflex takes its potential impact on our products into consideration, right from the development stage.

Concerns about safety have also prompted Technoflex to develop its own specific boat port, with a stronger weld between the bag and the connector and improved dispensing of the product to be injected that reduces the residual volume.

Finally, organizational changes have been made with a view to further improving the quality of our customer service. Customer Service has taken on new responsibilities, and two dedicated departments have been set up to respectively optimize the supply chain and formally define the multi-year continuous improvement plans.

More details on the following pages. Enjoy reading Flexmag!

Olivier Chesnoy
Chief Executive Officer

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FLEXmag, a world of connections:

FLEXmag

The Technoflex group magazine
Zone Artisanale de Bassilour
64210 BIDART – France

Web: www.technoflex.net
E-mail: flexmag@technoflex.net

Publishing Director: Olivier Chesnoy
Editor in Chief: Sylvie Ponlot
Contributors to this issue: Fabien Pruvot, Jean-Yves Bauer

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Quick facts

The boom in counterfeit products

More counterfeit medicaments are confiscated than any other product category. 68% of them come from China and, according to the World Health Organization, more than 50% of these medicaments are on offer on the Internet. This year alone, counterfeits of a famous product to treat cancer impacted 19 medical companies in the United States (source FDA). The product does not even contain the active principle. In the past, fake medicaments came mainly in the form of tablets or pills, whereas today, increasing numbers of injectable products are victims of counterfeit too. There is a fear in the United States that the numbers of counterfeit anti-cancer drugs is set to increase. The FDA, the agency that controls drugs in the United States, recently issued a warning against the appearance of unauthorized products on the market and called for greater vigilance.

An unprecedented association

Ten pharmaceuticals companies[1] recently grouped together to form the "TransCelerate BioPharma" non-profit organization. The purpose of this organization is to improve the quality of clinical research and to make new and innovative medicaments available to patients more quickly. "TransCelerate BioPharma's mission is to work together in the field of R&D and to pool the results of our research and our solutions in order to simplify and speed up the release of new medicaments that are of significant interest to patients", declared Garry Neil, interim CEO of the new organization.

[1] Abbott, AstraZeneca, Boehringer Ingelheim, Bristol-Myers Squibb, Eli Lilly and Company, GlaxoSmithKline, Johnson & Johnson, Pfizer, Roche and Sanofi

Access to healthcare for all in India

Last August, Indian Health Minister, Manmohan Singh, looked into the possibility of setting up a means-tested system to establish reference prices for medicines. The system could cut the bill for certain products by one third. The retail price would then be adjusted to the user's income. This calculation would only apply if there is no therapeutic alternative to the medicament in question. At the same time, the Indian government is looking into the possibility of providing generic medicaments for patients in public hospitals free of charge. These measures reflect the wish to broaden access to medicine in countries like India, where 79% of patients pay for their own healthcare, one of the highest ratios in the world.

Schedule

November 14 to 16 2012

COMPAMED

Compamed International Trade Fair

Düsseldorf, Germany - Hall 8B Stand G10A

- The international forum for innovative solution providers in the pharmaceuticals industry.

November 21 to 23 2012

iCSE pharma contract services

CPhI India Bombay Exhibition Centre

Mumbai , India - Hall 2 Stand Q2

- With 825 exhibitors from 21 countries and more than 27,000 visitors from 96 countries, CPhI is the major event in the pharmaceuticals industry in south Asia.

February 13 and 14 2013

Pharmapack EUROPE

Pharmapack Europe

Grande Halle de la Villette - Paris , France - Stand 350

- Putting patients at the heart of innovation.

Manmohan Singh
Indian Health Minister

Terminal sterilization: crucial every time!

SP. Jean-Yves Bauer

Sterility is the absolute criterion of an injectable product. Pathogenic elements are neutralized essentially by exposure to heat [1]. Autoclave terminal sterilization is essential for the safety of patients and does not allow the slightest error. A look at the risks and best practices.

The lack of knowledge of the polymers that make up the bags or connectors can result in burst or deformed bags, damage to the twist-off or a milky appearance during terminal sterilization. But these problems can be avoided. How? First, by gaining a better understanding of the molecules' resistance to heat, and by using sterilization methods that are adapted to the contents. But also through the perfect command of the sterilization cycle, from the temperature and the length of the cycle phases, to the pressure, the volume and shape of the bags to be sterilized, the number of bags in each load, etc.

PVC bags with over-wrap may turn white when terminal sterilization takes place in a spray or stream autoclave. This occurs when the vapor works its way between the macromolecules that make up the material. The only alternative is an air-vapor autoclave with ventilation that cools down the load.

The solution itself represents another threat. When the solution is exposed to heat, it expands and applies pressure to the walls of the bag. This pressure results in deformation that can sometimes cause the bag to burst. Regulating the pressure inside the autoclave can solve this problem.

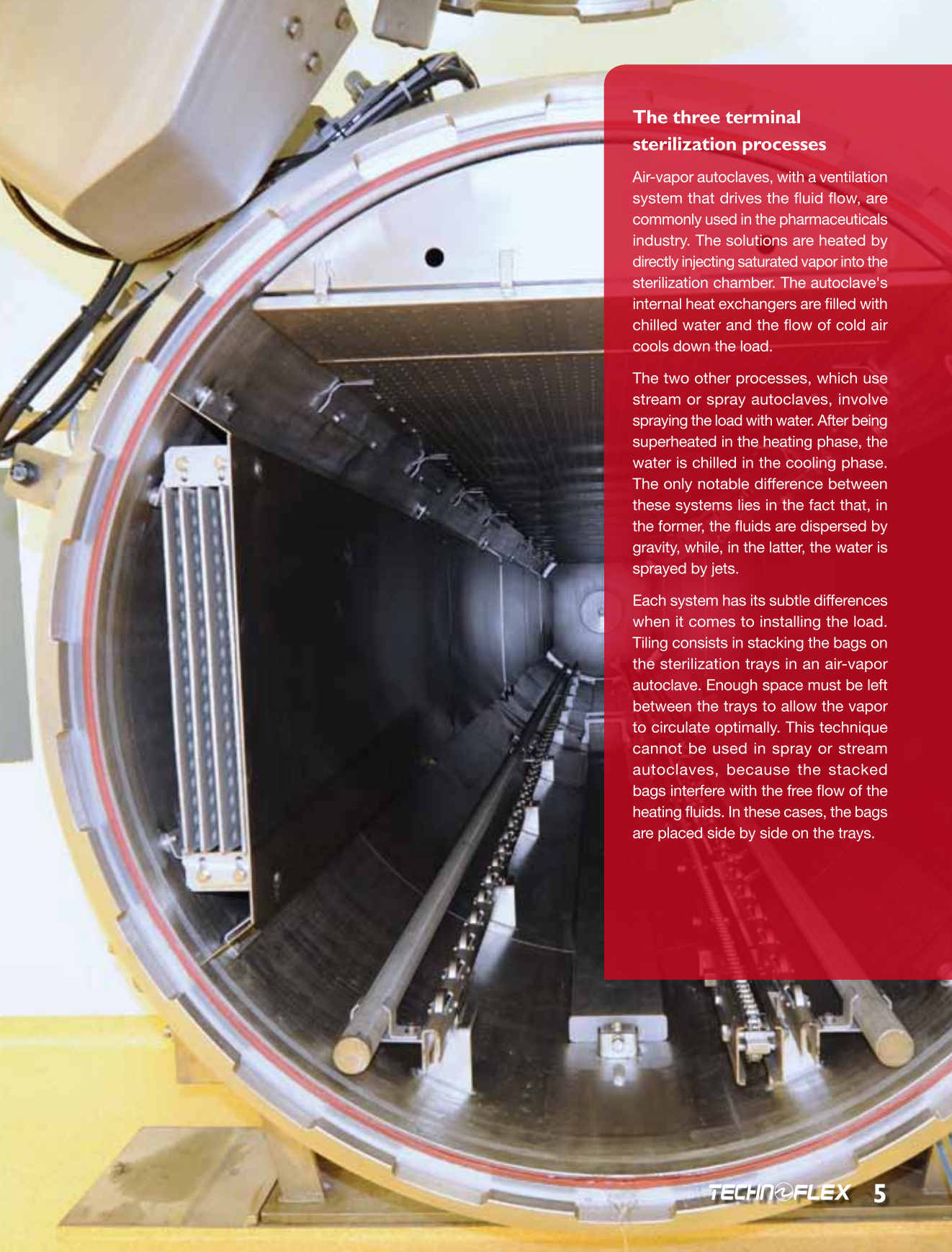
And when it comes to the temperature, each material has its own limits. Polypropylene bags must not be heated to more than 125°C, while the limit for PVC bags is just 122°C.

There are also a few special cases. Proteins that do not tolerate severe heat, such as albumin, must be pasteurized. In this case, stream autoclaves are used to expose the solution to a temperature of 60°C for about 10 hours.

Sterilization is a critical process in the pharmaceuticals industry that demands in-depth knowledge of all the parameters in play. Technoflex inspects and tests its bags under the real-life conditions of use of the products. Strict monitoring and regular checks of the autoclaves are also necessary. All new appliances must undergo initial qualification, or retrospective qualification for autoclaves that are already routinely used [2]. The conformity, quality and safety of the injectable products depend on it.

[1] Apart from molecules that do not tolerate heat and are conditioned in aseptic media

[2] GMP recommendations, Chapters 3 and 4 - § 4.26 & 4.28



The three terminal sterilization processes

Air-vapor autoclaves, with a ventilation system that drives the fluid flow, are commonly used in the pharmaceuticals industry. The solutions are heated by directly injecting saturated vapor into the sterilization chamber. The autoclave's internal heat exchangers are filled with chilled water and the flow of cold air cools down the load.

The two other processes, which use stream or spray autoclaves, involve spraying the load with water. After being superheated in the heating phase, the water is chilled in the cooling phase. The only notable difference between these systems lies in the fact that, in the former, the fluids are dispersed by gravity, while, in the latter, the water is sprayed by jets.

Each system has its subtle differences when it comes to installing the load. Tiling consists in stacking the bags on the sterilization trays in an air-vapor autoclave. Enough space must be left between the trays to allow the vapor to circulate optimally. This technique cannot be used in spray or stream autoclaves, because the stacked bags interfere with the free flow of the heating fluids. In these cases, the bags are placed side by side on the trays.

Design and innovation in boat ports

Sylvie Ponlot

Patients are exposed to a number of potential risks when undergoing IV therapy, from under or overdoses, to gas embolism and infection. Installing a drip may be a common, everyday practice, but it remains crucially important due to the risks inherent in the therapeutic operation and its impact on the administration of active principles. The success of an IV drip depends on both the caregiver's know-how and the equipment, which must be reliable and easy to use.

Technical incidents include the discovery of tears between the tubes of an injection bag when unpacking the equipment. Tearing usually occurs when the tube becomes stuck to the over-wrap during sterilization. The boat port developed by Technoflex is fitted with vanes inside the bag weld that prevent this type of problem by optimizing resistance to tearing.

And this coupling connector is just as supple as the tubes that are traditionally used. The elastic return allows the tubular part to be clamped, when necessary, without reducing the flow of the solution, once the clamp has been removed.

Finally, the internal reinforcers of the boat port are fitted with side channels that allow all the solution to be administered, without any residual volume. This important benefit means that caregivers can be sure that the complete prescribed dose has been administered.

Fabien Pruvot,
Project Development Manager

Sylvie Ponlot : *Fabien, you were part of the team that designed and developed the boat port. What were your priorities?*

Fabien Pruvot : We were guided by a number of priorities: reinforcing the fragile zones of bags with two tubes, facilitating the flow of all of the injectable solution, reducing risks of leakage and contamination at the weld between the bag and the tubes, etc. And they all served the same objective: improving the use of the bags and protecting the patient's safety, Technoflex's permanent priorities.

SP : *Is it a long haul from the idea to industrial production?*

FP : The first version was ready in 2009, but it required additional operations that we were not happy with. So we developed the product further. It took 3 more years to develop the definitive version that went into industrial production. We also decided to develop a long version for aseptic applications.

SP : *Does the use of the boat port involve any major changes for customers?*

FP : No, none at all! The diameter of the tubular section is identical to that of the usual tubes. This means that conventional connectors and the connectors in Technoflex's range can be inserted. Our customers also appreciate the fact that the boat port is made of the same material as the tube. Consequently, the stability studies required to check compatibility with the medicament are simplified, as is the amendment of the authorization to market.

SP : Is it only available in one material?

FP : This is true of the standard range. But we have already worked on other formulations for the boat port. This has helped us to make faster progress on a project for one of our customers with special needs. A project that has already been completed! Obviously, we offer the standard ranges, but we can also adapt to our customers' needs by proposing made-to-measure formulations. This is one of Technoflex's strengths.

SP : Does the replacement of the tube with the boat port impact the filling process?

FP : The impact is strictly positive! Since the boat port is an injected part, its geometry is perfectly controlled, the edges are straight and the diameter is precise. These benefits mean that the bags can be filled and automatically closed very quickly (aseptic or otherwise). When filling manually, the collar on the tubular part allows the bag to be held comfortably by the operator when inserting the twist-off.

Open day at Technoflex

Technoflex organized an open day for its employees' families on July 20. Almost 150 people took this opportunity to learn more about the company. The tour itineraries, which featured photos of the company employees, were designed to allow these very special guests to discover and understand the environment in which their loved ones work, the workings of the production plants, life at the company and the products manufactured by Technoflex. A number of interactive workshops, from dressing procedures or washing your hands before entering the clean room, were also organized to illustrate the regulatory standards that govern everyday work at Technoflex.

A new organization adapted to customer requirements

Sylvie Ponlot

Biomedicaments, more stringent regulatory standards and the rise of generics are causing some deep-seated changes in the world of pharmaceuticals. And these changes inevitably impact the entire production chain of healthcare products. In an effort to stay one step ahead of the needs of its international clientele, and to better meet its requirements, Technoflex has introduced some organizational changes.

Xavier Erguy
Continuous Improvement

Evelyne Sabatou
Supply Chain

A new **Continuous Improvement** department has been set up as part of Manufacturing. In addition to addressing the usual issues of performance and reactivity, this new department will also develop cross-functional solutions to permanently optimize processes.

The strategically important **Supply Chain** function has been reinforced. It now coordinates and centralizes the data and actions pertaining to orders, from procurement and production orders to shipments. Supply Chain works very closely with **Customer Service** in order to respond effectively to the fast-changing demands of Technoflex's customers.

Marie Anna Curutcharry
Customer Service

The deployment of these new resources illustrates Technoflex's ambition to stay one step ahead of a changing market and to further improve the quality of service delivered to its customers.