FLEX mag

December 2014 #08 The news magazine of the Technoflex Group

Focus

The shared objective of ongoing improvement

Business :
A chronic shortage of injectable drugs

Perspectives :
The Argentine pharmaceutical industry boom

TECHNOFLEX

Editorial

The permanent availability of drugs is an emblematic feature of access to healthcare, and yet it is shrouded in uncertainty – and not only in the developing countries, as you might easily be led to believe. The developed countries are far from immune to shortage issues, as recent situations have highlighted, including on the American market. In the latter case, the FDA says that 80% of stock-outs are for injectable products: this is a topic of particular concern to us, as you will see in this issue of Flexmag.

To offer a contrast with the winter season in the northern hemisphere, Flexmag also takes you to South America, and more specifically Argentina, a country that is enjoying a certain dynamism and is looking to significantly develop its position in the healthcare market. Particular effort is being made the highly promising biotech sector, with the stated ambition of establishing a foothold in the field of monoclonal antibodies.

Lastly, we present one of the flagship projects set up recently at Technoflex: while the initial quality of our products and processes is subject to very close attention as early as the design phase, the job doesn't stop there. An ongoing improvement procedure has been engaged by our teams, starting at the production stage, in order to ensure regular optimisation of our quality and customer service, efficiency, simplification, and the working environment for the people who manufacture the bags and connectors we produce for you. You can find out about this procedure in our Focus.

Lastly, as this issue N° 8 of Flexmag is being published in December, we would like to take the opportunity to wish you all an **Outstanding 2015**, both personally for each of our readers and their friends and family, and professionally for all our partners. Season's Greetings to all of you from the Technoflex team!

Happy reading!

Olivier Chesnoy
Chief Executive Officer

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Frontpage picture:
Xavier Erguy, Ongoing Improvement Manager, in front of his "Ideas Table"

FLEXmag

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Quick facts

South Korea, the new stem cell El Dorado:

Strongly supported by the government, Pangyo Techno Valley is a cluster dedicated to research. The research undertaken by its universities, laboratories and biotech firms has one point in common: embryonic stem cells. In 2012, no fewer than 45 clinical trials were authorised by the government in the field of cell regeneration. This cluster includes the ChaBiotech Centre, which now contains the country's largest stem cell bank.

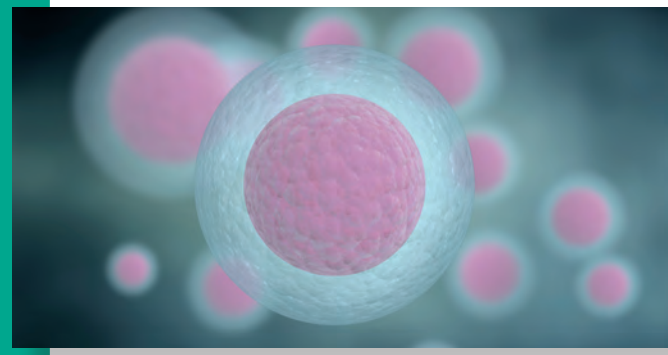
Towards quicker accreditation for generics:

A pilot programme initiated by Brussels is looking to set up an international generics regulation committee. The aim is for its members *(European Union, Australia, Canada, Taiwan and Switzerland)* to share their data on generic drugs in real time so as to accelerate the approval process. The programme could then go on to host organisations from other countries, such as Korea, New Zealand, Russia and Japan.

Creation of a "biobank":

Pluripotent stem cells *(PSC)* are now used to develop numerous medicines. However, in the scientific community there is a distinct lack of cells for the necessary trials, in terms of both quantity and quality. The creation of this European "biobank"1in Germany should help fill this gap, providing readily available "ready-to-use" stem cells. Around 1000 types of cell lines2could be used in this way to produce about a hundred million cells over the next three years.

[1] Association of the Fraunhofer Institute for biomedical techniques and 26 partners
[2] Cell lines are "immortal" cells that can be maintained in culture indefinitely.



Schedule

1st quarter 2015	Show / Venue	Technoflex Booth
February 11th & 12th	Pharmapack EUROPE Paris Expo, Porte de Versailles	Hall 5 Booth 650

The shared objective of ongoing improvement

Sylvie Ponlot

Keeping full control over a product means mastery of the manufacturing process. Like any industrial firm, Technoflex controls all the complex production techniques used, right from the origin of the product. But we also have to make sure that our processes progress constantly, and must adapt them to any new constraints that emerge. This is where the ongoing improvement procedure comes in. Set up three years ago, it is under the responsibility of an expert from the Industrial Department, Xavier Erguy.

He is like a conductor directing several orchestras at once. His roles range from practical organisation in clean rooms to the implementation of acknowledged methods of industrial optimisation. Xavier mentions the action plan carried out with regard to the position of product bins in the production workshops: they used to be arranged directly around the machines. Discussions held between the production cell manager, the operators and the technician showed that this theoretically *"logical"* system actually resulted in extra operations and thus time-wasting, and created unexpected difficulties for those concerned. After reflection with the teams, the area was completely reorganised. As a result there are fewer operations, more working space and a calmer, more efficient environment!

Another participative procedure is the "5S" method. At Technoflex it is applied by taking full account of the quality requirements of the products manufactured and the teams involved.

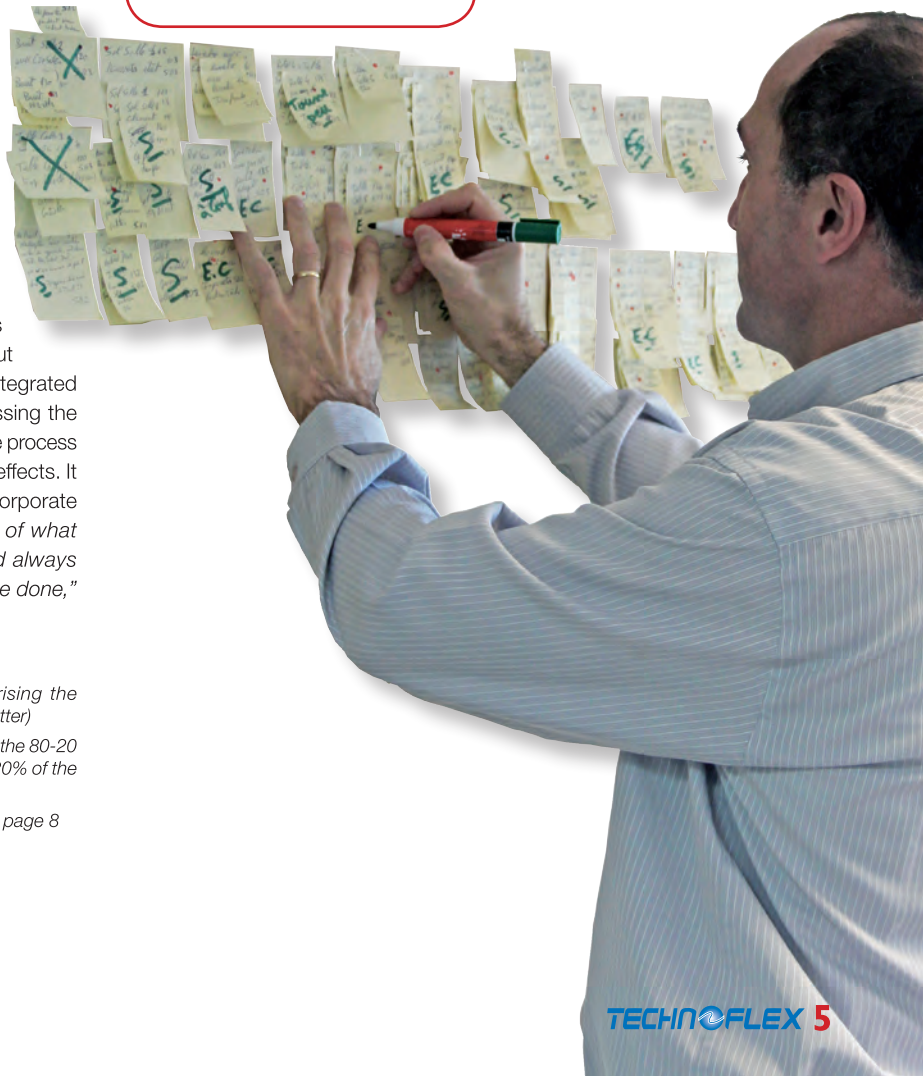
In any improvement campaign, solutions can only be provided after a study of the initial situation by the people directly concerned. Each person's working conditions, visual communication and ideas must be taken on board. In this particular case the storage of raw materials, their visibility and position and physical flows were thus reorganised. "*The order, storage methods, cleanliness and visual organisation recommended by the "5S" method allow us to build a functional working environment*", indicates Xavier. "*And it's all the more important for us because we work in shifts!*"

Unlike disruptive improvement, which involves a completely fresh start *(new equipment, new technology)*, the Kaizen [1] method used by Technoflex advocates continuous analysis.

In line with the company's regulated framework, it is a mind-set that Xavier promotes on a daily basis. *"I use widely acknowledged principles and methods –PDCA, 5M, Pareto [2] – and have adopted a Lean management vision"*, he says, *"in other words the quest for performance by eliminating waste. Along with Jennifer Hitte [3], our Safety and Environment Coordinator, we also promote awareness among our teams about waste treatment, pollution and energy consumption."* The target is to adapt to the working environment and to in-house needs, and to be responsive to all the teams and involve them in a shared objective.

Planning, performance, measurement and improvement are the four phases of ongoing improvement. But this procedure cannot be integrated by itself. It is only by harnessing the strengths of each player in the process that it can really produce its effects. It then becomes part of the corporate culture. *"We can be proud of what we've achieved, but should always be aware of what is still to be done,"* concludes Xavier Erguy.

In order to improve the quality of our production, we use the Lean method. This method requires the use of various tools, including the "5M" to identify the possible causes of a problem, the "5S" to create a functional working environment, and the Deming Wheel *(Plan-Do-Check-Adjust)* to organise production, until the expected standard is achieved.



[1] Japanese expression comprising the words Kai (change) and Zen (better)

[2] Pareto Principle, also known as the 80-20 rule (80% of effects come from 20% of the causes)

[3] Interview with Jennifer Hitte on page 8

A chronic shortage of injectable drugs

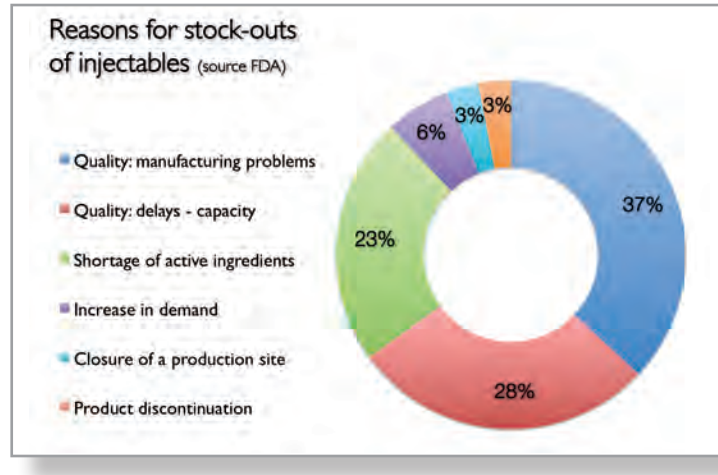
Sylvie Ponlot

Delayed surgery and suspended clinical treatments are among the dramatic consequences of an issue that has become widespread over the last few years: a shortage of injectable drugs. Faced with ever-increasing demand, producers of indispensable drugs [1] are having trouble keeping up. Numerous supply tensions have resulted at global level.

Production difficulties and, on occasion, natural disasters *(protamine, which is produced from extracts of salmon fished off the Japanese coast, is no longer usable due to the Fukushima disaster)* are two of the many factors responsible for this worldwide phenomenon. But management of these crucial products, particularly the supply chain policies of hospitals, also has an impact. In order to bring down costs, hospital Purchasing Groups put out calls for tender for their drugs *(including injectables)*. The contract is awarded to a single supplier for a period of around three years. While financially this strategy pays off, the downside is a risky one. The system encourages suppliers to break the contract or simply cease production due to lack of profitability. If the supplier fails in its commitments, the hospital is left high and dry.

The time required for healthcare products to receive official approval exacerbates the situation. Taking several years, this process lengthens the time to market for drugs that could be replaced. Another damaging aspect is the externalisation of production of pharmaceutical active ingredients.

Whereas 80% of these raw materials were manufactured in Europe thirty years ago, the trend has now been reversed. Mostly concentrated in Asia, these manufacturing sites make controls more complex due to the distance, and there are inevitable repercussions on the overall chain.



To counter these risks of shortages, industrial firms build up strategic stocks or implement dual sourcing. The same cannot be said of healthcare establishments. Forcing them to ration essential medication, stock-outs put their patients in serious danger *(development of illnesses, longer hospitalisation, deaths, etc.)*.

What measures could reduce the number and severity of shortages? The example of Australia could be adopted, whereby single-supplier sourcing contracts are prohibited. Referencing of other suppliers and allowing replacement options. Similarly, a system of collaboration between the regulatory bodies would speed up accreditations and the replacement of certain products. While industrial groups have a key role to play in the prevention and management of stock-outs by reporting any failures in a timely manner, only a system in which information is shared internationally between health authorities, hospitals and laboratories would substantially scale back a problem that blights the world health system.

[1] Oncology, anti-infectives, cardio-vascular diseases, the central nervous system and pain relief are the five therapeutic areas most affected.

Sources: FDA; ASCO (American Society of Clinical Oncology); LEEM; WHO; IMS; British Medical Journal

Perspectives

The Argentine pharmaceutical industry boom

During the 1990s, many pharmaceutical firms were attracted by Argentina and its low production costs, enabling them to dominate the local market. Since the turn of the century, however, with the arrival of generics, the trend has been reversed. National firms have reconquered the domestic market and 70% of the drugs consumed in Argentina today are produced in the country.

Argentina currently has over 200 pharmaceutical firms accounting for turnover of €3.3 billion in 2013, against €2.5 billion in 2012. The Argentine market boasts growth of 23%, ranking it second behind Venezuela and way ahead of Brazil. Argentina was one of the first countries in South America to implement the WHO guidelines on GMPs and inspection standards, a step which now makes it an attractive destination for clinical trials.

Biotechnologies are not lagging behind, either, with over a hundred firms in the sector, 93% of which are domestic. In 2013, the country presented its research into skin regeneration and recombinant protein development. Argentina is innovating and expects to inaugurate a plant this year dedicated to production of monoclonal antibodies for the treatment of cancer and auto-immune diseases. This production plant, the fruit of a public-private partnership, will be the first of its kind in Latin America.

A few obstacles remain to be overcome, however, such as the level of Research and Development investments. They need to be boosted to increase the country's ability to produce innovative molecules. Finally, the capacities of local production plants, which currently are not enough to compete with those of Chinese or Indian manufacturers, must be increased. Such steps will enable Argentina to pursue its development and increase its competitiveness in the face of multinational pharmaceutical firms.

Sources: UBI France; Bulletins électroniques; IMS Health; Reuters

The major concern of Safety and Environment

Sylvie Ponlot: Jennifer, for the last year you have been Safety and Environment Coordinator. What exactly does your job consist of?

Jennifer Hitte : My job covers two distinct areas. First of all, I have to ensure the safety of Technoflex employees at their work-stations, whether in production or in the offices. The majority of my time is spent in the warehouses and in the bag and connector production area. In addition, I am also responsible for the environmental side of things.

SP: How do you ensure the safety of Technoflex employees?

JH : As operators of a facility, we are responsible for carrying out all the statutory checks on the on-site equipment, and that makes a long list! We check the electrical installations, hoisting equipment, machines, pressure vessels and fire safety system. Safety training courses are organised throughout the year, for example on autoclave operation or electrical qualifications. A prevention plan has been implemented covering risks related to the facilities, activities and equipment. There are also rules governing all the technical operations on machines or the cleaning of clean rooms.

SP: What about the environmental aspect?

JH : By its business in plastics processing and storage, Technoflex is what is called a Classified Installation for the Protection of the Environment *(ICPE)*. It can generate risks of accidents which could be detrimental to people or the natural environment. There are therefore operating rules to be observed and we must ensure that they are complied with.

SP: Such as, precisely?

JH : The bags, for example, are tested and undergo autoclave sterilisation. The water used is then treated by filtration before being discharged. Every six months, we check and analyse the wastewater and ground water.

Then there is the waste classified as dangerous by the regulations that is carefully monitored. It is listed by quantity, by category and according to the recycling or disposal method. Some waste is used for energy production, such as organic solvent or laboratory waste. Other forms, such as acids, are destroyed. Finally, the neon tubes and batteries are recycled.

SP: What are the consequences of non-compliance with these technical requirements?

JH : In the best-case scenario, we would be sent a formal order to solve the problem within an allotted time. If we were to fail to do so or if the situation should recur, the consequences would be more serious, such as a suspension of the authorisation to operate, which would effectively shut down Technoflex. However, we work on the basis that the primary purpose of these requirements is to guarantee the safety of our staff and our environment, so there can be no question of not complying with them!

Jennifer Hitte,
Safety and Environment Coordinator

SP: Do you have other responsibilities?

JH : Since July, I have been a "qualified employee" in occupational risk prevention. I regularly take part in meetings of the Health, Safety and Working Conditions Committee where we pursue our objective of ongoing improvement. For example, we have achieved extremely positive results in the ergonomics of the various work-stations thanks to the efforts of Xavier Erguy, our Ongoing Improvement Manager, and a consultant ergonomist.