FLEXmag

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June 2019

The Technoflex group news magazine

LASA drugs under high surveillance

All change in Technoflex connectors department!

Unprecedented clinical trials in Japan

Editorial

Olivier Chesnoy
President & CEO

Since the first medical perfusions in the middle of the 19th century, injectable drugs have more than proved their worth. Whether under patent or generic, they now play an essential role in modern therapeutics. As with all active products, they can have side effects and should therefore be used carefully and wisely. But beyond the side effects inherent in their therapeutic properties, it is sometimes forgotten that factors quite independent of the molecules themselves can also present a risk. With the multiplication of presentations and brands, many of them for example with similar-sounding names and similar appearances are found together in hospital pharmacies. In the English-speaking world, they are referred to as "look-alike" and "sound-alike drugs". These additional risks are the subject of much debate and discussion: learn about them in our Focus section.

On the other side of the world, in the land of the rising sun, gene therapies are progressing rapidly and accumulating exploits in this area. Stem cells are more than ever the main focus, as testified by the latest Japanese clinical trial that is underway. A first, which you can read about in our "Prospects" section.

Finally, the Business and Profiles sections will unveil the major developments in our connectors department. This is a major cornerstone of our business, both for supplying customers directly, or for use with our bags, and is undergoing tremendous change. Expansion, reorganization and new equipment, as well as new executive staff with the arrival of a new production manager, whom we will be introducing to you.

Happy reading!

Flexmag, a world of connections

Flexmag

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Quick facts

Explosion in counterfeit drugs

In five years, incidents involving fake drugs have increased by 60%. Benefiting greatly from online sales, the traffic in counterfeit products is today estimated to be worth $200 billion and represents 20% of the global pharmaceutical market. Although the European States calculate fiscal losses due to this illegal market at more than €1.5 billion, it is the African countries that pay the heaviest price. Almost seven in ten drugs are counterfeit or of lower quality and are directly involved in the deaths of hundreds of thousands of people.

More effective than ever!

A trailblazer in this area, Rwanda has enlarged its fleet of drones[1]. The new devices will deliver loads of 1.7 kilograms and can cover 160 km at a speed of 101 km/h. Their fixed wing allows them to fly at high altitude even in bad weather conditions. Since 2016, 4,000 flights have delivered 7,000 bags of blood!

[1] *Flexmag 12 – The new allies in health care*

Dr Nteziryayo waiting for drug delivery by drones

Agenda

3rd & 4th quarter 2019

Healthcare Packaging Expo	September 23–25	United States, Las Vegas, NV Convention Center	Healthcare+ PACKAGING EXPO	**Booth N-305**
AABB	October 19–22	United States, San Antonio, TX Henry B. Gonzáles Convention Center	AABB 19 SAN ANTONIO	**Stand 518**
Innopack Worldwide	November 5–7	Germany, Frankfort Messe Frankfurt	2019 ISCT melbourne MAY 29–JUNE 1	**Hall 11 Level 1 Booth B20**
ISBT	November 16–19	Thailand, Bangkok Central World Convention Center		*Pending*
CPhI India	November 26–28	India, Delhi India Expo Mart, Greater Noida	CPhI india	*Pending*

Events listing available at www.technoflex.net

Focus

LASA drugs under high surveillance

The greater the number of steps involved in preparing a drug, the higher the risks. This is the case for injectables which have a wide range of applications. They are used in anesthesia, intensive care, chemotherapy, nutrition, and antibiotic therapy. Taking the administration route used into account, they require care and vigilance through to administration and demand increased surveillance when the prescription involves drugs referred to as Look-Alike and/or Sound-Alike drugs (LASA).

Sylvie Ponlot

At the end of the 1960s, only around ten products were affected by such similarities, whether visual *(Look-Alike)* or phonetic *(Sound-Alike)*. This resemblance is found in the name, the shape or the packaging. Today, the number of pairs or trios of LASA drugs is estimated at more than 3,000. The main factor responsible? The decline in patents. It has triggered the arrival of many generic drugs with similar names and the same active principle. This is particularly the case for anti-infective agents. The confusion causes many accidents with potentially fatal consequences, as they sometimes involve dangerous substances such as powerful tranquillizers or anticancer drugs.

LASA drugs alone account for a quarter of the drug-related errors reported in the United States. To reduce their impact on patient safety, multiple measures have been undertaken. First of all, the first critical step of reading the prescription when it is handwritten, is gradually being computerized. It contains precise, important information about the drug and its preparation. Concentration, dose, diluent, speed of perfusion, all information essential to avoid confusion, to safeguard reconstitution in the hospital pharmacy and administration to the patient. Still in the hospital environment, numerous recommendations have been drafted. Among other things, they recommend not buying several generic drugs with the same active principle, as well as better organization of injectables storage by separating dangerous products from the rest or additional labelling to better identify them.

Another concrete preventive action relates to the drug typography used on primary and secondary packaging. Alternate cases, lower case and capitals, have been used to better identify the different syllables. The use of capital letters has noticeably improved the legibility of the product name. More recently in the United States, the Institute for Safe Medication Practices *(ISMP)* has gone further.

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It now recommends enhancing visibility by incorporating bold characters: **LOOK-**Alike & **SOUND-**Alike.

Regulations and packaging, solutions exist

Many government bodies such as the ANSM or the FDA have published a list of all LASA drugs. It is updated regularly, but it is difficult, even impossible, to standardize these lists at international level as many pharmaceutical products have different names in the different countries where they are marketed. Still from a regulatory perspective, it is possible to act upstream, particularly before granting a marketing authorization. When filing an application, a commercial name which is not similar to a product that already exists could be required under penalty of refusal of approval.

Regarding packaging, another solution is conceivable and is easily carried out: the attribution of a color code per product category that would be visible on the primary and secondary packaging. In the case of injectable drugs packaged in flexible bags, administration ports such as twist-off or luer-lock ports could display specific colors *(blue, red, green, etc.)* according to product. For the other formulations, the color would appear on the secondary packaging and the product label.

Many avenues for improvement may therefore be envisaged to reduce the risk of errors associated with Look-Alike and Sound-Alike drugs. But to implement them, only international collaboration between the pharmaceutical industry, packaging manufacturers, regulatory bodies and final users would remove the remaining barriers.

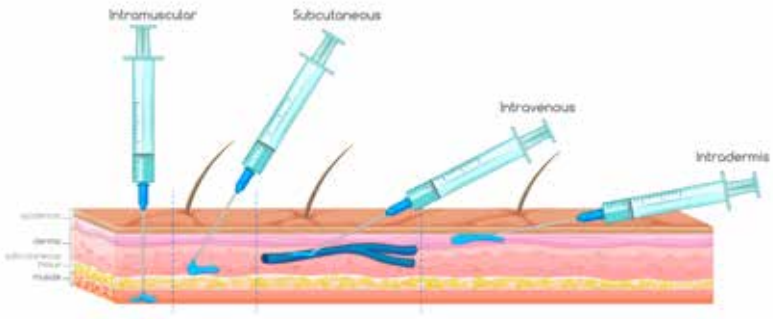
4 injection methods, 4 levels of action

Intradermal injection is generally used during vaccination or allergy sensitivity tests. It is performed using a short needle around 1.5 centimeters long.

Subcutaneous injection reaches the tissue located under the skin, superficial to the muscles. It is suited to products which should be absorbed more slowly such as analgesics and some antibiotics.

There is then the intramuscular, or IM injection. It is an alternative and rapid administration route. The muscles, with a profuse blood supply, absorb the active principle more quickly, allowing it to act just as quickly. The intravenous route bypasses the absorption barrier.

The product is injected directly into the circulatory system and its action is practically instantaneous. Finally, we speak of a bolus when the drug must be injected in a single solitary dose. Rapid and speedy, it is administered by continuous intravenous perfusion, which acts as a drug vehicle.



All change in Technoflex connectors department!

The regulations governing the activities of the pharmaceutical industry are constantly changing and are ever more rigorous, as anticipated by Technoflex. Over the last ten years, the company has made many investments which allow it to offer new-generation connectors adapted to the requirements of pharma companies.

Sylvie Ponlot

The connectors department is a hive of activity, operating 24/7 with machines which are only shut down once a year for maintenance operations. It is composed of two distinct zones, injection and assembly. The first project stream involved the plastic injection division with the installation of new injection molding machines. Six of these are entirely electric and perfectly suited to use in clean rooms. They handle high-speed operation with ease, while improving the work environment for our teams by reducing noise rating technological innovation at the center of levels. Another area of improvement, incorporating technological innovation at the center of our quality approach: conformity checks, checks of appearance or counting and sorting, the automatic vision feature detects potential defects in the assembled products. Installed on the assembly machines, the inspection camera scrutinizes the twist-off, injection site and other components. It performs faster and more reliably in repetitive tasks, freeing staff from tedious manual inspections.

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A new zone commissioned!

After several months of work, the plastic injection zone clean rooms extension has just been commissioned. Adding a surface area of one hundred and seventy square meters, it now brings the total surface area devoted to the production and assembly of connectors to more than 1,600 m^2. This new Controlled Atmosphere Area *(CAA)* recently welcomed four new hydraulic injection molding machines weighing between 80 and 150 tons. The greater the volume to be injected, and the larger the mold cavity, the higher the clamping force required. This determines the tonnage of the molding machine. These investments now allow the production of more complex connectors, that are still as innovative.

This new high-tech, diversified equipment ensures production at industrial speeds meeting the demands of our customers, whether these are pharmaceutical or biotechnological. And further equipment items are planned!

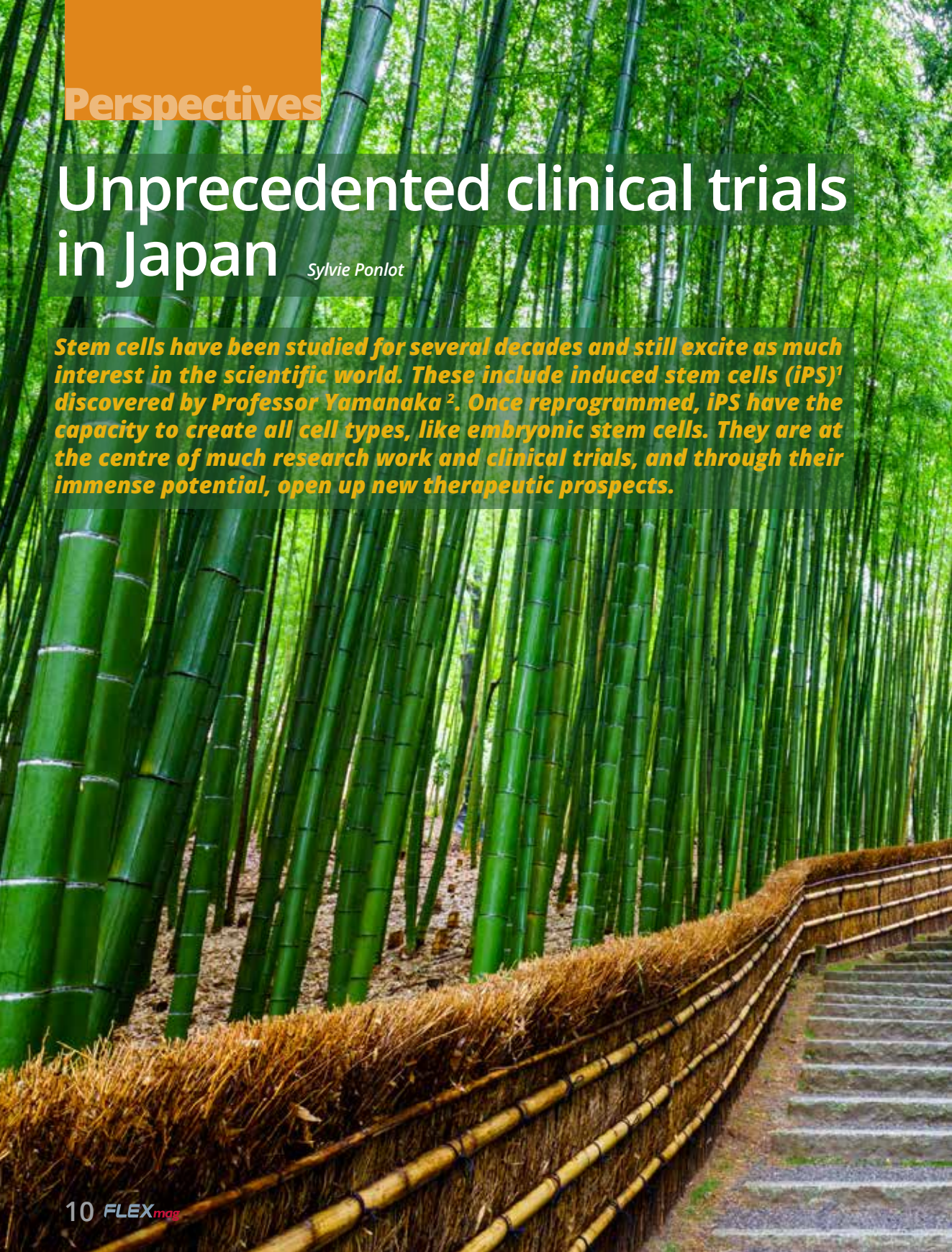
Electric press

Inspection with automated vision systems

Unprecedented clinical trials in Japan

Sylvie Ponlot

Stem cells have been studied for several decades and still excite as much interest in the scientific world. These include induced stem cells (iPS)[1] discovered by Professor Yamanaka [2]. Once reprogrammed, iPS have the capacity to create all cell types, like embryonic stem cells. They are at the centre of much research work and clinical trials, and through their immense potential, open up new therapeutic prospects.



En Last February, the Japanese Minister of Health authorised the fifth gene therapy trial. The application, filed by the team of Professor Hideyuki Okano of Keio University in Tokyo, targets the treatment of spinal cord lesions. It plans to inject several million iPS cells into the dorsal spine. A world first which aims to demonstrate the safety of grafted cells and to validate the transplantation process. The trial will be conducted in four patients injured recently, with spinal cord lesions. They will receive two million iPS cells over two to four weeks following the accident, the period during which the treatment is considered effective. The patients treated will then be monitored for one year.

In the autumn of 2018, a gene therapy trial evaluating the treatment of Parkinson's disease was also conducted. The team of Professor Jun Takahashi of the University of Kyoto transplanted more than two million iPS cells into the left hemisphere of the brain of a 50-year-old patient. After a postoperative period of six months without complications, the right side of the brain will also receive a transplant. The trial provides for a monitoring period of two years.

The subject of the first trial in 2017 was the treatment of age-related macular degeneration (ARMD). During surgery, five patients received an injection of iPS cells in their eyes. Two years later, the results are positive: the vision of four patients has ceased to decline, and that of the last patient has improved. The surgeons of Kobe Hospital and the researchers of the Riken Institute now envisage new trials to optimise the fields of application.

[1] Flexmag 11 – Stem cells, 50 years of discoveries and progress

[2] Flexmag 11 – Reprogramming the cells of the human body

Khalid Fekni,
Connectors Production Manager

Sylvie Ponlot

For six months now, the connectors division of Technoflex has been under the responsibility of Khalid Fekni. A native of Clermont-Ferrand, this engineer and graduate of the ENIT *(École Nationale d'Ingénieurs de Tarbes)* knows plastic injection like the back of his hand. He has been working in this field for more than 30 years! After a 10 year spell in the automotive sector at Plastics Vallée in Oyonnax, Khalid Fekni decided to move abroad to Luxembourg where he worked in food packaging. Now, Khalid has made the leap to pharmaceutical packaging: a specialist in high-speed molds, he is putting his plastic injection engineering skills to good use within Technoflex.

"The arrival of Khalid Fekni to direct our revamped connector teams represents a key asset for Technoflex. One of his main missions will be in particular to continue the development and modernization of our production equipment. His experience and maturity allows us to tackle upcoming projects with serenity" said Jean-François Soulé-Susbielle, Technoflex Industrial Director.

On a more personal level, Khalid did not choose to settle in the South-West by chance. *"I am a simple person, I am a nature lover. My wife and I discovered the region several years ago. We loved this place immediately. Here there are the mountains, the beach and plastic injection! What more could I want?"* he said with a smile. This enthusiastic cook takes full advantage of the assets offered by the Basque Country in this area. He also regularly engages in sporting activities such as running and mountain biking. The region is perfect for him!

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