FLEXmag

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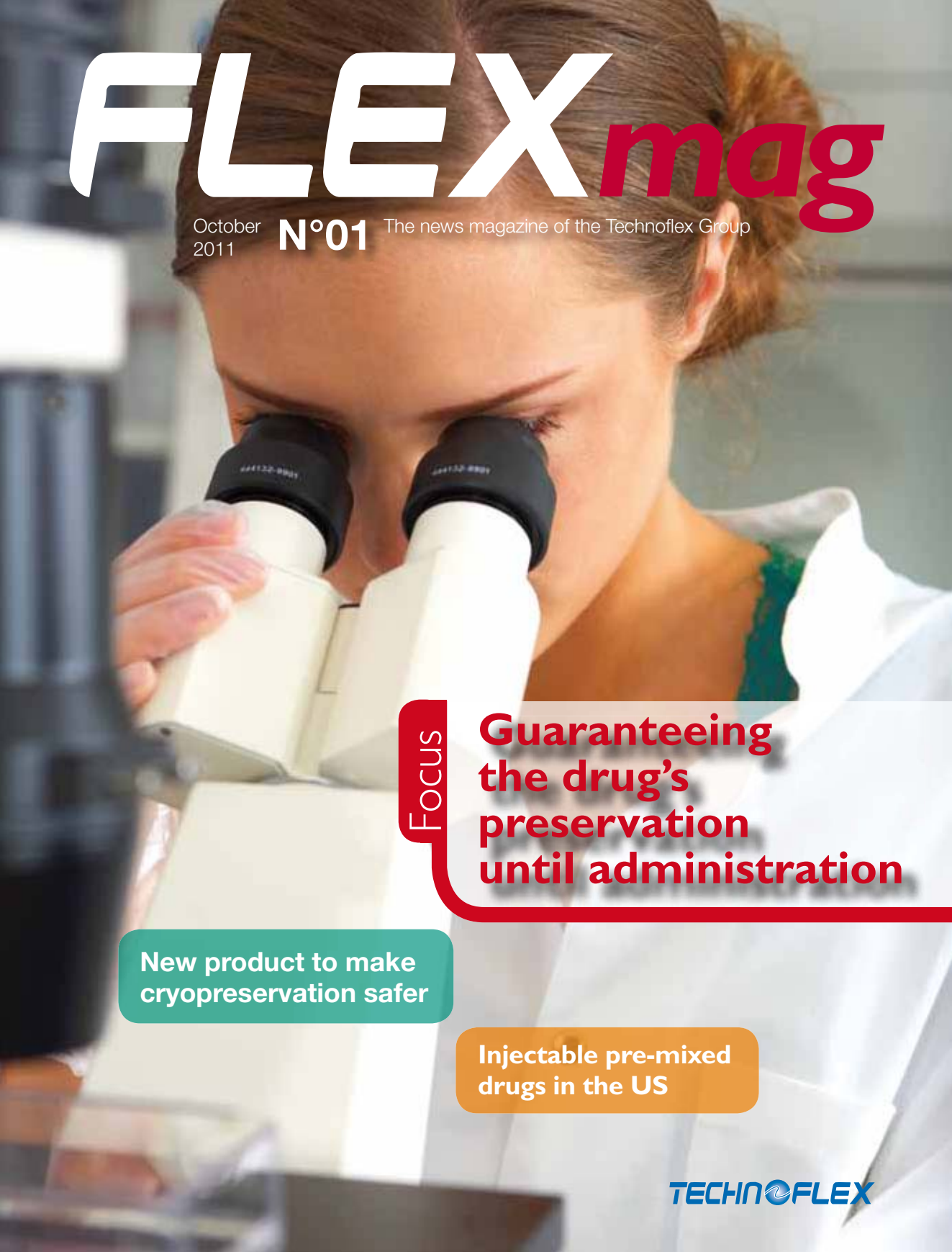

Focus

Guaranteeing the drug's preservation until administration

New product to make cryopreservation safer

Injectable pre-mixed drugs in the US

TECHNOFLEX

Editorial

Since its creation 40 years ago, Technoflex has grown from a subcontracting company to an innovative firm and a European leader in the design and manufacture of flexible bags and medical devices for the pharmaceutical industry. Our cutting edge technology and internal R&D resources enable us today to provide all-inclusive solutions, which are innovative, reliable and easy-to-use, offering our clients significant competitive advantages in their business.

Today, we develop true partnerships with our clients, with Technoflex getting involved upstream to meet their needs, so as to immediately optimize the design of future flexible bags and related connectors. This integrated, innovative approach enables us to prepare our future growth, by anticipating on technical, environmental and regulatory evolutions.

With a €38 million turnover in 2010, the Technoflex group already exports 65% of its production in about fifteen countries. Our goal is to strengthen our presence worldwide, notably in high-potential markets such as the United States, India and South America.

New markets, new needs, new products, new techniques… These are the issues we would like to share with you via our brand new information magazine, "**FLEXmag**". We hope it will answer your questions and foster connections.

Enjoy your reading!

Olivier Chesnoy
Chief Executive Officer

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Issue 01 – October 2011

Quick facts

Technoflex in Brazil

August 2011 - Transamerica Expo Center, Sao Paulo, Brazil.
Confirming its international strategy, Technoflex participated in the CPHI ICSE show - which welcomes 4000 attendees from the Pharmaceutical Industry, - the most important South-American forum, making it possible to develop partnerships and access a fast-expanding pharmaceutical market. A first-rate opportunity to be known and recognized!

Technoflex trebles its polypropylene production capacity

With three new automatic machines manufacturing polypropylene bags arriving between September 2011 and January 2012, Technoflex will significantly increase its production lines. The tailor-made, German-designed equipment will bring the current capacity from €3 million up to €4 million units a year – in order to best fit all our customers' needs!

A new seal of approval for Technoflex

In July, Technoflex received the AJE certification, granted by the Association Jeunesse et Entreprises. This seal of approval is the first certification to promote exchanges between schools and firms, with a view to help young people enter the business world. An organism which collaborates with the Education, Work, Economy and Industry ministers, AJE boasts a 25-year experience, with 30 Clubs nationwide. The AJE-Technoflex collaboration aims at making the evolutions of our trade better known, so as to improve young people's integration in the job market. This partnership has a bright future!

Schedule

October **22-25** - 2011

AABB-CTTXPO Annual Meeting

San Diego, California

- The premier event for transfusion and cellular therapy professionals, with more than 5500 attendees.

October **25-27** - 2011

CPHI Worlwide

Franfurt, Germany

- The best event for meeting representatives from the Pharma (outsourcing) industry.

November **16-18** - 2011

COMPAMED

Düsseldorf, Germany

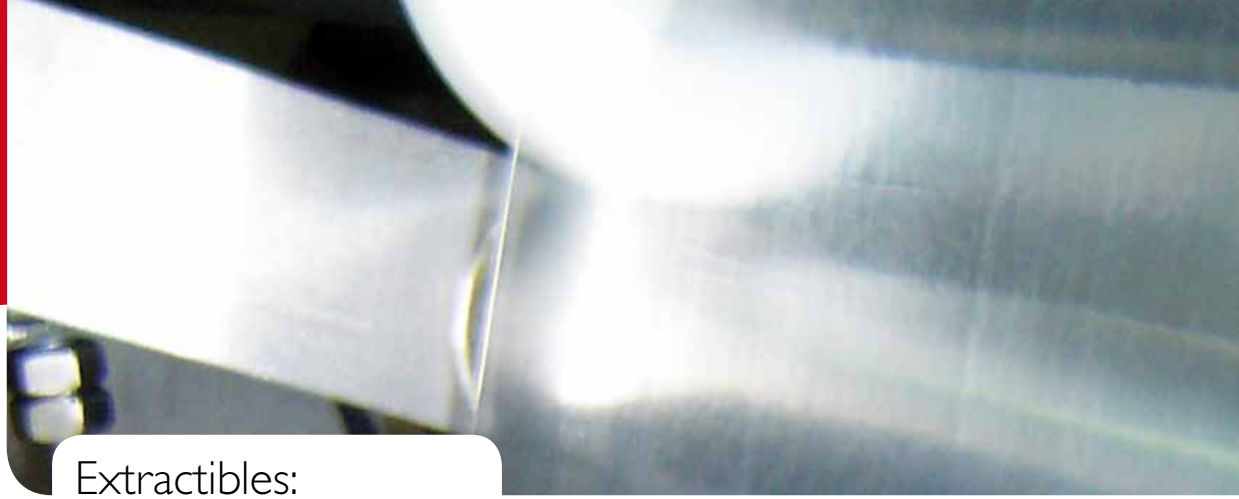
- High Tech solutions for medical Technology.

November **30** - December **2** - 2011

CPHI India

Mumbaï, India

- The most important and most comprehensive event of the pharmaceutical industry in South Asia.



Extractibles:

Guaranteeing the drug's preservation until administration

Author: Sylvie Ponlot, with support from Jean Yves Bauer

For a drug to be granted its commercial authorization *(Drug Approval)*, pharmaceutical companies have to submit a file to the relevant regulatory authorities *(AFSSAPS in France, FDA in the US, ...)*. The latters pay specific attention to the analyses of extractible substances from material in direct contact with the solution. Interaction problems between container and content are monitored with extreme care to ensure the drug's integrity.

Inerta®, a perfect control on the film's formulation

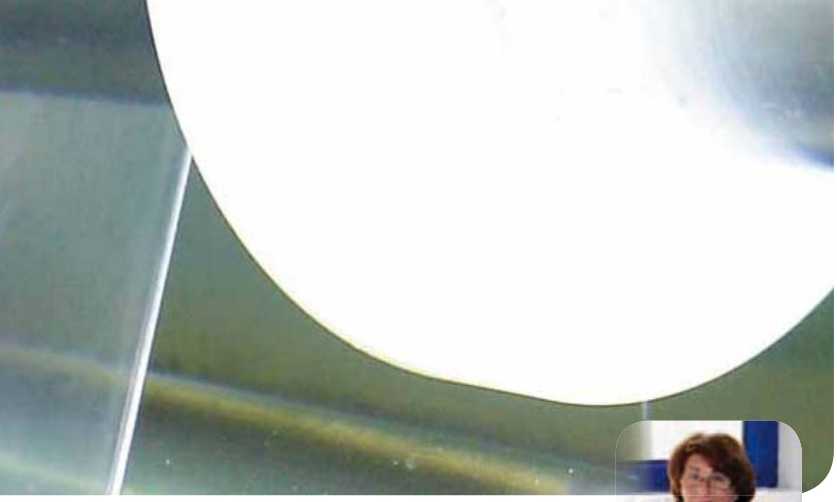
To meet drug preservation requirements with utmost precision, Technoflex has developed its own polypropylene-based formulation since 2004: Inerta®.

The Inerta® film is composed of three co-extruded layers:

- an external layer resisting autoclave terminal sterilization
- a middle layer providing great flexibility to the whole film
- an internal layer, in contact with the solution, enabling the bag's sealing

This highly inert polymer is used to manufacture the flexible conditioning and its related connectors. It is compliant with European and American pharmacopoeia (EP 3.1.3 & EP 3.1.6 / 21 CFR 77.18.10 / USP class VI) and registered at the FDA (DMF #19057) and in Canada (DMF # 2007-070). Moreover, all the extra tests to which Inerta® was submitted – transparency studies, residual volumes, integrity test, permeability measuring,… - support the fast conditioning of molecules in a reliable and already-tested container. Using this unique material significantly increases the end product's performances.

Thanks to these properties, Technoflex raises quality standards by offering a product range aimed at conditioning solutions with ever-greater sensitivity.



"We meet the most stringent requirements"

Sylvie Ponlot: *With what regulatory requirements must Technoflex comply today?*

Dominique Saint Ellier - *Director of Quality Assurance / Regulatory Affairs at Technoflex*
These requirements are grouped in aguideline publishedby the EMEA *(European Medecines Evaluation Agency)* entitled ICH *(International Conference Harmonization),* which sums up the body of information which a client has to submit in a marketing authorization Drug Approval file. The section dealing with primary plastic ackaging for drugs compels Technoflex to provide a full description of the bag and its material: extractible studies, leachables and migrations (interaction analyses between container and content). These studies have to be conducted with the end product, prior to stability tests.

SP: *What is Technoflex's interest in meeting these requirements?*

DSE: The stake here is to demonstrate the inertia of the Inerta® material, when in contact with the solution. To anticipate and satisfy our clients' expectations, we conducted four complementary extractible studies, which covered all aspects of the contact between Inerta® and different solutions: WFI water, ethanol, acid (pH<2) and alkaline (pH> 11) solutions. Hence, our clients are provided with the basic data for their own stability tests, which should enable them to submit their file more quickly.

SP: *Are these requirements likely to evolve?*

DSE: Yes, because they are sensitive to two factors: current events, which authorities take into account, and the Reach Regulation, which was implemented on June 1st, 2007. This European legislation compels industries to monitor the rates of chemicals used in manufactured and delivered products, but also their impact on man and the environment.

SP: *What is Technoflex's positioning regarding these constraints?*

DSE: Our constant regulation watch enables us to monitor what is going on in the market, especially from a regulatory point of view. Hence, we are able to identify and assess these evolutions in order to anticipate their integration in our future products.

SP: *Technoflex is currently renewing a certification. Can you tell us more about it?*

DSE: We are renewing the ISO 15378 standard. This standard for manufacturers of drugs' primary packaging integrates all GMPs (Good Manufacturing Practices) to be respected.

Tailor-made Inerta®

Marie Anna Curutcharry

In the early 2000s, Technoflex realized that its clients lacked a reliable product that would comply with pharmaceutical regulatory requirements. This realization led to the creation and launch of the Inerta® range in 2004.

Although similar products are available on the market today, none offers as many safety advantages: chemical inertia – a claimed and proven feature -, well-known raw material, guaranteed supply…

"We create bespoke formulations when specific properties are needed, especially mechanical properties such as flexibility or heat resistance, or chemical ones, such as the exclusion of a specific component if the drug is no longer stable in its presence," explains François Capitaine, Head of R&D.

The direct control on the technical data and extrusion processes of raw materials makes it possible for Technoflex to react quickly to the technical, regulatory and commercial information requests from its clients.

"It should also be noted that Inerta®-based bags and medical devices manufactured by Technoflex are already registered and sold worldwide for many applications and molecules, giving us significant feedback," François Capitaine concludes.

These medical devices are injected according to need and subject to EC labeling.

François Capitaine,
Head of R&D

New product to make cryopreservation safer

Sylvie Ponlot

One of the main issues with the preservation of live tissues is the possible cracks appearing on the container when released from liquid nitrogen into ambient air. To respond to this major technical concern, Technoflex's R&D department has developed an innovative EVA *(ethylene vinyl acetate)*-based bag, specifically designed for stem cell preservation, organ preservation liquids or blood-derived products.

Thanks to the mastery of the industrial process developed by Technoflex, the bag's integrity is ensured when it is submitted to the high thermal amplitudes in thawing. It keeps the products at temperatures ranging from -10 to -196°C.

The specificity of this kind of bags lies in their EVA-based, High-Frequency welded tubing and connectors, which ensure the integrity of a perfectly sealed system once filling is complete *(Container Closer Integrity System)*. This process, already used in Technoflex's sterilized bags, replaces the glue generally used to attach connectors, which poorly resists temperature variations. It also prevents contamination risks, migration problems between container and content, and suppresses assembly costs for the filler.

Manufactured in an ISO 8 clean room, the EVA bag is is assessed through numerous tests, in compliance with Good Manufacturing Practices: endotoxin levels per kinetic colorimetry counting, tightness test…

Bags capacity ranges from 5 to 500 ml. They can be specifically adapted to meet our clients' needs, and can be sterilized via beta or gamma radiation by request. Technoflex offers global, "all-in-one" sterilization for bags, tubes and connectors.

Medical issue

Why use stem cell treatments?

Stem cell treatments can be useful in a great variety of diseases and medical conditions, since they cause a degradation leading to cell death. This kind of treatment makes it possible to create new cells and to regenerate existing cells. 1998 marked the start of the first derivations of human embryonic stem cells. Since then, different therapies have been studied for heart diseases, bone marrow injuries, degenerative diseases (Parkinson's, Huntington's) and multiple sclerosis.

Pharmaceutical industry:

Who is driving the global growth?

Four emerging countries – Brazil, Russia, India and China, known as the BRICs – will drive the growth of the global pharmaceutical market, which should rise from 3 to 6% a year by 2015. China should witness an average annual growth of 20%, India of 15%, Russia of 12% and Brazil of 11%. In years to come, China will become the first contributor to the global pharmaceutical market, replacing the United States. « There is going to be an even greater polarity between mature countries, whose growth will be around 0 to 5% in years to come, and emerging markets » explained IMS Health France, which headed the study.

Injectable pre-mixed drugs in the US

Dave Dornan, San Diego, California

The market for pre-mixed drugs has expanded substantially in recent years due to the value of ready-to-use drugs in bags in the hospital setting. Safety concerns surrounding hospital pharmacy admixture programs has shown that 9% of drugs compounded in hospitals were done in error, according to a recent study. As a result of these safety concerns, the new USP 797 guideline increases hospital pharmacy drug compounding requirements to more closely comply with cGMP's, which has driven more use of pre-mixed bags.

USP 797, a reminder:

In the United States Pharmacopoeia (USP), 797 is the title of the chapter " Pharmaceutical Compounding & Sterile Preparations". The primary objectives of this chapter are ensuring sterility and accuracy of compounded sterile preparation. Physicians, nurses, pharmacists, technicians –anyone who compounds sterile medications or pharmaceutical products- are subject to this guideline. If the chapter 797 deals with the pre-administration manipulations for sterile compounding in specific areas such as the whole arena of compounding, transportation and storage, it is important to note that the IV drug administration itself is not covered.

For more information: www.usp.org

ISPA, a school created by business people for business people

France's plastics processing industry is ranked 4th worldwide, after the US, Japan and Germany. It is a fast-changing business, which relies on constant technological and raw material innovations, notably in the medical field.

The ISPA group was created in 1985 to meet the essential needs of plastics processing firms, and bridge the lack of a university-level degree in plastics processing. It is run by the Fédération Française de Plasturgie and the Chamber of Commerce in Alençon, and its board of directors is composed of Company Managers. This institute is the only one to provide cooperative training (with students working part-time in a company) that is fully centred on plastics processing, with degrees ranging from work-based, two-year courses (BTS) and BSs, to Masters' in Engineering.

With 16 permanent and 30 temporary teachers with academic or industrial backgrounds, the 190 students in 2011 will benefit from the innovative means the group has secured, with analytical labs, processing rooms, etc.

Olivier Chesnoy appointed Technoflex's Chief Executive Officer

Last summer, Olivier Chesnoy was appointed Technoflex's Chief Executive Officer. A physician by training with a degree from the French business school ESSEC, he brings Technoflex over 20 years of experience worldwide in health industries (pharmaceutical, biotechnology...). Among other things, he developed and established subsidiaries in Asia, including China, for the Fournier group, for which he also directed the Spanish division. After heading a biotechnology company (specialized in the discovery and development of therapeutic molecules acting on the modulation of cell death), he was most recently based in Spain, where he managed the turnaround of Laboratoire Urgo's subsidiary.

A hiking enthusiast, he has also practiced sailing for years, ever since his studies on the Normandy coast when he was a skipper in a cruising school. "In fact, I prefer activities in places where there is no phone coverage…" he jests, even if he now lacks time to engage in them! More seriously, he underlines the similarities between his different trainings: medicine, sailing and management require the same qualities - a quick diagnosis, the ability to define a precise course, the training of a highly capable staff to adapt more quickly. Plus, as on a boat, as he likes to remind, the most important thing is to stand united!

Julien Cavelier's experience for Flexmag:

Since September 2009, I've been in the engineering program at ISPA, which combines scientific and technical cultures with industrial concerns throughout the apprenticeship.

I did not want to be an apprentice in a manufacturing unit or in the subsidiary of a major industrial group. A former teacher of mine talked to me about Technoflex, claiming there was what I was looking for. Indeed, the firm's human scale and my interest for pharmaceutical industry motivated my decision to join in.

Technologies and innovations are the two essential elements in the theoretical training provided at ISPA, and those two components naturally combine in my work at the R&D department. Most projects I am entrusted with aim at turning an idea into a product while striving to optimize every step of the product's life cycle from the design on, so that it is respectful of man and the environment."

Apprentices are popular

"Welcoming apprentices following a sandwich course in our department paves the way for the possible hiring of future collaborators, but it also gives us a different vision, which may make us reconsider our habits. The contribution of new ideas is a definite advantage," notes François Capitaine, Head of R&D.