

# FLEXmag

April 2013 **#05** The news magazine of the Technoflex Group

## Parenteral nutrition

Focus

European big pharma  
in the inevitable  
biotech race!

PP multi-chamber  
bags for parenteral  
nutrition

TECHNOFLEX

**W**hen a patient can no longer eat normally, either temporarily or longer-term, medical staff sometimes need to turn to alternative feeding techniques. For such purposes, parenteral nutrition provides patients with the nutrients they need while the medical teams go to work on the pathologies at the root of the problem. In this respect flexible packaging also facilitates the implementation process, as our Focus explains. Technoflex offers its expertise in transfer sets and multi-chamber bags, among other things, in order to provide useful innovations to the sector.

We also closely monitor developments in the pharmaceutical industry, in which all our clients work: the growing importance of biotech firms in the eyes of the traditional big pharma is also reflected in the need to offer bag solutions that go well beyond simple chemical molecules. Here again, our R&D teams are permanently active.

Lastly, we never forget that our core business is performed on a daily basis by our teams, who put the greatest care and attention – day and night – into the manufacture of the bags and connectors that end up on the patient's bed: these are the people who are best able to speak about the interest and relevance of their work. You can see for yourselves when you read the interview with one of our experienced production line operator!



**Olivier Chesnoy**  
*Chief Executive Officer*

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## FLEXmag

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## Quick facts

### “Bisphenol A” law enacted

Enacted and published in the French Journal Officiel, the law suspending the manufacture, importation and marketing of any food packaging containing Bisphenol A has entered into force. It is enforceable as of 1st January 2013 for infants and young children, and will be for the rest of the population from 1st January 2015.

This law also prohibits the use of tubing made with DEHP in pediatric, neonatology and maternity services from 1st July 2015. Within a period of one year from the enactment of the law, the government will submit a report on endocrine disruptors. This report will specify the health and environmental consequences of their presence and will discuss the right time for prohibiting the use of 3 phthalates (DEHP, DBP and BBP) in all medical devices. The French authorities will notify the law to the European Commission, which will then be obliged to extend it to the other Member States if it considers the reasons invoked as acceptable. It will bear in mind the opinion of the European Food Safety Authority, which is expected to be issued in May 2013.

### A biodegradable polymer

Scientists at the Centre for Research on Materials in Brno (Czech Republic) have recently developed a “bioplastic” by recycling waste oil from canteens. Bacteria synthesize a polymer from this oil which serves as an energy reserve. This polymer appears to have identical properties to those of plastics, with the added advantage of being biodegradable. The researchers who have managed to produce a small quantity plastic hope that this performance will improve when the process is industrialized. This bioplastic could have numerous applications, including in medical packaging. Worth keeping an eye on!

### 2012 – a good year for pharmaceutical innovation

In the USA the number of new drugs authorized by the FDA reached a new high, with 39 market authorizations. And in Europe the EMA authorized 52 new drugs. The European Agency is expecting a better result in 2013 with 64 new drugs, including 20 orphan drugs and 20 generics. These are encouraging results as most of these drugs are new molecular entities (NME) that have never previously been used in a treatment.

## Schedule

April **23** to **25** 2013

### Interphex

New York, Javits Center

- The key venue where pharmaceutical industry professionals get together to find innovative solutions to assure the quality and efficacy of pharmaceutical and biopharmaceutical products. Technoflex is taking part in the event and will welcome you at stand 2335.



June **18** and **19** 2013

### Pharmapack North America

Philadelphia, Convention Center hall F

- Pharmapack North America showcases the latest innovations in pharmaceutical packaging and drug delivery systems. For this second edition, you can come and meet Technoflex at stand 414.

# Parenteral nutrition: a risky treatment but one that produces positive results

Sylvie Ponlot

**P**arenteral nutrition is prescribed in the event of a deficiency of the gastrointestinal tract, and consists in feeding a patient intravenously. Although the treatment has been mastered, it is nonetheless a complex solution. From preparation through to administration, pitfalls abound. And yet the protocol saves lives. Below is a detailed review.

Introduced into medical care during the 1960s, parenteral nutrition has saved many lives. Children, particularly prematurely born babies, are the patients that have benefited most from the technique.

Parenteral nutrition (PN) is prescribed when a patient has a gastrointestinal disorder preventing him or her from

feeding orally. Numerous clinical situations result in the prescription of PN: postoperative complications, Crohn's disease, cystic fibrosis, etc. It is also used in oncology and intensive care units, as well as in pediatrics and neonatology. Parenteral nutrition serves to meet patients' energy needs and correct any micronutrient deficiencies.

It can be administered via a peripheral venous catheter or central venous catheter (CVC). The choice between the two depends on the duration of administration, the composition of the admixture and the venous state of the patient. Peripheral venous catheter is preferred for short-term prescriptions (7 to 10 days) of partial nutrition as a complement to oral intake. CVC is used if the venous network is insufficient or when high-concentration admixtures

are administered. This is the case with total parenteral nutrition (TPN) which requires high caloric intakes. It involves the set-up of catheters in the operating theatre under sterile conditions. Whether it is cyclical or continuous, parenteral nutrition must be very closely monitored. Its efficacy has to be measured and complications (technical, infectious, metabolic or nutritional) must be avoided at all costs.

## Two groups of nutrients with forty highly unstable compounds

Parenteral nutrition includes micronutrients and macronutrients, encompassing glucose, lipids and amino acids. As the primary source of energy, glucose is required for the blood and kidney cells to function properly.



Lipids, in the form of lipid emulsions, provide essential fatty acids. They are indispensable for the structure of molecules and cell membranes. Lastly, amino acids act on the immune system and the digestive system. They renew the dead cells in our muscles, eyes and hair. Of the 22 existing amino acids, 8 are not synthesized by the body. They therefore have to be provided by our food. Micronutrients include vitamins, electrolytes (mineral salts) and dietary minerals (metals). They contribute to the good working of the metabolism (i.e. transport of oxygen).

All these components can interact chemically with each other. To conserve their stability, several precautions therefore need to be taken. The absence of oxygen guarantees the integrity of amino acids and vitamins. Due to their extreme sensitivity, vitamins are also protected from UV rays during storage and are added to the solution just before administration. But certain compound breakdowns are inevitable, such as the “Maillard reaction” which occurs spontaneously when amino acids are mixed with glucose. Over time, the solution takes on a yellowish-brown colour and becomes unsuitable for use – hence the importance of rapid administration after reconstitution.

### **Compounded or ready-to-use preparations?**

Pharmaceutical companies have standardized parenteral nutrition admixtures for many years. The use of bags has extended the shelf life of these standard formulations and has allowed them to be used in hospitals. But despite numerous advantages (reduced handling and contamination risk, etc.), ready-to-use formulations are not always suitable for all patients, particularly in pediatrics. And there is no MA (Market Authorization) for infants aged under two. This is something of a paradox: due to their digestive immaturity, premature babies<sup>1</sup> are the patient group

with the greatest need for parenteral nutrition. Furthermore, from the premature baby through to the adolescent, children have different nutritional needs that vary according to age, weight and clinical situation. The prescription and composition of parenteral nutrition are thus defined on a case-by-case basis.

These mixtures, known as “magistral” or “compounded” formulations, are prepared by the hospital pharmacy. They offer the advantage of great flexibility in the choice of products and are perfectly suited to the patient. But they have to be sterile and pyrogen-free, because terminal sterilization is impossible: the mixture components would be irrevocably altered. They must therefore be manufactured in a Controlled Atmosphere Area (CAA), requiring sophisticated equipment such as an isolator, laminar flow hoods and an air ceiling. The product is prepared with a robot – a robot, inspected (for sterility, endotoxins, particle contamination) and then quarantined inside a cold chamber. When the final inspections and checks have been performed the nutrition solution is released and delivered to the patient.

Parenteral nutrition has come a long way over the last 50 years. Industrial ready-to-use formulations are used alongside pharmacy preparations. The former have significantly facilitated nutritional care in small establishments, outpatient and home care, but remain unsuitable for pediatrics and neonatology. A further step forward is therefore required in the future to adapt this type of “ready-to-use” formulation to the infant population.

<sup>1</sup> 2012: 65,000 premature births in France



*Compounded preparation*



*Mixing amino acids and lipids*



# PP multi-chamber bags for parenteral nutrition

Sylvie Ponlot

**T**he multi-chamber bags developed by Technoflex are made of a polypropylene-based film with a high oxygen barrier. This particular property protects amino acids against oxidation, the main factor in their degradation.

The bags are compartmentalized into two or three chambers containing macronutrients in the form of binary mixtures (glucose and amino acids) or ternary mixtures (lipids, amino acids and glucose). These standard mixtures are suitable for the majority of patients. To prevent the inevitable interactions between some of these macronutrients, peelable welds (removable thermo-welds) are put in place to separate them from each other. In order to reconstitute the mixture, the welds are simply squeezed by hand to break them.

Multi-chamber bags offer many advantages. They enhance patient safety as they reduce handling and thus the risks of contamination of the nutritional mixture. They bring down the waiting time linked to the opening hours of manufacturing units (the solutions are prepared in hospital pharmacies). The drugs can therefore be dispensed by healthcare staff as soon as they are prescribed. The bags also come in more extensive ranges with simplified storage conditions. All these advantages have allowed the widespread use of these ready-to-use parenteral nutrition bags in hospitals.

There remains the issue of micro-nutrient supplementing (dietary minerals and vitamins). Due to their high level of instability, these components have to be added just before administration. This operation can sometimes be forgotten. A way of remedying this problem would be to create a new chamber dedicated to dietary minerals. But the main difficulty is the dosage form of the vitamins. Packaged as lyophilisates in bottles, they have to be used within 24 hours following reconstitution. So an extension of the "all in one" concept to include vitamins and dietary minerals would be a significant improvement. The recent R&D developments at Technoflex have resulted in the adaptation of the TTS101 transfer set<sup>1</sup>: welded directly on the bag, it is used to fix the vitamin bottle securely. This system facilitates the reconstitution of the vitamin solution when the mixture is used. The aim is to improve the safety of parenteral nutrition. It could be used by healthcare departments in hospitals, but also in HAH<sup>2</sup>. In this respect the handling operations would be vastly reduced and the addition of micronutrients would no longer be forgotten.

<sup>1</sup> Flexmag n°2

<sup>2</sup> Healthcare at Home



# European big pharma in the inevitable biotech race!

Sylvie Ponlot

**W**ith the increased regulation of drug expenditure and the fall of patents, it is the emerging countries that represent a means of expansion for European pharmaceutical firms. And since they have already laid down markers in these countries, the "big pharma" in Europe are actually in a better position than their American competitors to profit from this growth. According to a study by Standard&Poor's, despite falling sales in Western Europe, the revenues of pharmaceutical companies have been boosted by sales in the emerging countries.

To date, no European pharmaceutical firm has yet launched a patented drug in these emerging markets. That will be the next stage in their development. The roll-out of such products will depend on how intellectual property laws in China, Brazil and India evolve. They have yet to be fully integrated into local law or to be properly implemented, despite some progress in the protection of intellectual property\*. Faced with this problem, certain pharmaceutical firms may initially enter the market with biological products which are harder to copy. Indeed, standard molecules are all currently in the process of being manufactured as generics and the majority of innovative drugs are now being discovered by biotech firms. As well as enhancing their global product portfolio, one significant interest justifying the massive investments

made by the big pharma in biotech is also to consolidate their positions in the BRICS (Brazil, Russia, India, China and South Africa).

## **R&D: between externalization and partnerships**

For many years the pharmaceutical industry internalized all the stages in drug development, from initial research through to clinical development and production, and encompassing packaging design, marketing and commercialization. To cope with the soaring costs of these developments and increasingly uncertain results, some companies have chosen to reorganize their R&D (abandoning certain therapeutic areas, reducing the number of

countries in which clinical trials are conducted). Others prefer to externalize their R&D for the first stages of drug development by forming partnerships with biotech firms and academic centers. These new strategies allow the large companies in the sector to distance themselves from some of the inherent risks of these developments whilst offering young biotech firms new financing sources and increased autonomy.

*\*(ANSIVA in Brazil, Flexmag N° 03)  
Source IMS, Standard & Poor's  
Source Bulletins Électroniques*





## Olivier Chabay, production line operator

by Julia Beauquis

*Julia Beauquis: You're a production line operator at Technoflex. Can you describe your career so far?*

**Olivier Chabay:** I graduated in Industrial Sciences and Technologies with an option in mechanical engineering, before taking a higher education diploma in Industrial Maintenance. I joined Technoflex as a temporary worker, then on a fixed-term contract. I have now been in the Technoflex production team for 13 years.

*J B: Tell us about your various tasks.*

**OC:** As a production line operator I make sure the manufacture and packaging of bags run smoothly. My role is to monitor the machines and carry out maintenance on them with the technicians. I also have to control the quality and quantity of bags produced, and supply the production lines with film rolls.

*J B: Is teamwork important?*

**OC:** A "cleanroom"<sup>1</sup> is like a mini-world where everyone works together! I work with the team managers, production workers, adjusters, technicians and warehousemen. Teamwork and team spirit are therefore very important. Information has to circulate easily and instructions have to be clear.

*J B: Is it a job you would describe as routine?*

**OC:** Not at all – and that's what makes it so good! The scope of my job is broad enough for me to do things that are different. Also, there is always the risk of a line malfunction which requires a rapid intervention to be able to restart production. I love the technical aspect of my job. I'm putting all the theory I learned at school into practice.

*J B: Technoflex has increased its polypropylene activity. Has this changed the way you work?*

**OC:** The switch from PVC to PP involved a period of adaptation. We had to review our working habits, particular in terms of dress. It's completely different, since we are working in ISO 7 certified cleanrooms. In the PP area there is also a lot more sampling. Some of the samples are analyzed in our in-house laboratory and the rest goes to our clients, who do their own checks.

*J B: In your view, what qualities do you need to do this job?*

**OC:** You need to have a rigorous and methodical approach, and above all team spirit, as communication is really important. The expertise you gain with experience. But we sometimes put ourselves under pressure! You have to remember that the purpose of our products is to improve the safety of patients. They must therefore be of irreproachable quality.

<sup>1</sup> Controlled Atmosphere Area

