Injectable drugs: a long, winding road

by **Sylvie Ponlot**, Technoflex

FROM RESEARCH INTO MOLECULES THROUGH TO SALE OF THE END PRODUCT, MORE THAN TEN YEARS ARE REQUIRED TO DEVELOP AN INJECTABLE DRUG. THE "GESTATION" OF MEDICINES IN BAGS INVOLVES FOUR PHASES, AS WITH STANDARD DRUGS, BUT WITH A FEW MORE SPECIFIC CONSTRAINTS. TECHNOFLEX, A EUROPEAN LEADER IN DESIGNING AND MANUFACTURING IV BAGS AND CONNECTORS, SHINES A SPOTLIGHT ON A ROAD POTENTIALLY FRAUGHT WITH PITFALLS.

Once exploratory research and preclinical testing of the molecules have been completed, Phase I clinical trials start with healthy volunteers (50 to 100). The goal is to determine the maximum dose tolerated by man, as well as the administration method. Phase II, peformed on a few hundred people, evaluates the dose-effects relationship, defines the drug dosage and detects short-term adverse effects. It is also the starting point for development of the primary packaging. In order to be compatible with the drug and to guarantee perfect stability, the material used for the bag has to conform to numerous parameters. The aim is to avoid any interaction with the product that may pose a threat to the quality of the injectable drug and hence to the patient's safety.

A key point to consider is the raw material from which the bag is made. This material undergoes a study of extractables and leachables, then an assessment of toxicity and risks. Extractables are compounds of plastics that can be extracted by solvents with physical and chemical properties that differ under aggressive conditions. Leachables refer to compounds that can be released by plastics into the pharmaceutical products under normal conditions of use.

At this stage, Technoflex's R&D department also verifies that compatibility between bag and spout is optimal. Decisions are made about criteria like diameter, whether to have an aseptic filling or not, and so on.

Factors other than the composition of the drug can affect the stability of the product in contact with the container. This is the case with ambient temperature and humidity. The stability study carried out also has to take account of low temperatures as well as the freezing/thawing cycles, particularly for biotechnologies and blood derivatives. For certain preparations it is also essential to consider the effects of exposure to light.

Phase III could be called the "comparative testing" phase. It is the main clinical trial and includes several thousand people. The drug's properties are compared with a placebo or an existing drug. Only if an acceptable benefit-risk ratio is proven can a market authorisation (MA) be awarded. At this stage of testing, the injectable's primary packaging is ready: polypropylene, polyethylene, EVA or PVC depending on the nature of the drug. The final phase starts when the drug is marketed: this is pharmacovigilance. Knowledge of the drug in actual conditions of use is furthered in this way. Phase IV is also called post marketing surveillance.

The goal of therapeutic research is to develop high-quality, efficient injectable drugs. It is a long, complex process. The expertise of all the main players is required for innovative treatments to emerge.

<< Jérôme de Monpezat at work at Technoflex. Jérôme is in charge of the development and prototyping of packaging and connectors for IV drugs. >>

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Sylvie Ponlot is in charge of communication at Technoflex. She is the editor in chief of Flexmag, the company's magazine and a passionate photographer who exhibits regularly.