

## **Plastics for Specialty Medical Devices: A processors perspective**

As plastics suppliers play an increasingly critical role in the manufacture of specialty medical devices, Steve Lovatt, Head of Regulatory Compliance at Bespak explains why the duty of care for Good Manufacturing Process goes beyond the 'plastic processor' through to the original plastics manufacturer.

### **Patient safety**

The design, development and manufacture of specialty medical devices and pharmaceutical components are conducted within highly regulated environments, and for good reason. There is often intimate and prolonged contact between the plastic component, the drug therapy and the patient. An undisclosed material in the plastic could enter the formulation and ultimately be absorbed into the patient's bloodstream. As plastics are often used in inhalation devices, this potential hazard is particularly critical as the lungs are sensitive organs and do not have some of the more robust protective mechanisms that have evolved, for example, in the Gastrointestinal (GI) tract.

To avoid any such harmful consequences, the US Food & Drug Administration (FDA), who review all new drug applications, provide a number of criteria that need to be fully satisfied before any product can be launched.

### **Material specification**

A 'leachable' is a substance that migrates out of the plastic into the formulation over the period of the product's shelf life. The FDA and other regulatory authorities require that these substances be identified, that their safety profile assessed and controlled. Studies are required to establish exactly what substances can leach out of the plastic into the product. For such substances, a specification is agreed with the regulators and they are then subject to routine monitoring controls. As leachables may take months to enter the formulation, what is actually routinely monitored is the 'extractables' profile. Extractables testing employs aggressive solvents and higher temperatures to establish a measure of what may come out of the plastic over an otherwise longer period of normal storage and use. Placing the plastics into a deliberately more aggressive environment allows them to be assessed within the shorter timescales available for quality control testing. If you can establish a correlation between the leachables and extractables profile, the regulators will allow you to routinely monitor extractables.

All of the above means that it is critical for the polymer supplier to ensure consistency of their material formulations. Obviously a low level of leachables, and low toxicity of the substances concerned will make initial approval and ongoing monitoring easier.

Specialist medical device manufacturers will have vast experience of the FDA approval process and can, with a clear understanding of the plastic formulation, assist suppliers with the early regulatory validation work. This does of course require both parties to be transparent in their working relationship.

### **Design and Development**

It is a feature of the regulatory approval process that material decisions made in the early years of a device's development can be fixed for the lifetime of that device. If a specific material is used in device development and the critical safety and efficacy studies have begun, a change in any part of the specification will almost certainly delay the product development, as work may have to be repeated. Clearly any delay to product launch means lost sales for the duration of the delay.

Given that timescales for pharmaceutical product development can typically be in excess of five years, with the lifetime of a marketed product often running into decades, it is in the interests of both supplier and manufacturer to choose materials where the continuity of supply can be guaranteed and maintained for the duration of the device's life.

### **Ongoing Supply**

Improvement and cost containment are typical reasons for change and whilst these are welcome, the benefits always need to be weighed against the sometimes formidable costs associated with testing and approving any changes. Continuity, reliability and consistency are powerful drivers in this industry sector. Changes can be made, but the planning process needs to start early and be approached as a partnership between all parties in the product supply-chain. For approved products it is possible that re-registration may have to take place, and two years notice should be considered the absolute minimum.

During routine supply the cost of failure is very severe. If there is any risk of patient harm, or non-compliance, product will be recalled and costs can easily rise into millions of pounds. Given this risk enormous focus is placed on the controls and measures taken to avoid errors. This normally follows a code of practices known as 'Good Manufacturing Practices' (GMP). Plastic suppliers will be expected to demonstrate that they have the level of control required.

All of the above may appear problematic, however if good development choices are made, change control and manufacturing are well managed, the plastic supplier and device manufacturer can enjoy a long-term and profitable relationship.