Blow-Fill-Seal for Ophthalmic Packaging

The high levels of quality assurance and wide variety of pack designs offered by blow-fill-seal technology makes it particularly suited to the packaging of ophthalmic products.

By Urs Lichtenstein at rommelag ag

Urs Lichtenstein joined rommelag (Buchs, Switzerland) in 1974 as an Assistant to the Sales Manager and, after a couple of years, was promoted to the position of Area Sales Manager. Since 1989, he has worked as Sales Manager for rommelag, focusing primarily on Key Account Management.

Blow-fill-seal (BFS) technology is an automated packaging process whereby plastic containers are blow-moulded, filled and sealed in one continuous protected operation. First invented by rommelag in the 1960s, BFS technology was originally used for the packaging of consumer products, but development of the bottelpack® range of aseptic BFS machines in the 1970s extended its use to pharmaceutical applications.

The BFS process begins with a polymer (usually polyethylene or polypropylene) being heated and extruded under pressure. The polymer melt is formed via a circular orifice into a hollow tube (known as a parison), which is prevented from collapsing via a stream of sterile filtered air. The mould that forms the body of the container is in two halves; the lower half closes to seal the bottom of the open parison and the parison wall is then blown and/or sucked to the cooled mould walls to form the lower part of the container. Filling needles draw the stipulated volume of sterile product into the container, and after withdrawal of the needles, the upper part of the mould closes to form and seal the upper part of the container. The forming, filling and sealing steps are thus carried out in one unit operation, taking just 10-12 seconds. The moulds contain up to 50 cavities (or even more), depending on the machine, container size and design.

By its very nature, the BFS process offers high levels of quality assurance. By integrating container manufacture with product filling, BFS removes a major step from the production process, together with its associated risks. At the end of 2004, the US FDA defined for the first time regulatory requirements on the use of BFS technology. As a rule, the filling process is considered to be a case of aseptic processing and is therefore subject to the strict GMP requirements on these processes. Special attention needs to be paid to some of the central requirements such as environmental monitoring, the absence of particles in the product and validation of the processes by media fill.

Any shape that can be blow-moulded can be blow-fill-sealed. This creates the possibility of making endless different packaging forms, in various different shapes and sizes, and designed with specific patient needs in mind. As a result, BFS technology is used in the manufacture of a wide range of products including large- and small-volume parenterals, inhalation solutions, surgical irrigation water, nose and ear drops, creams and ointments – and, in particular, ophthalmic products.

OPHTHALMIC APPLICATIONS

Back in the 1970s, the rommelag bottelpack system became established in the field of eye drops and ocular medicine for volumes of between approximately 0.3ml and 1ml as a unit-dose presentation, and between 5ml and 15ml for multi-dose applications. The BFS process is particularly suited to the filling of ophthalmic solutions; most of these products are heat-labile and hence will not withstand terminal sterilisation. The sterility assurance level of the BFS process is extraordinary, and has been proven by millions of containers manufactured in media-fill validation runs. The
Blow-fill-seal technology is recognised as an efficient, advanced aseptic processing technology for liquid pharmaceutical products. It provides far higher levels of quality assurance, together with definite cost advantages, compared with traditional aseptic filling techniques. The technology has been well-established in the field of ophthalmic products for a long period of time, and has shown an excellent record of successful launches of new products and designs of benefit to the patient.

Multi-doses are usually single containers with volumes ranging between 5 and approximately 15ml. Traditionally, the containers have a standard thread fitted with a piercing cap. When the product is to be used, the cap is screwed down as far as it will go; the spike inside the cap pierces the upper membrane in the neck of the bottle. The regular flow and size of the drops depends upon the diameter of the hole, the surface tension of the product and the pressure exerted by the user. Continuous pressure transforms the flow drops into a spray. This system is simple, safe, practical and efficient. However, it may not be considered suitable for special products which require the strict observance of dosage instructions. The alternative is a drop-counting measuring cap. This is a complete closing-opening-dosing-re-closing assembly consisting of two distinct components. The instruction for use are:

- The closing assembly is screwed down as far as it will go in order to open the bottle
- The upper cap is removed
- The bottle is squeezed to dispense the exact number of drops required

The weight of these drops is constant, regardless of the pressure exerted and its duration. This innovation makes the insertion of a dropper part into the container obsolete.

CONCLUSION

Blow-fill-seal technology is recognised as an efficient, advanced aseptic processing technology for liquid pharmaceutical products. It provides far higher levels of quality assurance, together with definite cost advantages, compared with traditional aseptic filling techniques. The technology has been well-established in the field of ophthalmic products for a long period of time, and has shown an excellent record of successful launches of new products and designs of benefit to the patient. Worldwide acceptance in the ophthalmic market has confirmed the particular suitability of this form of packaging for ophthalmic applications.

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