Automating the De-blistering Process

PEER REVIEWED

This article provides an overview of why de-blistering is required, what issues this creates, and how automated de-blistering technology can be implemented to improve run rates, increase efficiency, lower costs and help reduce risks to staff.

Blister-packing Process

Blister-packs are a very common means of packaging pharmaceutical tablets, capsules and soft gels. Such packs generally comprise a sheet of initially flat plastic or aluminium base material in which are formed a series of wells. A tablet is inserted into each of the wells, the open ends of which are sealed by means of a sheet of aluminium foil which is attached to the base material sheet. Each tablet is thus sealed in its own well until use, when the base material well is depressed by finger pressure and the tablet is forced out through the foil backing

Reasons for De-blistering

Although de-blistering would normally only be done by the consumer, there are various reasons that blistered product would need to be removed from the primary packaging and this occurs at multiple points along the product lifespan. During initial product packaging, when the blistering machine is being set up, product is required to be run through but is rejected until quality approval of the final blister is signed off. When you are dealing with high-value and in some cases very low batch sizes of capsules / tablets, these set-up blisters will be required to be de-blistered. Furthermore, any reject blisters generated throughout the run due to malformed blisters, leaks or out-of-registration sealing may also need to be de-blistered to ensure acceptable wastage limits are met and minimal reject capsules / tables are created. Another reason for de-blistering is related to incorrectly packed products, specifically issues with the blister-pack itself. This can be an incorrect livery, strength, language or variable data (batch number and expiry date) on the lidding foil or embossed into the base material. This would require the stock to be rejected, destroyed or recovered by de-blistering. Again based on the cost, availability of the drug and required timelines, a decision will be made on the necessity for de-blistering. Another reason for de-blistering could be in the case of a product recall where the drugs are out in the market and a problem is found and the entire batch of that drug would be recalled to be inspected and evaluated. During this process, depending on the reason for the recall, the individual tablets / capsules may need to be tested and a large amount of de-blistering may be required. During clinical trials it is sometimes required to test the trial drug against a comparator. A comparator trial, rather than a placebo-controlled trial, means that the experimental drug is not being compared to a placebo, but rather to a drug that is already being used to treat patients. In this case, when a comparator drug is already on the market in a blister-pack format these will have to be purchased, unpacked, de-blistered and then re-packed or over-encapsulated (if this is to be used on a blinded trail) and then compared to the new drug during the clinical trial. If this is a large Phase III trial, then the quantity of blister-packs that require de-blistering can be very high. Finally when the drug product reaches the end of its shelf-life, it needs to be destroyed. For expired blisters containing toxic product, there is often an expensive disposal process if the product is not separated from its packaging. In this case, a highly-controlled and safe method of de-blistering is required.

Issues with De-blistering

Blister-packs are designed to be opened by the end user and as such, hand processing is one method of de-blistering. This can be appropriate for small numbers of packs and on an ad hoc basis, but if a large number of packs are planned to be de-blistered, carrying out this operation by hand is both time-consuming and costly. Furthermore, a recent study carried out by the Health and Safety Executive found that manual de-blistering required operators to use forceful pinch grips, with the greatest force being exerted through the thumbs. Discomfort and other upper limb symptoms were seen to be commonplace after a shift involving de-blistering. It was established that during the de-blistering task, the wrists were held in bent and awkward postures and there was also rotation and flexion of the supporting wrist as the strips of tablets must be turned frequently. The posture taken up by the operators to allow them easy access to the blisters required them to sit resting their feet on the bar underneath the table. This posture created extra tension in the arms and neck, but it also meant that they could not comfortably place their feet flat onto the floor, leading to discomfort in the legs and back. The de-blistering task can be a long process, sometimes lasting an entire shift or more and it was reported that some operators find the task very monotonous and become fatigued and under-stimulated within this area. The outcome of this study points to the requirement of a better solution than a manual de-blistering process.

Methods of De-blistering

Due to the issues raised regarding manual de-blistering of large quantities of blisters, a number of machines have been devised for this task and each has benefits and drawbacks based on the volume, blister type and nature of the

drug to be de-blistered. Working in a clinical trial supply chain company, we have experience of hand-processing, manual and semi-automated de-blistering machines, choosing the most suitable process for the job. The first type of machine we utilise is a Poppitt dispensing digital aid which uses a single pneumatic punch to remove the tablets. This eliminates the necessity for repetitive thumb movements and awkward seated postures, and reduces the amount of force required to de-blister the tablets, eliminating the musculoskeletal risk. The blister strip is presented one pocket at a time into the machine, and when the tablet reaches the correct position it is automatically popped out of the strip and collected in a tray below. These machines are relatively small, portable and low-cost, and work with many sizes and shapes of blister and drug product. However this is still a slow and labour-intensive process and can cause damage to the drug products if they are very friable, and is not recommended for use with capsules, soft gels or tablets with a score mark. These are best suited to small volumes of blisters containing robust tablets as they are quick to set up and do not require lots of specific change parts. A second type of machine we use to improve the de-blistering process is the Sepha press-out manual. This machine can empty tablets and capsules from blister-packs at a rate of up to 20 blisters per minute and is designed for use on small batches of push-through blisters in linear formats. They are portable, easy to set up and run, have a single change part making them very flexible and quickly adjusted, and they are fully cGMP compliant. This machine is best suited in operations which need flexibility for lots of different blister push-through formats. The mechanism is based around a set of rollers which the blisters are fed through; pressure is then applied to the well of the blister, which forces the tablets through the foil lidding and out of the pack into a collection tray. This machine does not require any electricity or air supply as the rollers are turned by a hand crank. While this machine is quicker than processing by hand or by the single pneumatic punch-style machine, it is still not suited to large runs of blister-packs and can cause damage to some kinds of tablets and capsules. There have also been issues with pieces of foil from the lidding material separating from the pack and falling into the tablet collection tray. This leads to the tablets having to be inspected or passed through a metal detector to ensure that no foil fragments are left in with the recovered tablets. As this is an additional process, the time, number of operators and cost of the job as a whole is increased. A third type of machine, which we have recently purchased, has been designed to eliminate the risk of foil contamination in the recovered tablets and increase throughput for large de-blistering runs. The Pharma Engineering Stripfoil de-blistering machine process is built around a highly-specialised adhesive tape. This has the primary function of stripping the aluminium lidding foil from beneath each pocket on the blister, allowing the tablets to be easily removed with very little force. This has the twin benefits of reducing the amount of waste due to damaged drug product and removing the risk of foil contamination in the recovered drug product. The blister strips are fed into the machine using a magazine stacking system, allowing a large number of packs to be prepared quickly and easily. The blisters are then presented to the adhesive tape which pulls them into the drive rollers and across the removal station. The adhesive tape removes the aluminium foil covering the blister pocket and a second roller then gently pushes the drug product from the back side out of the blister and into a collection bag. The machine is easy to set up and has variable change parts, allowing for a variety of blister sizes, shapes and formats to be processed quickly and efficiently. The machine can run at a rate of up to 60 blisters per minute, making it the perfect tool for large de-blistering jobs. We have run direct comparisons on manual de-blistering and using the three various machines, showing an increase in productivity, reduction in operator health issues and improvement in quality and yield when using the automated options. In fact, we found that the Stripfoil machine was able to run with less than half the staff normally used on a manual run and had a per-shift output more than five times that of the manual process. The Stripfoil machine has been fully validated and has cut lead times and costs on comparator-based trials where we are required to de-blister large numbers of commercially-available drugs prior to the over-encapsulation process.

Conclusion

We have found that the use of automated machines for the de-blistering process has provided an increase in the quality, yield, speed and efficiency over the traditional hand de-blistering method. Even when the set-up and validation is taken into account, we have been able to shorten customer's timelines and reduce costs based on the increased throughput and reduction in additional quality inspection. However, we are still conscious that hand de-blistering and some of the less automated machine solutions for de-blistering are still the best option when only a very small quantity of blisters is required to be re-worked, and as such, each job should be assessed and the most suitable method of de-blistering should be employed.

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