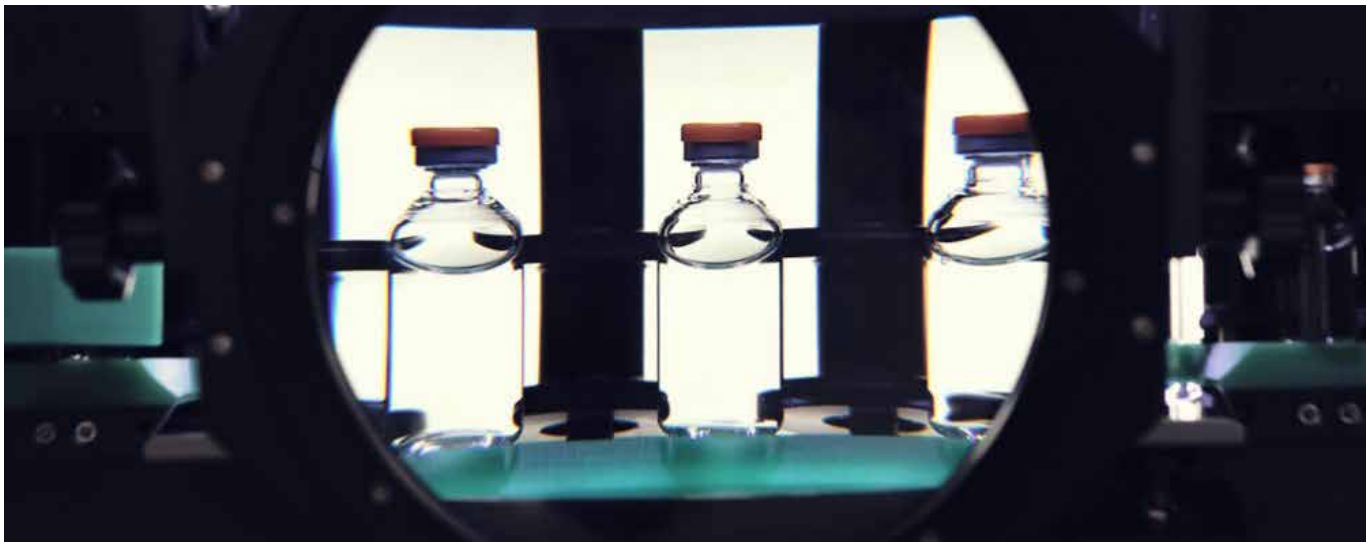
european
PHARMACEUTICAL
manufacturer

The advances being made in vial processing

by John Erdner

John Erdner, product manager, aseptic fill-finish systems, SP Scientific PennTech, discusses the advances being made in vial processing to help reduce the risk of vial damage and particle contamination.



There has been at least one recall for parenteral products packaged in vials with chipped rim surfaces and a number of US Food & Drug Administration (FDA) 483 notices issued to pharmaceutical manufacturers for glass particles found in vials. When this occurs, it is obviously a critical event for the manufacturer of parenteral products. Sometimes these instances can go undetected – the vial progresses to filling, is stoppered and capped before inspection. If the vial is capped, this defect will be difficult to identify.

Manual inspection and most automated inspection systems use rear-source lighting to look for particles within the product. Particles block the light and appear as black spots, however, glass particles are easily missed in this process. Some more advanced inspection systems are entering the market which use bottom-source lighting to help identify fibre and glass fragments via reflectance measurement, however, these are costly and it would be prudent and more efficient to address the issue of glassware damage at its source.

Figure 1: Chipped vial rim and resultant particulate generation

Sources of glassware for the filling line

Glass vials may be sourced and then washed and sterilised prior to filling as part of a continuous process, which is typical for higher throughput lines filling larger batches. Here, glass vials are washed to remove loose particles from the inside and outside of the vials; vials are then feed through a depyrogenation tunnel for sterilisation. Vials leaving the tunnel enter the most sterile area of the facility and are now ready to be filled.

Many smaller batch applications use sterilised glass supplied directly to the filling station as a cost- and space-saving alternative to operating a washing and sterilising line. Pre-sterilised glass vials are washed and depyrogenated by the supplier, double bagged and then gamma irradiated to sterilise before being shipped to the end user for use. This convenience, however, may introduce additional risk to the process. Even though the glass is sealed to protect against contamination, the glass is not under full control during shipment where vibration and manual handling are inconsistent. Typically, the vials are tightly bagged to hold them together in a formation or pack. Vials rub against each other or may collide if the pack loses shape, leading to damage, seen as cracks and chips, resulting in the creation of glass particles. The use of dividers or other packaging separating the vials for protection is not normally possible as they may compromise sterility or themselves create dust particles.

For small batch applications there are companies that provide a vial washer and tunnel suited to lower throughput processes of 50 vials per minute, or less. Modern systems (Figure 2) are compact, occupying 3m/9ft or less, and are sized for small batches giving the drug manufacturer complete control of the process, thus minimising the risks of human intervention and contamination.

Eliminating vial damage during washing

Vials are usually manually unwrapped and loaded into vial washing machines, when the operators have the opportunity to identify damage or debris and remove the defective glass. Besides transport damage, another cause for chipped vials can be vial washers themselves. Many washing systems use stainless steel needles to transfer the washing

Figure 2: Modern washing and depyrogenation installation featuring washing needles

media to the inside the vials. The needle enters the mouth of the vial before the washing phase begins.

To achieve high vial throughputs, rotary washers have dozens of needles and some linear washers have hundreds of needles entering the vial multiple times during the washing process. A 2cc vial can have a neck opening as small as 7mm diameter and the spray nozzles may be as thick as 4mm,

Figure 3: High Pressure Washing Jet Manifold for Vial Washing Without Needles

leaving little clearance (Figure 3). Thin needles can easily be accidentally bent during storage or installation, or misaligned during set up or service. The result is that the needle impacts the rim of the vial causing chipping to the vial mouth and glass debris. This interaction between the needle and vial occurs inside the machine during the washing process and is virtually undetectable as the vial is filled, stoppered and capped, and depending on the closure used, may not even be detected during the final inspection process.

The most advanced vial washers have eliminated the use of needles entirely, yet still achieve a 3-log reduction of particles required by the FDA during vial washing. This is accomplished by positioning a vial above the washing manifold which has precisely machined orifices to generate a high velocity water jet. This design creates a water stream that maintains its convergent nature until it impacts the base of the vial (Figure 4), ultimately eliminating the risk of misalignment and therefore the chipping and debris associated with the use of washing needles.

Summary

The use of pre-sterilised glass has inherent risks of glass particles and sterility assurance as the process is outside the drug manufacturer's control. When introducing a new washing process in-house, vial washers which do not use penetrating needles should be selected to minimise the risk of chipping glass and creating debris. Small systems are available today that fit within smaller facilities, reducing the dependence on supplies of pre-sterilised glassware.