

The Importance of Defining a Practical Performance Test for Vial Washers



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Background

In the pharmaceutical industry, containers used for injectable drugs must be clean, sterile and pyrogen free. For vials, this preparation process normally is comprised of vial washers and depyrogenation tunnels or ovens. The purpose of a vial washer is to remove particulate matter and microorganisms from the inside of vials. The ovens or tunnels are used for depyrogenation of the vials to reduce the quantity of endotoxins to an acceptable level.

Vial washers use water for injection (WFI) to remove particulate from the inside and the outside of the vials. The removal process is accomplished by dilution, however temperature and water pressure will improve the efficiency of the washing cycle through thermal expansion and flushing action during the cleaning process.

There are several methods for validating the cleaning effectiveness of washers, but all include some sort of contamination and then an evaluation of the effectiveness of the removal of the contamination. Different pharmaceutical companies have different preferences in test methods (salt tests, particulate tests or riboflavin test) but it is important to define the expected results so they are achievable and evaluate the cleaning effectiveness of the important parts of the vial.

Even though all portions of the vial will be washed, the critical portion of the vial is the surface area that contacts the product. Whether it be a log reduction of particulate or removal of all visible riboflavin, it is important to focus your challenges on the inside of the vial. Many protocols are written with the same cleaning expectation on all surfaces of the vial, or use the general terminology “inside and outside” of the vial when defining the boundaries of the challenge. This broad definition of the cleaning surfaces ignores the degree of importance between different areas of the vial.

All manufacturers of vial washers do a good job of cleaning the inside portion of the vial. There are subtle differences between different manufacturers, as some use needles to go inside the neck of the vial to get closer to the glass surface but risk chipping the vial during the cleaning process [Fig 1]. Others eliminate the use of needles and use a very small opening in a manifold to obtain high-pressure low flow rate to save WFI usage and eliminate the risk of chipping vials. All manufacturers effectively pass the different validation challenges when it comes to cleaning the inside of the vial.

Cleaning the outside of the vial is nice to achieve and will minimize the chances of re-contamination during vial movement but can be extremely challenging and sometimes impossible depending on the washing equipment. All washers capture the vial in some manner to retain its position relative to the washing media.



Figure 1 Washing needles penetrating vials

Linear Washers

Linear washers insert the vial upside down within a bucket [Fig 2] or basket to position the vial so the washing needle, which is on a vertical moving carriage, can enter the mouth of the vial from underneath. All outside cleaning should be accomplished by a spray nozzle that is located directly above the base of the upside down vial [Fig 3]. The sides of the vial get no direct impact from this spray and the shoulders of the vials are extremely challenging to clean.



Figure 2: Loading linear washer buckets with vials

Rotary Carriage Style Washers

There are two different types of rotary washers. SP i-Dositecno [Fig 4] and Calumatic use a carriage to capture a group of vials and rotate the vials into an upside down position. A custom spacer [Fig 5] block maintains the centering of the vials over a spray tube. The spray tube has dedicated orifices that line up with the openings of the vials and effectively clean with minimal WFI usage. There is no risk of chipping the mouth of the vial, as there are no moving nozzles with these types of rotary washers [Fig 6].

Two external spray washers per station are angled at 30° towards the position of the vial. There is some clearance between the carriage and the vials to allow a better chance for external washing of the shoulder but depending on the vial profile, the shoulder may not be 100% cleaned sufficiently to remove all of the riboflavin [Fig 7].

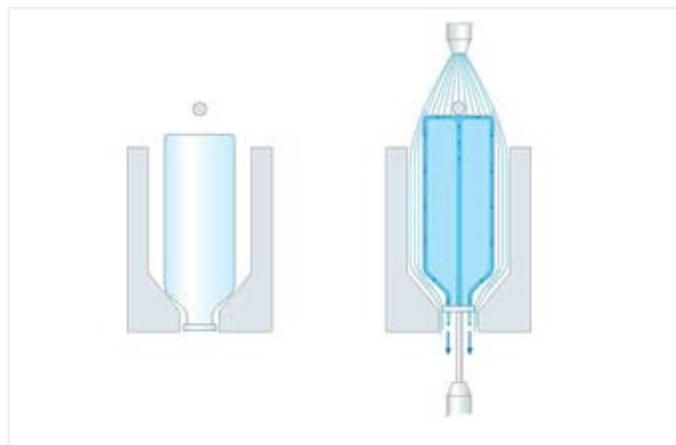


Figure 3: Illustration of washing the external surface of a vial on a linear washer

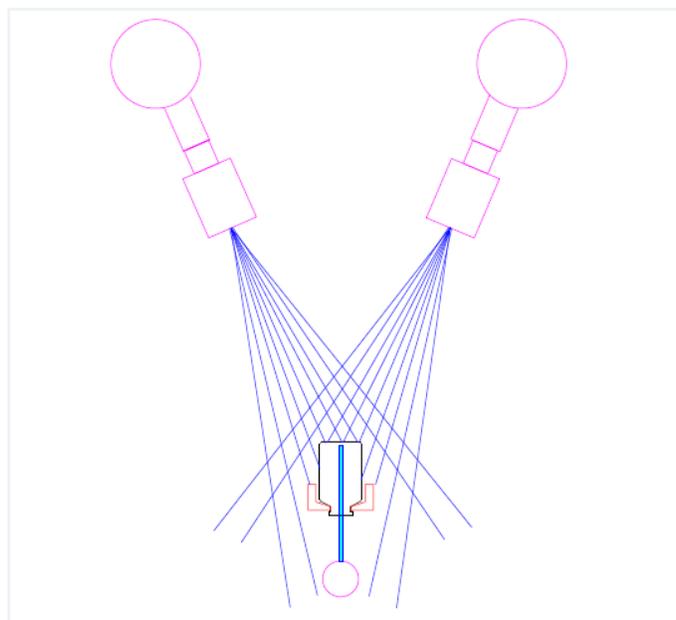


Figure 7: SP i-Dositecno washing of external surface of the vial



Figure 4: SP i-Dositecno rotary washer

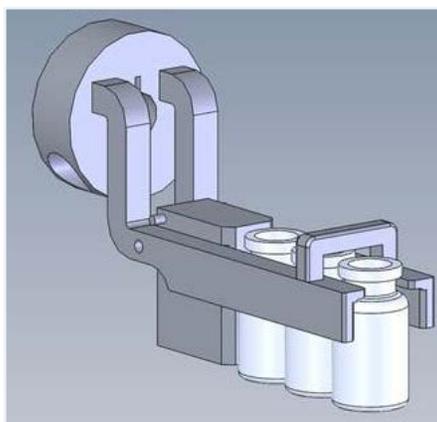


Figure 5: SP i-Dositecno rotary washer cassette supporting vials washing

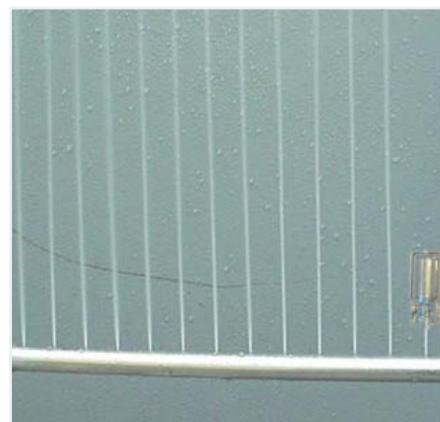


Figure 6: SP i-Dositecno rotary washers spray pattern without washing needles

Rotary Circumference Washers

The second type of rotary washer [Fig 8] captures the vial or ampule in grippers around the neck. A single line of vials moves around the circumference of the machine to progress through the cleaning process. The grippers rotate the vials 180° to align with moving nozzles that enter the vials for internal cleaning. The external washing nozzles have direct exposure to all the outside vial surfaces except for under the grippers, which will never see any water or cleaning affect [Fig 9].

Conclusion

We all want to demonstrate the quality of our pharmaceutical processes. However, through risk mitigation, we can evaluate the process from a practical perspective and only challenge the effectiveness of those portions of the process that protect the product quality and safety.

In other words, in any washing challenge, it is important to aggressively challenge the washing process of the internal surfaces of the vial but have a more lenient standard of acceptance for the outside of the vial which is not really considered a product contact surface.



Figure 8: Rotary style washer with grippers

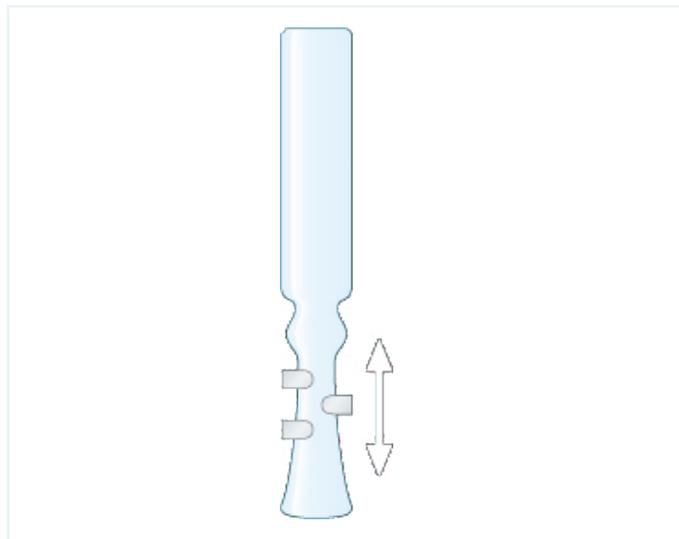


Figure 9: Washing will never occur beneath grippers hold vials or ampules