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Make the right container choice

Products used in critical environments need to conform to the accepted standards of cleanliness, in order to ensure valuable products contained within maintain their integrity and do not become compromised. Even the smallest quantities of foreign materials can render batches unusable, something which has significant implications in terms of both time and cost. As such, it is vital that users understand the different cleanliness standards and select the best containers to meet the demands of their application.

There are a number of factors to be taken into consideration when selecting containers for use within a critical environment. In order for companies to internally process the containers and other materials that conform to the required levels of cleanliness, they need to have sufficient time, money, and expertise, which can be lacking. This is why outsourcing is often a more viable option.

The meaning of clean

There are numerous terms and complexities surrounding cleanliness that make it naturally challenging to ensure a comprehensive understanding. The main drivers behind selecting a particular product are often around levels of particulates and pyrogens, but there are other factors that often need clarification. For example, does irradiating or autoclaving mean a product is sterile? Often there can be more than one answer to such a question, which is why having clear definitions of these terms is important for maintaining conditions in a critical environment. Different applications will often require different processes in order to achieve the required levels of cleanliness, as shown in Figure 1.

Clean room produced

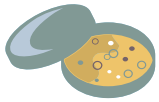
Provides a level of confidence in container cleanliness, but does not indicate any product certification

Washed

Can remove particulates and reduce endotoxins, but cannot qualify without validation

Irradiated/ autoclaved

Indicates that a process was applied, but not that the product is validated as sterile



Low particulate

Validated compliance with standards such as USP <788> indicates a qualified particulate load and is likely lot-to-lot tested

Low pyrogen

Pyrogen levels can be validated according to USP <85> and may include lot-to-lot testing

Sterility assurance

Validated sterility ensures every lot meets a sterility assurance level as defined (e.g., USP <71>), but may include lot-to-lot testing

Figure 1. Common processes associated with standards of cleanliness

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The importance of validation

One of the first factors to take into consideration when assessing container choices is validation. Having an understanding of validation of a process and its equipment (autoclaving, irradiation, washing), and the difference between this and product claim validation (e.g., sterility assurance levels, particulate levels) is key. The former builds confidence that a process is repeatable, but only the latter can confirm a quantifiable product claim can be reliably and repeatably met.

Process validation data assures users that the processes will consistently yield a product of a predetermined quality, and facilitates the validation of product claims later on. In contrast, product validation ensures it consistently meets a specific criteria or claim. For example, the presence of particulates will influence sensitive applications, which is why the United States Pharmacopoeia (USP) <788> is in place and enforced by the Food and Drug Administration (FDA). These contaminants can come from several different sources and can be dangerous if introduced into the bloodstream. As such, it is vital that particulate levels are validated across all containers used within a cleanroom environment.

The validation options selected are based on the user's choice and decision making, but the risks need to be weighed as they relate to the intended application.

Insourcing vs. outsourcing

Once the level of validation and cleanliness required has been decided, the equipment needs to be cleaned and prepared to critical-environment standards. When looking at particulate levels, this can be challenging since the processes involved require significant expertise along with an investment of both time and capital expense. In order to process containers so they are USP <788> compliant, there are several important components required:

- Dedicated facility space
- Purchase, installation, validation, and routine maintenance of autoclaves, washers, dryers, and water systems
- Protocol development
- Validation of report development
- Sourcing of base materials to be washed
- Revalidation and upkeep, as required
- Personnel to perform all processes

For some companies, performing the validation, collecting, and reviewing of all of this data can be a daunting prospect. Outsourcing can prove to be a cost-effective alternative that enables companies to ensure their containers are validated as compliant, without the need for such high levels of input, both in terms of finance and time. Vendors that offer such services inherently have in-house personnel with high levels of expertise, along with the space and equipment. Tapping into this allows pharmaceutical and biotech companies to benefit from their expertise, and to be confident in the quality of their critical-environment validation data, without the need to set up dedicated facilities themselves.

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Conclusion

It is pivotal that the equipment and materials used within critical environments are able to meet the required cleanliness demands, such as those outlined in USP <788>. Although understanding and implementing clean parameters can prove challenging, it is necessary that they are effected to ensure that product integrity is maintained. Users need to be able to select the right container and ensure it is chosen based on the application needs, not just convenience, in order to save time and cost in the long run. Highly sensitive formulations, for example, will require extremely low particulate levels in order to ensure they are safe for use. And, the only way to ensure that necessarily low levels are maintained is to undergo the correct cleaning procedures and validations, whether they be performed in-house, or outsourced to a trusted partner.

Find out more at **thermofisher.com/criticalenvironment**

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