Qualification and Validation of Disposables in Biopharmaceutical Processes

The biopharmaceutical industry has embraced the use of disposables for a variety of reasons. At smaller scales, such as in R&D and process development, the convenience of disposables has driven their use. At larger scales, where decisions are made more formally, the convenience experienced earlier translates to true economic benefits. The key drivers for the implementation of disposables have been grouped into four main categories: increased capacity, reduced time to market, reduced process risk and reduced direct costs. As driven by these factors, the use of disposables in biopharmaceutical processes has grown. With this growth, the trend has been from single use components, such as stand-alone filter capsules, tubing and flexible bags to integrated “systems” that incorporate any number of components, arriving presterilized from a supplier. These systems are now being tasked with accomplishing true process steps, rather than simply replacing a stainless tank or filter housing.

A key motivating factor often cited for the move to disposables is the elimination of validation (predominantly for cleaning and sterilization) or outsourcing to the vendor of the responsibility for validation. While this is to some extent true, processors will benefit from the model provided by the qualification and process validation of sterilizing grade filters. Sterilizing grade filters are subject to a strict set of performance criteria before they can be considered suitable to sterilize liquids within a particular process. One such criteria is that all sterilizing grade filters must pass a bacterial challenge according to an established ASTM standard method in order to qualify for a sterilizing grade application. Furthermore, as the market has evolved, so have the requirements. Sterilizing grade filters must now be accompanied by a plethora of validation data that knowledgeable filter users utilize to evaluate suitability. This is simply the price of entry to the market.

Despite all of the requirements, none of the data provided by the filter manufacturers, however, allows the processor to do anything more than make an informed selection and properly design processes and process specific validation studies. Even though the filter manufacturer provides bacterial challenge information establishing a correlation of integrity test values to bacterial retention under defined conditions, the processor still must validate bacterial retention under worst-case process conditions with the actual formulation.

The users of disposable bioprocess systems face a similar task. Quality suppliers of disposables to the biopharm industry supply an ever-growing catalog of “validation” data. But the user needs to be aware of the scope and limitations of the data presented. Does the validation data cover just the bag chamber film, a completed bag chamber, or the whole assembly? Was the data produced after irradiation and aging? How much is applicable to the users custom assembly and the conditions of use?

The data, while generally produced in a “validation,” may only serve as qualification data for the end user because the scope of the work performed may not match the requirements of a process specific validation. Careful consideration of the validation data presented by the supplier must be compared to the data required. The end user then needs to make an informed, risk-based decision of the process specific validation work to be performed for the implementation of disposables into their process.

The validation data produced for Sartorius’ Gammasart BioSystem SA line of standard filter and bags assemblies covers the entire assembly and includes physical properties, gamma sterilization, extractables with ethanol and WFI at 20 °C and 50 °C for one week, one month, six months and one year. The data also includes biocompatibility, cytotoxicity and a variety of what have become standard USP tests such as, endotoxin, particles etc. The validation protocol for each specification has been written broadly to intentionally cover the standard designs as well as a variety of custom designs and applications that may relieve the end user of some validation efforts.

Just as the industry has accepted the support of filter validations by filter manufacturers due to the specialized nature of the work to be performed, so it will be with disposable suppliers. The Sartorius CONFIDENCE® validation service is ready to serve all validation efforts required for implementation of disposables into biopharmaceutical processes. Services include gamma sterilization validation, extractables analysis, chemical compatibility, adsorption and integrity testing.

While cleaning and autoclave cycle validation efforts are no longer part of the work to be performed by a processor, the validation requirements have not been completely eliminated. Working together with a dedicated quality partner, experienced in the qualification and validation of critical processes, will ensure success.

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