Biotech

Technical Regulatory Topic

During Filter Validation, Can Pall Perform One Set of Testing to Cover Both Gamma and Steam Sterilization?

Sterile Filter Validation

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Author: Morven McAlister

Answer

Although Pall will readily accommodate specific end user requirements for filter validation testing, in accordance with the guidelines indicated in PDA Technical Report 26, Pall recommends that test filters be sterilized using the same method as used in the customer process. A filter that is gamma irradiated may produce a different extractables profile compared to a steam sterilized filter of the same membrane type and configuration. Consequently, to cover these potential chemical differences, two sets of extractables testing would be required.

Similarly, Pall recommends that two independent bacterial retention tests would be required to validate both steam and gamma sterilized filters. This is in adherence with the technical guidance of PDA Technical Report 26 which states in section 6.1 “Factors influencing bacterial retention”:

> *“…process conditions (reuse, sterilization and resterilization, temperature, pressure differential, flow rate, process time)”.*

Exposure of filter membrane to gamma irradiation has the potential to modify the surface chemistry of the membrane, which hypothetically, could change adsorptive and bacterial retention properties. PDA Technical Report 26 also states in section 4.1.1 “Revalidation” that if sterilization procedure changes revalidation may be required.[1]

Although Pall considers that bacterial retention would probably not be impacted irrespective if the filter was steam or gamma irradiated, in our experience, performing two separate studies presents the least risk of not meeting regulatory expectations. Pall is aware of at least one situation where a regulatory submission was rejected due to use of steam sterilized filters in a process-specific bacterial retention test to simulate gamma irradiated process filters. Additionally, Pall is aware of an FDA reviewer's opinion that

> *"…the test filter for retention studies should be sterilized in the same manner as the production filter."*

However, development of product-wet integrity test (PWIT) limits is not influenced by the membrane surface chemistry or adsorptive properties. Rather, integrity test measurements depend on the surface area of the filter, the membrane polymer, the wetting fluid, the pore size of the membrane, and the gas used to perform the test. As neither autoclaving nor gamma irradiation change these parameters, it is technically justified to apply the results to either a steam sterilized or a gamma irradiated filter.

The recommendations presented here are based on over 20 years of experience of Pall performing filter validation studies, participation in industry standard committees and engagement with regulatory bodies.

Based on the explanations given above, we do recommend that end-users discuss their proposed validation testing plans with the appropriate regulatory authorities prior to study initiation, when any concerns can be addressed.

References

[1] PDA Technical Report 26, "Sterilizing Filtration of Liquids. (Revised 2008)."

PALL Biotech

Corporate Headquarters
Port Washington, NY, USA
+1.800.717.7255 toll free (USA)
+1.516.484.5400 phone

European Headquarters
Fribourg, Switzerland
+41 (0)26 350 53 00 phone

Asia-Pacific Headquarters
Singapore
+65 6389 6500 phone

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