BioReliance®

Pharma & Biopharma Manufacturing & Testing Services

Application Note

Drug Product-Based Integrity Testing to Establish Product/Filter Test Specification Value

Our integrity test specifications are accurate and reliable. We test filters wet with standard wetting fluids (water for hydrophilic filters and alcohol for hydrophobic filters) that are ideal for pre-use integrity testing.

Our Efficient Approach

After use, the filter is still wet with the process fluid (drug product) that it filtered. Most drug products have a surface tension that differs from that of the standard wetting fluid. In most cases, this alters the integrity test results. Likewise, process fluid that tends to increase bubble point may cause a faulty filter to pass. To minimize delays in production and product release caused by these false test results, we conduct drug product-based integrity testing.

Our experience has also proven that it is ineffective to determine product bubble point values by simply using a surface tension ratio and mathematical calculation. Variables such as the wetting contact angle can affect integrity test (bubble point and/or diffusion) values. To account for this, we do physical integrity tests to determine the product-based value.

Our Validation Specialists perform water and product integrity testing on filters to establish the water/product integrity ratio. The ratio is then used to calculate the acceptable integrity test value for filters wet with process fluid.

We have developped two levels of testing, based on:

- 1 product lot: fits for purpose, usable for the majority of pharmaceutical drug products
- 3 product lots: recommended when formulation contains surface active ingredients or very low alcohol concentrations or when product to test are not from the manufacturing line.

What You Need to Know to Begin

- How many lots of process fluid you would like to test, and when?
- Do you have an SDS for the candidate test solution?
- Is this a controlled drug? If so, what are the classification and code?
- Test is designed to model key process parameters:
  - What are the room and fluid temperatures?
  - What is the test gas?
- What is the filter catalog number?
- What are the integrity tests used for batch release? Bubble point? Diffusion? Both?

Product-Based Integrity Ratio Testing is Required When…

- Product is not or cannot be rinsed off of the filter prior to measuring the integrity value
- The filter is sterilizing grade with a sterilizing claim

Test Approach

Testing begins once you sign our standard test protocol, and we approve it.

Testing is conducted on our sterilizing-grade membrane discs or filter devices with a minimum of 200ml of process fluid, and following your key process parameters.

Upon completion of testing, we analyze the data to ensure stable and reproducible results among the test replicates.

We will send you a standard report summarizing testing data.

This scale-down study will provide you a reference for your Drug Product-based Integrity Testing Specification Value.

It is recommended to verify the data under normal manufacturing conditions, as an in-process confirmation using large scale filters.

Our highly experienced, industry-leading team of scientists will:

- Determine the correct testing for your process and customize test systems
- Cut costs by using the least amount of product necessary
- Provide accurate test protocols and reports
- Maintain raw data files
- Ensure confidentiality

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Why Integrity Testing is Important

To ensure product sterility and regulatory compliance, membrane filters must be integrity tested after filtration of a drug product. Integrity testing ensures that the correct pore size filter was used, the filter was installed properly, and the filter was defect free. Integrity testing is highly dependent on the physical characteristics of the wetting solution, and even small changes to the test solution can substantially alter integrity test results. When physical characteristics of the process fluid alter integrity test results, there are two options available. The process fluid must either be completely flushed out to fully wet the membrane with a solvent of known integrity test values, or the effect of the drug product on integrity test results must be determined. Completely flushing the process fluid from the membrane can be time-consuming and costly. Additionally, some components may bind to the membrane regardless of the volume passed through the filter, and not readily flush out. Integrity tests are quicker, less expensive, and yield more reliable results.

Regulatory Compliance

Filter integrity testing is a critical step in the manufacturing of sterile drug products and is required by regulatory bodies worldwide. The United States Food and Drug Administration's Guideline on Sterile Drug Products Produced by Aseptic Processing recommends post-use integrity testing to check for leaks or filter damage. PDA's Technical Report 26 further outlines the test methods. Our testing entirely complies with these guidelines.

Ordering Information

We encourage you to audit our worldwide laboratory facilities. Let our years of filtration and process optimization experience save you time and resources. We have committed Validation Specialists in our BioReliance® Validation Laboratories located in the U.S., Brazil, Europe, India, China and Japan.

Contact your local BioReliance® Validation Laboratory or sales representative for the request form. The scope of your project will be then determined and a quote provided accordingly. Let us help you get your product on the market!

References

Filter Integrity Tests

Bubble Point	Diffusion	Bubble Point and Diffusion
Level 1: 3 filters from 1 lot/ 1product lot		
VSERVBUP1	VSERVDIF1	VSERVENH1
Level 2: 9 filters from 3 lots/ 3 product lots		
VSERVBUP2	VSERVDIF2	VSERVENH2

Additional information on in-process IT confirmation: Establishing product specific bubble point values for sterilizing grade filters (AN1505EN00)

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