BIOTECH

Application Note

USD 3593

Identifying False Failures Using the Water Intrusion Test

A Decision Tree to Help Correctly Identify Non-Integral Sterilizing Grade Gas Filters

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1 Introduction

Sterilizing-grade gas filters play a critical role in the maintenance of sterile boundaries in pharmaceutical processes by preventing the movement of microorganisms into or out of systems whilst allowing pressure equilibration as fluids fill or empty vessels. Such filters incorporate hydrophobic membranes to prevent wetting during operation in humid environments, which would cause a subsequent loss of filter performance. Despite being an intentional design characteristic of sterilizing-grade gas filters, the membrane's hydrophobicity makes filter integrity testing more challenging as the widely accepted bubble point (BP) and forward flow (FF) tests rely upon a filter membrane being wetted out to establish the filter's integrity. One method employed to overcome the non-wettability of these hydrophobic membranes with water is to use an organic solvent, such as isopropyl alcohol, mixed with water. This does, however, introduce a potential contaminant to the system meaning the tests become unsuitable for performance *in situ*. It also means that, if the test is performed pre-use, a flushing and drying period must be implemented, adding time and complexity to filter installation.

An alternative strategy is to employ the water intrusion test (WIT) which utilizes the hydrophobicity of the filter membrane to establish the filter's integrity. In a WIT, only water and a gas, such as air or nitrogen, are used as test media meaning that the filter does not need to be flushed and dried post-test. Furthermore, the WIT only requires the non-sterile side of the filter to be exposed to these test media. This means that the filter can be tested *in situ* as only a negligible amount of water will cross the membrane of any integral filter into the system.

Studies have shown that the basis of the WIT is the evaporative loss of water through the filter membrane.[1] A number of factors which have been shown to influence this evaporation and/or which cause an additional passage of water through the membrane can induce a failure reading from the WIT due to such an additional water loss during the WIT. Care needs to be taken to avoid incorrect assessment of the filter integrity and to identify these false failures using the WIT[2]. The decision tree shown in this document establishes a logical procedure that an end-user can consult when utilizing the WIT as their integrity test method for sterilizing-grade gas filters.

2 Considerations

The following factors and system characteristics need to be taken into special consideration when a failure result is obtained using the WIT method. Each step is numbered and subsequently shown in the decision tree to identify at which step it is relevant:

2.1 System Leaks

The water flow during the WIT measurement of an integral filter device is extremely low so that even small leaks within the system on the upstream side of the filter, can have a significant effect on the measured water flow during the test. Care should be taken to ensure that any valves and connections used between the integrity test device and the filter housing or in the test system to ensure closure of the non-sterile side of the filter assembly are gas tight prior to and during testing.

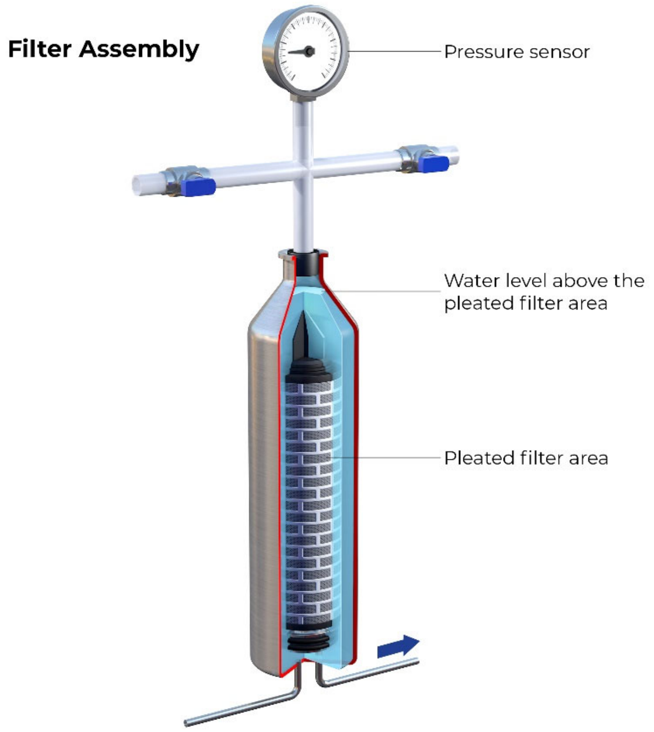
2.2 Filter Orientation

The filter capsule or cartridge housing must be in the vertical (upright) position as shown in

Figure 1. This ensures that the water level within the filter is above the highest visible pleated part of the filter. If the water level drops below this point, dry parts of the membrane become exposed to compressed gas allowing the bypass of air through the exposed parts of the membrane resulting in WIT failures.

Figure 1

Typical set up for the water intrusion test, highlighting the correct water fill level

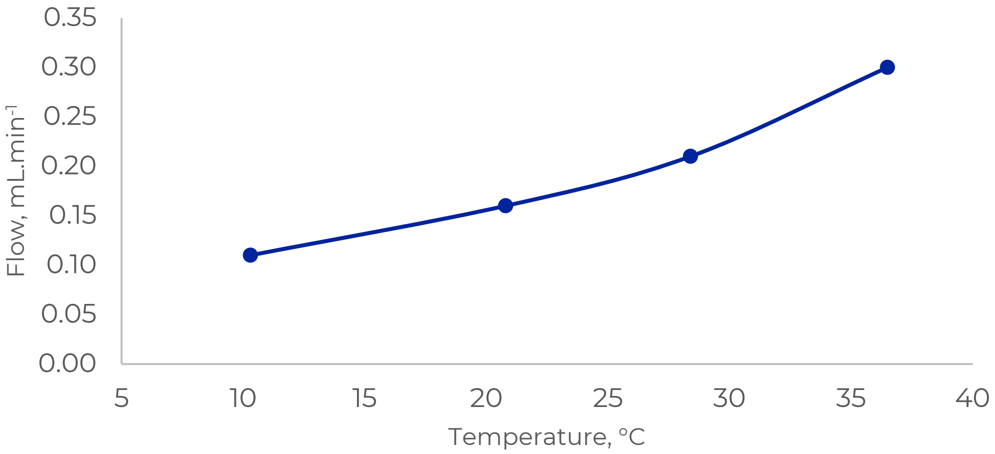


2.3 Test Medium Temperature

The WIT relies on the evaporative flow of water across an integral membrane at a temperature of between 18 and 24 °C[1]. The graph in Figure 2 shows the relationship between temperature and evaporative flow. As the temperature increases more water will evaporate appearing as an increase in water flow through the membrane. It is therefore important that the temperature of the test fluids does not vary by more than 1 °C during the test.

Figure 2

Relationship between temperature and evaporative flow across a typical hydrophobic membrane

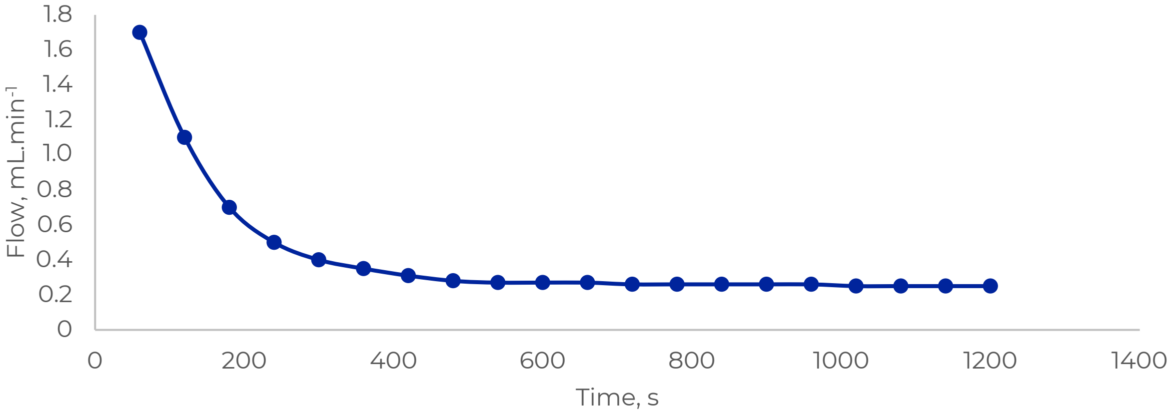


2.4 Stabilization Period

During the WIT, the upstream side of the filter assembly is filled with water and a test gas is applied against the water to increase the pressure acting upon the membrane. Pressurization of the upstream system with compressed air will lead to small system instabilities due to temperature effects (temperature increases with pressurization), pleat compression (as the filter is compressed) and dissolution of air in the water phase. These effects will initially result in higher test gas flow rates being measured, which subsequently decreases with time until it stabilizes at a constant low flow rate, identifying an integral filter. An example of the decrease of flow to a stabilized rate is shown in Figure 3. If at the end of the WIT a decrease of the water flow is still visible at rates higher than the limit value, then the test time should be extended, and the test repeated to make sure the test system pressure has an opportunity to stabilize.

Figure 3

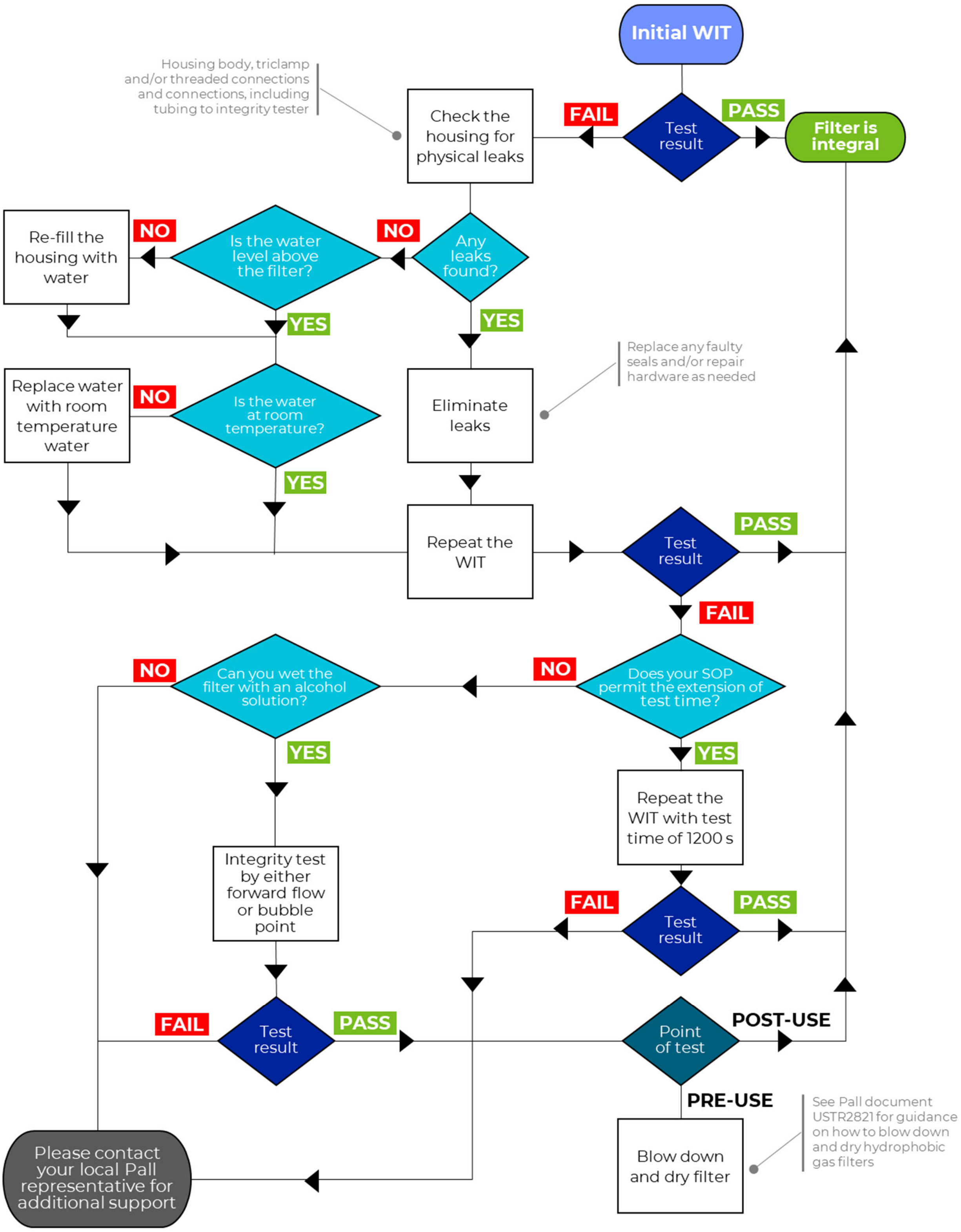
Typical gas flow measurement curve observed during a WIT



2.5 Alternative Test Methods

The WIT relies on the membrane being completely hydrophobic. In certain circumstances the membrane can become wetted out if water or the product comes into contact with it for a prolonged period of time and/or if the surrounding temperature is elevated. This can cause water to pass through the membrane at the WIT pressure resulting in test failures. In such cases, the membrane may be wetted with a low surface tension fluid (such as 60 - 70% isopropyl alcohol in water) and tested using either forward flow or bubble point test method as described earlier in this document.

3 Decision Tree



4 Summary and Recommendations

Whilst the WIT can be challenging as a result of the low water flows typically being measured, it holds a relevant place amongst other test methods due its ability to test hydrophobic filters without the use of alcohol solutions. Using the WIT can save time and money by following the decision tree shown in this document in order to confirm whether a filter failure result is true or false in order to make a correct assessment of the filter integrity.

5 References

1. R. Jaenchen *et al*., "Studies on the Theoretical Basis of the Water Intrusion Test (WIT) USTR2047", Pall Corporation (2002)

2. I. Johnson, M. Cardona, "Best Practices for Successful Integrity Testing using the Water Intrusion (WIT) Method USD 3033", Pall Corporation (2015)

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