Filter Validation Protocol

Agilent 850-DS Dissolution Sampling Station

Technical Overview

The Agilent 850-DS Dissolution Sampling Station is optionally equipped with a filtering option that greatly improves dissolution sample processing through the use of innovatively designed filter plates. The Whatman™ 850-DS 8-Channel Filter Plates from GE Healthcare, are consistent with filtration membranes and housing materials currently used for dissolution sampling. The only differences between traditional luer-type syringe filters and the filter plates are the absence of the luer fittings, and eight disks are incorporated on a flat plate. The compact arrangement of the filters on the plate also make it much easier for the automated equipment to process and filter samples over traditional automation-ready filters.

To minimize the effort that your laboratory would have to invest to evaluate and validate the new filter plates, the following is an example of a filter validation. It is a straightforward procedure and it should be maintained with your method validation documentation. The filter validation protocol includes filter selection guidance, as well as three tests to challenge the filter's efficiency, adsorption and leachability.

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Filter Validation Protocol

Filtration is an essential component of the dissolution test. The dissolution process stops at the moment that a sample is withdrawn and immediately filtered. The sample, once clarified of solid particles and excipient material, is now ready for the second phase of the test—analysis of the filtered sample.

This analysis is generally performed by a UV-Vis spectrophotometric or HPLC procedure. Additionally, filtration is needed to alleviate potential blockage of HPLC column inlets, caused by particulates and excipient matter from sample solutions, that ultimately results in reducing the normal lifetime of the column.

Filter selection

Selecting the correct filter material is quite simple. Depending on your method, you will typically use glass fiber or membrane filters for HPLC anlaysis. Table 1 provides information on the four types of filters that can be used with the 850-DS for automated filtration of dissolution samples. The table also cross references the corresponding 25 mm luer lock individual syringe filters that may be used for the validation tests mentioned below.

Filter tests

Whether a dissolution method is performed manually or automatically, the filter must be challenged in three primary areas:

- efficiency
- leachability
- adsorption

If a filter is being qualified as an equivalent filter for an existing method, the efficiency challenge may be omitted unless the pore size of the filter has changed. If excessive absorption of the active drug occurs, excipient interference is high, or filters become clogged, alternative filters may be required.

Table 1. Whatman 25 mm syringe filters, corresponding filter plates, and recommended applications.

Item description	Whatman 25 mm Individual Puradisc Filter part numbers	Whatman 850-DS 8-Channel Filter Plate part numbers (8 filter disks/plate)	Recommended application
PTFE membrane filter, 25 mm, 0.45 µm	6784-2504 (50/pk) 6785-2504 (200/pk)	7707-3000 (50/pk)	Chemically stable and inert, suitable for acidic aqueous solutions
Nylon membrane filter, 25 mm, 0.45 µm	6750-2504 (50/pk) 6751-2504 (200/pk)	7707-3100 (50/pk)	Robust hydrophilic membrane for applications where protein binding is not critical
Polyethersulfone (PES) membrane filter, 25 mm, 0.45 µm	6781-2504 (200/pk)	7707-3200 (50/pk)	Hydrophilic, low protein binding membrane recommended for aqueous samples
Glass fiber (GMF) filter, 25 mm, 0.7 µm*	6825-2517 (50/pk) 6825-2527(200/pk)	7707-3300 (50/pk)	The standard for difficult-to-filter samples to retain coarse particles; also, a good filter for gelatinous capsules

*Retention rating rather than pore size.

Efficiency test

Filters used in the dissolution method must be sufficient to stop the dissolution process. The efficiency of the filter is its ability to remove undissolved active pharmaceutical ingredient (API) from a sample solution. See Figure 1.

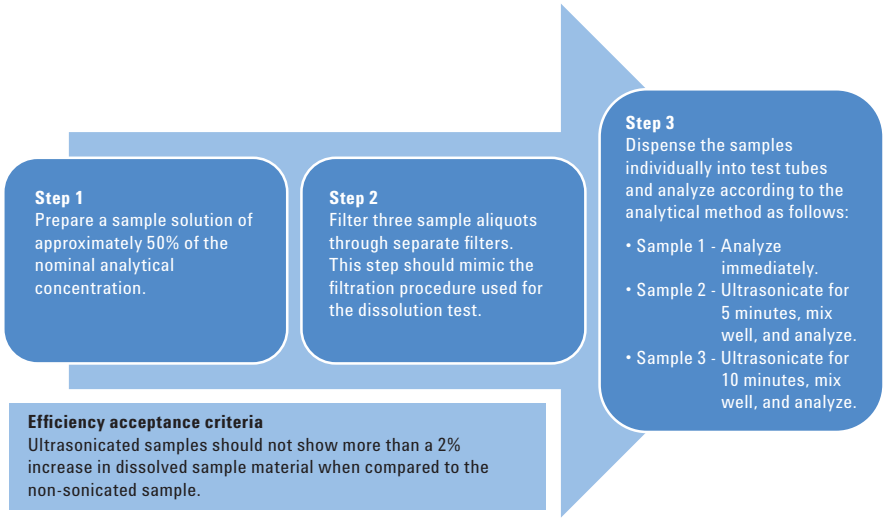

Figure 1. Typical efficiency test.

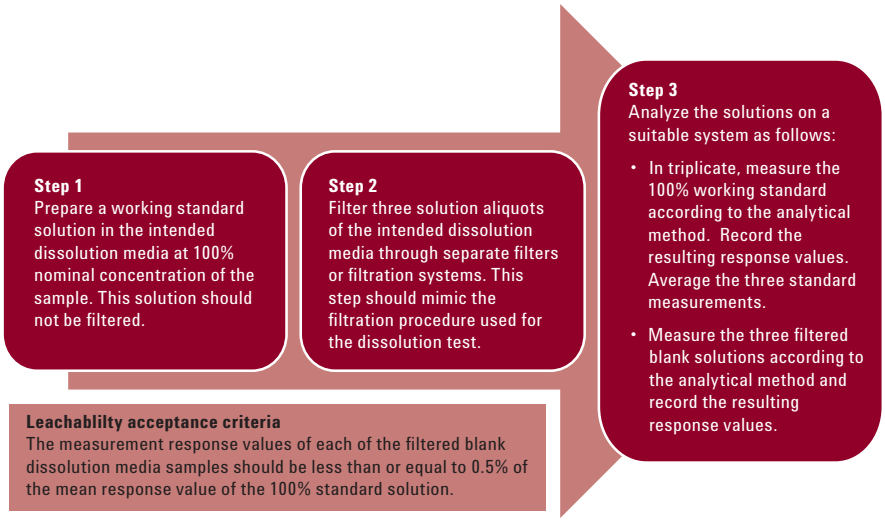

Figure 2. Typical leachability test.

Leachability test

Filters used to clarify samples must not contribute to the UV spectra at the wavelength of measurement. Additionally, leachable substances must not affect the quantitative integrity of dissolved active pharmaceutical ingredient (API). See Figure 2.

Adsorbance test

Filters used to clarify dissolution sample solutions should not adsorb dissolved API material onto their surfaces. Membrane technology typically adsorbs drug product onto the surface of the membrane. The extent of this adsorbance must be challenged. The final method should state that a specific volume be discarded prior to collecting the sample for analysis. The unique challenge with dissolution is that the initial sample of a typical dissolution profile may only be 20% of the final concentration at 100% of label claim (% LC). For this reason, a working standard should be made with the nominal concentration of the first timepoint. It will take more of this concentration to condition the filter with active drug. For example, if you have to flush 3 mL through a filter at 100% of label claim, you may have to flush 15 mL through the filter to condition it at around 20% of label claim. See Figure 3.

Table 2. Typical adsorptivity test data.

Aliquot no.	Total volume filtered (mL)	% Recovered
1	1	80*
2	2	90*
3	3	95*
4	4	98*
5	5	100*
6	6	100
7	7	100
8	8	100
9	9	100
10	10	100

*In this example, the first 5 mL must be discarded prior to sample collection.

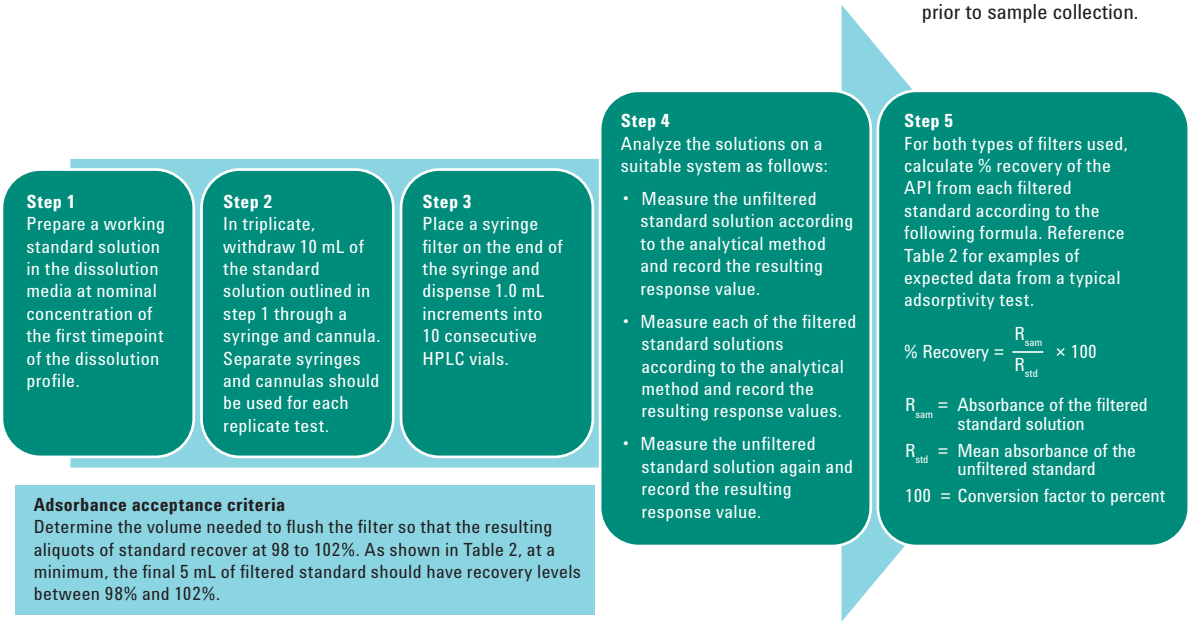

Figure 3. Typical adsorptivity test.

Filter Validation Summary

Although validated dissolution methods may contain a filter statement such as "Whatman 25 mm Puradisc filters, or equivalent," this generally covers the use of alternative generic filters that were originally validated. In the case of the filter plates with eight individual filters that were co-developed by Agilent and GE Healthcare, the filter should be considered as an equivalent to the individual 25 mm Puradisc filters outlined in Table 1.

The decision of equivalence rests solely with the interpretation of the end user and in the event further validation is warranted, Agilent offers this filter validation to supplement the adoption of the Whatman filter plates designed for the 850-DS. The filter plates are designed to group the filters in a single manageable plate for ease of use and automation. Only the outer physical appearance was modified to a plate design and the internal product and contact components of the Puredisc filters remain unchanged.

Whatman filters and filter plates are supplied by authorized GE Healthcare representatives worldwide. Each filter plate consists of eight individual 25 mm filters configured for use with the Agilent 850-DS filter changer option. Agilent recommends using each filter plate for a single timepoint to avoid clogging and potential carryover issues.

Should you have questions regarding this protocol or the suitability of these filter plates in your dissolution testing, please contact the Agilent Dissolution Hotline at **dissolution-hotline@agilent.com**.

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