Whatman™ Roby syringe filter validation kit

cytiva

Introduction

Filtration is an essential step in the dissolution process. When a sample is withdrawn from the dissolution vessel and is immediately filtered, the dissolution process stops. The sample, once clarified of solid particles and excipient material, is now ready for the second phase of the test: the analysis of the filtered sample – generally performed by a UV-Vis spectrophotometric or HPLC procedure.

The filtration step seperates the dissolution phase from the analytical phase of the dissolution assay. Additionally, filtration is needed to prevent potential blockage of HPLC columns and components caused by particulates and excipient matter from sample solutions. Failure to filter samples may ultimately lead to instrument downtime and reduce the normal lifetime of the column.

Filter performance for dissolution testing must be investigated in three primary areas: efficiency, adsorption and leachability. If a filter is being qualified as an equivalent filter, the efficiency test may be omitted unless the pore size of the replacement filter is different to that of the qualified filter.

Filter selection guide

The filter validation kit simplifies filter media selection. The test kit contains five different types of Roby filters (see table). With an easily performed manual test you can determine which Roby filter gives the best result.

The filters are divided into 3 categories:

- Glass fiber filter media (depth filter)
- Membrane filter media (surface filter)
- A stack of membrane plus glass fiber prefilter (depth filter followed by surface filter)

Use a depth filter when the dissolution media contains a large amount of coarse particulates. Start the validation with Roby 25/GF 92. For the filtration of dissolved gel capsules we recommend a Roby 25/GF 55.

Use a surface filter when the amount of coarse particulates in the dissolution media is low. Start the validation with the highly versatile Roby 2/0.45 RC.

Use a combined depth and surface filter when a standard depth filter does not provide a clear filtrate and/or a surface filter gets clogged. Start the validation with Roby 25/0.45 RC – GF 92.

Category	Filter material	Product name	Pore size	Recommended application
Depth	Glass fiber filter GF92	Roby 25/GF92	> 1.0 µm	The standard filter for samples with large amounts of coarse particles
Depth	Glass fiber filter GF55	Roby 25/GF55	~ 0.7 µm	The preferred filter for gel capsules
Surface	Regenerated cellulose membrane (RC)	Roby 25/0.45 RC	0.45 µm	The filter of choice for HPLC analysis Very low protein binding, better than PVDF Very low extractables
Surface	Polyamide/Nylon (NYL) membrane	Roby 25/0.45 NL	0.45 µm	Robust membrane for applications where protein binding is not critical
Combined depth and surface	Glass fiber prefilter plus membrane	Roby 25/0.45 RC-GF92	0.45 µm	When a membrane filter (surface filter) gets clogged and a glass fiber filter (depth filter) alone is not sufficient.

Follow the three described test procedures on pages 4–5 to find the best filter for your application.

Efficiency challenge

The efficiency of a filter for dissolution testing is its ability to remove undissolved active pharmaceutical ingredient (API) from a sample solution.

Typical efficiency test:

- Prepare a sample solution of about 50% of the nominal analytical concentration.
- Filter three sample aliquots through separate filters – this step should mimic the filtration procedure used for the dissolution test.
- Dispense the samples individually into test tubes and analyze according to the analytical method as follows:
  - Sample 1 – analyze immediately.
  - Sample 2 – ultrasonicate for 5 minutes, mix well and analyze.
  - Sample 3 – ultrasonicate for 10 minutes, mix well and analyze.

Acceptance criterion:

Ultrasonicated samples should not show more than a 2% increase in dissolved sample material when compared to the non-sonicated sample.

Leachability challenge

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 API.

Typical leachibility test:

- Prepare a working standard solution in the intended dissolution media at 100% nominal concentration of the sample. Do not filter this solution.
- Filter three media solution aliquots through separate filters. This step should mimic the filtration procedure used for the dissolution test.
- Analyze the solutions on a suitable system as follows:
  - In triplicate, measure the 100% working standard according to the analytical method. Record the resulting response values. Average the three standard measurements.
  - Measure the three filtered blank solutions according to the analytical method and record the resulting response values.

Acceptance criterion:

The measurement response values of each of the filtered dissolution media samples should be less than or equal to 1% of the mean response value of the 100% standard solution.

Adsorbance challenge

Filters used to clarify dissolution sample solutions should not adsorb dissolved API material onto their surfaces. Membranes typically adsorb drug products onto the surface of the membrane. The extent of this adsorbance must be determined. The final method should state that a specific volume should be discarded prior to collecting the sample for analysis.

As this test requires analysis of unfiltered sample, we recommend UV-VIS spectography.

Typical adsorptivity test for membrane syringe filters:

- Prepare a working standard solution in the dissolution media at the lowest nominal concentration of the sample. For example, if the expected results of first dissolution time point is approximately 25% of the label claim, then a working standard at 25% of label claim should be used for this study.
- In triplicate, withdraw 10 mL of the above standard solution through a syringe and cannula or other equivalent method. Separate equipment should be used for each replicate test.
- Place a syringe filter on the end of the syringe and dispense 1 mL increments into consecutive cuvettes.
- Analyze the solutions by UV-VIS spectography as follows:
  - Analyze the unfiltered standard solution according to the analytical method and record the resulting response value.
  - Analyze each of the filtered standard solutions according to the analytical method and record the resulting response values.
  - Analyze the unfiltered standard solution again and record the resulting response value.
  - Calculate % recovery of the API from each filtered standard according to the following formula:

$$\% \text{ Recovery} = \frac{R_{sam}}{R_{std}} \times 100$$

Where:

R_{sam} = Adsorbance of the filtered standard solution

R_{std} = Mean adsorbance of the unfiltered standard

100 = Conversion factor to percent

Acceptance criterion:

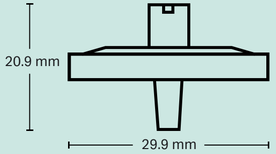
Determine the volume needed to flush the filter so that the resulting aliquots of filtered standard recover at 98% to 102%. At a minimum, the final 5 mL of filtered standard should have recovery levels between 98% and 102%.

The following is an example of the type of data typical of this test:

In this example, the first 3 mL are required to flush the filter and must be discarded prior to sample collection.

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

Roby 25 syringe filters – technical data

Max. operating pressure psi	Max. operating temperature °C	Effective filter area cm²	Hold-up Inlet after air purging µL	Inlet	Outlet	Dimensions (mm)
100	60	4.2	≤ 50	Luer-lock inner cone (female)	Luer (male) shortened	

Roby 25 syringe filters – ordering information

Catalog number	Description	Diameter (mm)	Pore size (µL)	Membrane/housing	Connection in/out	Color code	Quantity/pack
10 463 803	Roby 25 NL	25	0.45	NYL/PP	FLL/ML	yellow	200†
10 463 802	Roby 25 NL	25	0.45	NYL/PP	FLL/ML	yellow	1000
10 463 806	Roby 25 RC	25	0.45	RC/PP	FLL/ML	translucent brown	1000
10 463 809	Roby 25 RC-GF92	25	0.45	RC-GF/PP	FLL/ML	brown	200†
10 463 808	Roby 25 RC-GF92	25	0.45	RC-GF/PP	FLL/ML	brown	1000
10 463 814	Roby 25 GF55	25	0.7	GF/PP	FLL/ML	natural	200†
10 463 815	Roby 25 GF55	25	0.7	GF/PP	FLL/ML	natural	1000
10 463 801	Roby 25 GF92	25	> 1	GF/PP	FLL/ML	natural	200†
10 463 800	Roby 25 GF92	25	> 1	GF/PP	FLL/ML	natural	1000
10 463 898	Filter Validation Kit*	25	–	–	FLL/ML	–	125

* *Filter Validation Kit includes:*
Roby 25/GF92; Roby 25/GF55; Roby 25/RC; Roby 25/RC-GF92; Roby 25 NL (5 tubes of 25 pieces each)

† *8 tubes with 25 pieces each*

GF – Glass fiber
PP – Polypropylene
NYL – Nylon
CA – Cellulose acetate
RC – Regenerated cellulose
FLL – Female luer lock
ML – Male luer

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