

# Considerations for Selecting the Best Filtration Devices in Analytical Sample Preparation

*Filtering analytical samples and mobile-phase solutions using the correct filtration device is an economical way to reduce instrument downtime, maintenance, and associated costs.*



**Richard Pearce**  
Life Science Consultant

## **LCGC: Why is filtration used in analytical chemistry sample preparation?**

**PEARCE:** The purpose of filtration in analytical sample prep is to remove any particulate contamination that could impact the integrity of the analytical instrument. With a high-performance liquid chromatography (HPLC) instrument, for example, particulate contamination could cause blockages or wear and tear to parts of the system, the pump, the injector port, tubing, or even the detector.

Filtration is important for protecting those parts but also for protecting the column. Effective filtration can prevent particulate contamination from blocking the flow path within a chromatography column, prolonging the life of the column, and prevent the premature replacement of the column—basically filtration protects the instrument and the column, and it prevents system downtime and reduces maintenance costs. However, above all, it ensures the integrity of the testing, preventing noisy baselines and ensuring clear resolutions, which gives analysts clear, accurate, consistent results.

## **LCGC: What are some of the important considerations when you're selecting a filter to use for sample preparation?**

**PEARCE:** There are several factors to consider. First, the application and type of analysis. Pall, for example, offers syringe filters that are designed and certified for use in HPLC, liquid chromatography-mass spectrometry (LC-MS), and ion-chromatography applications. The type of analysis will help determine the pore size, the filter needed to effectively protect both the instrument and the column.

For example, if you're using a column with 3.0 µm packing, then the flow path will be 0.43 µm. Therefore, you need a 0.2 µm filter to prevent particulate from plugging that column. Typically, when using an HPLC column, a 0.45-micron filter will offer effective protection; however, if you're using an ultra-HPLC (UHPLC) column with a much smaller packing size, then it's better to use a 0.2 µm filter with a smaller pore size.

Second, how are you going to handle the filter? Will it be used manually, or will it be used in an automated-handling system? For dissolution testing, for example, the filter system must be compatible with the auto-handling system you're using.

And third, the filtration device needs to be chemically compatible with the sample. Chemical compatibility is influenced by more than just the membrane; the filter that houses the membrane and other construction materials used within the device need to be considered.

Pall offers a range of different membrane types based on the type of sample and solvent mix. Within their portfolio, they offer water-wettable polytetrafluoroethylene (PTFE). This is a good membrane because it's chemically compatible with most standard solvents, including both aqueous and aggressive organic solvents. This makes membrane selection more simplistic during method development and validation processing.

Sponsored by



Next, sample volume needs to be considered. How much sample do you have? This is important because many times there isn't a lot of sample available. There is a range of filtration devices that have different sizes and filter diameters based on the volumes of sample you're using. Users tend to think about the diameter of a device, but manufacturers use slightly different sealing mechanisms when making filtration devices, so it's important to look at the effective filtration area (EFA) of a filter. This is the amount of filter material that's exposed to the sample when filtering, so the larger the EFA, the larger the sample throughput; and the larger the device, the larger the EFA, so the greater the throughput, which makes filtration a lot easier. The flip side is if you're using a larger device, then the hold-up volume—the amount of sample that gets trapped in the device during filtration—will be greater. So, if you're filtering a small amount of sample, you have to account for the hold-up volume to ensure you're getting enough of your filtrate to do your analysis.

In summary, when selecting a filter, there are a number of things to consider: the application and analysis type, the pore size needed to effectively protect the system and column and how you're handling the filter, and finally, chemical compatibility and how much volume you have to start with.

#### **LCGC: What types of filtration devices can be used in sample-preparation applications?**

**PEARCE:** There are several filtration devices commercially available. The most commonly used for analytical sample prep is the syringe filter. They range in diameter from 4 mm - 37 mm, so they have different EFAs to suit different sample volume types. If you have a difficult-to-filter solution, Pall offers syringe filters with a built-in glass fiber pre-filter where both the pre-filter and the final membrane filter are encapsulated in one device. Pall's premium syringe filters are designed to be used manually, so with your hand and your thumb, or on automated platforms. They have designed features that ensure trouble-free operation when you're using them on a robotic system.

There are newer forms of filtration devices available as well, such as spin devices that filter under centrifuge and 96-well filter plates. These types of products are great if you have a lot of small-volume samples you want to process all at once. They feature the same membranes and construction materials as syringe filters, so you don't have to worry about revalidation.

#### **LCGC: What are extractables, and are they a concern?**

**PEARCE:** Extractables are undesirable artifacts or chemicals that can leach out of a filtration device and go into your sample. Extractables can arise from either the filter membrane or the housing—they can even come from chemicals in the product packaging, which is used to house the filtration device.

Extractable materials are a major concern for many analysts because they can jeopardize analytical results. They can cause coelution and extraneous peaks on chromatograms. Pall's membranes and devices have been tested for compatibility with common HPLC solvents—water, methanol, acetyl

nitrile, etc.—and they use established HPLC procedures to verify low levels of UV detectable extractables, ensuring the products are clean for use in HPLC. They also offer high-quality LC-MS syringe filter products that feature a certificate containing TIC chromatograms that show all the detected peaks relative to internal standards.

#### **LCGC: Are there any other quality concerns that users should consider when choosing the correct filtration device?**

**PEARCE:** In addition to extractables, binding is another quality concern: Are there analytes in your sample that could bind to your filtration device? Binding is a particular concern to researchers who are working with proteins, large-key molecules, for example. They are also a concern to analysts working in critical pharmaceutical quality control such as dissolution testing.

Pall performed an Active Pharmaceutical Ingredient (API) binding study. They've tested a variety of drug compounds having differing chemical structures, ionization properties, and molecular weights against wwPTEF syringe filters, and they have published data showing that the syringe filters have a very acceptable level of drug binding that won't give out-of-spec results. Ultimately, analysts want to ensure that they have consistency, reliability, and reproducible results, and the quality of the filtration device is key to them achieving this.

#### **LCGC: You discussed sample preparation filtration—is it also important to filter mobile-phase solutions used in HPLC?**

**PEARCE:** Yes, it is. Mobile-phase filtration is often overlooked. There is an assumption that HPLC-grade solvents can be used directly out of the bottle. However, it is as important to filter your mobile phase as it is your sample. It's never safe to assume your mobile phase is free from particulate contamination, especially if your mobile phase is a mixture that's been produced in a laboratory. It's a good idea to filter either with a 0.45 µm or 0.2 µm filter, depending on the needs of the system and the type of column being used. Also, when filtering a mobile phase, it's typically filtered under a vacuum, so you're degassing your solvent. Degassing the solvent prevents any bubble formation, which could shift baselines, create shifts in retention times, and ultimately give inaccurate data.

Some of the older style mobile-phase filtration devices were made of glass, and they were very difficult to set up and clean. Pall got around this problem by supplying the SolVac® filter holder for mobile-phase filtration. It's constructed from chemically resistant polypropylene plastic, so it's very safe to use. If you drop it, it won't break, unlike the glass setups, and it uses a magnetic seal to seal the membrane disc inside the unit. So, it's a lot easier to use compared to older glass-funnel systems.

One of the real benefits is it filters directly into your mobile-phase reservoir, so you can use it directly on an HPLC bottle, which simplifies the handling and washing steps involved. The SolVac filter holder uses a 47-mm membrane disc, and Pall provides the same selection of membranes for mobile-phase filtration as they do in all its other filtration devices.