Streamline your sample prep workflows for smarter research

Transform your sample prep workflow to enable you to focus on the science with expert guidance

THE QUEEN'S AWARDS FOR ENTERPRISE: INTERNATIONAL TRADE 2021

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Introduction

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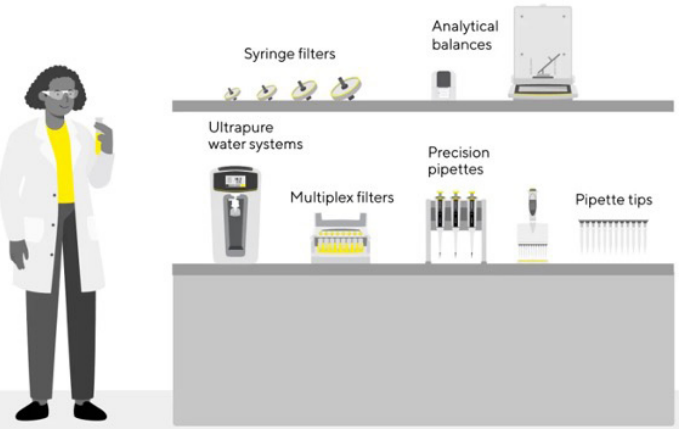


Inefficient sample preparation can disrupt even the most promising research. Whether it's inaccurate pipetting, inconsistent weighing, contaminated ultrapure water or inadequate filtration, the smallest variables can lead to unreliable results, lack of reproducibility, lost time and regulatory difficulties.

These setbacks are costly; therefore it is essential that every stage of your lab workflow is optimized. By taking a critical look at each stage of your workflow, you can prevent errors and get high quality, reproducible data the first time.

In this eBook, we tackle the common challenge in sample preparation, highlighting key technologies and simple changes you can make to ensure your workflows are reliable, efficient, and regulatory compliant.

Four steps to smarter sample preparation:

1. Reliable lab weighing

Accurate weighing is foundational to sample preparation protocols as the first step in mixing buffer and reagent stocks. Small discrepancies in measurement can impact the integrity and function of the sample, and ultimately the downstream data.

Proper maintenance is crucial for ensuring a well-functioning balance. This guide provides insights into how to select the right balance for your needs and keep it operating accurately. Key tips include daily cleaning procedures and environmental factors that can influence weighing accuracy.

Environmental factors such as drafts, humidity, and temperature can affect balance readings and lead to prolonged stabilization times. Some balances, like the Cubis® II Ultra-High Resolution Balances feature built-in systems that automatically adapt to changing lab conditions, ensuring consistent and reliable performance every time.

Another crucial consideration is compliance with the regulatory standards required by your lab. The Cubis® II, with full 21 CFR Part 11 compliance, is equipped to support current and evolving regulatory demands.

For further guidance, download your free copy of this guide from SelectScience to achieve lab weighing compliance with ease.

2. Efficient liquid handling

Pipetting is one of the most repetitive and error prone tasks in the lab. Whether you are preparing samples or reagents, it is vital to consider the

consistency and ergonomics of your pipette as they directly impact the accuracy of pipetting.

Contamination during pipetting is a significant concern for achieving reliable lab results. Common sources of contaminants include aerosols and particle suspensions, which frequently arise from routine lab activities. This guide addresses three types of pipetting-related contamination:

- Pipette-to-sample contamination,
- Sample-to-pipette contamination,
- Sample-to-sample contamination

– and discusses strategies for avoiding each.

Labs also face growing demands to increase throughput, requiring tools that improve workflow efficiency. Efficient pipettes that are easy to use and integrate with existing lab systems help to streamline sample preparation workflows. The Picus® 2 electronic pipette is an example of such a solution, due to its advanced connectivity and user-friendly operation that meet modern lab needs.

Download this ultimate pipetting guide from SelectScience to learn how to optimize your pipette workflows.

3. High quality lab water

Water is a universal reagent, and its quality is crucial for the success of experiments. Impurities such as ions or microbial contaminants can distort results, damage instruments, and waste valuable time spent troubleshooting preventable issues.

Despite its integral role, the advantages of having a reliable and accessible source of ultrapure water in the lab are often overlooked. Centralized systems for lab water are not efficient and may fluctuate in performance, posing risks to sample preparation workflows. Systems like the Arium® Mini Ultrapure Lab Water System that provide consistent, ASTM Type 1 ultrapure water directly at the bench can simplify access to quality lab water for day-to-day operations. The Arium® Mini system has the added benefit of a compact design, easy maintenance, and real-time purity checks, providing convenience and peace of mind.

Key considerations when choosing a lab water system must include understanding the different types of lab water and establishing the best type for your application. This informative guide outlines how to choose the right water purification system for your lab.

4. Fast and effective filtration

Filtering samples before chromatographic analysis is essential for preventing instrument clogging, enhancing accuracy, and reducing sample variability. For highly sensitive tasks such as HPLC, effective elimination of particles from your samples is critical to maintaining column integrity. However, not all filters are created equal; low-quality membranes can absorb or interact with analytes, leading to sample loss and affecting accurate quantitation.

Minisart® Syringe Filters with polypropylene housings and various membrane options are designed to optimize recovery and chemical compatibility. Their high flow rates and consistent pore sizes contribute to reproducibility and safeguard sensitive analyses. This resource compares four membranes used in syringe filters, emphasizing the importance of selecting high-quality membranes for sample preparation.

How to Ensure Accurate Weighing Results in Challenging Conditions

Best practices for achieving reliable data from high-capacity analytical balances

Lab balances play a critical role in workflows, due to the foundational data for downstream analytics.

Accurate weighing results depend on:

- Selecting the right balance for your application that is highly sensitive and has the capacity for your sample size
- Cleaning and maintaining the balance to rid of debris and sample spills/leakages that affect weighing accuracy
- Securing data integration to support data integrity and compliance
- Ensuring hardware and software configurations are modular for changing needs and to future-proof purchases

Environmental factors that affect accuracy

Vibration
From other equipment or systems can change sample distribution or disrupt mechanics.

Drafts
Can interfere with balance mechanisms or cause subtle air pressure changes.

Temperature
Changes can alter properties of materials and mechanics and/or affect humidity.

Magnetic interference
From nearby equipment or magnetic samples can cause inaccurate readings due to magnets in the weighing system.

Humidity
Changes can cause evaporative water loss or condensation in the sample or vessel.

Static electricity
Can contribute positive or negative forces leading to inaccurate and/or unstable readings.

How to clean balances and why

Proper cleaning and maintenance is crucial in order to protect performance and lengthen the instrument's lifespan. Balances must be cleaned regularly due to:

- Small debris particles, like dust and hair
- Spills, whether liquid or particles, affect accuracy and pose a contamination risk.

Daily Cleaning Steps:

To remove particulates and residues

Extensive Cleaning Steps:

Performed quarterly or whenever larger spills occur

Turn the balance off or on standby, unless using the cleaning app. Gather cleaning supplies: tissues, soft cloth, soft brush, stiff brush, forceps, water, and/or 70% ethanol or other mild cleaning solution.

Important! Check the manual to confirm compatibility of cleaning solution with surfaces.

Remove weighing pan or sample holder.

Remove components as the instrument permits: draft shields, weighing pan or sample holder, and base plate.

Wipe base plate and weighing pan with a soft brush or tissue wet with water or cleaning solution.

Wipe the balance and disassembled components with brushes, wet tissue, and other cleaning supplies as needed.

Important! Use caution to prevent particulates or liquid from entering any opening. Avoid compressed air, as it can lodge suspended particles within the mechanisms.

Reassemble pieces once they are thoroughly dry.

When dry, reassemble pieces in reverse order: base plate, weighing pan, draft shields and display.

Important! Reassembling damp components can lead to instrument damage or drift from evaporation.

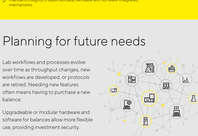
isoCAL

Run appropriate checks and tests to confirm function, including draft shield operation, leveling, and calibration.

Lab balance connectivity and data integrity

Lab digitalization requires full connectivity between analytical equipment and systems to realize the benefits:

- Paper-free workflows that eliminate manual data entry, reduce errors, transfer errors, and data falsification
- Improved data security with fully electronic data handling
- Streamlined workflows and operational efficiencies
- Increased workflow automation, removing data breaks



Data integrity measures work to further:

- Accelerate key timelines, e.g. discovery time and time to market
- Eliminate repeat work with reliable data and reporting

Maintaining compliance requires additional software considerations that center improved data handling and traceability:

- Audit trail
- Access control with personalized user and role management
- Electronic signatures
- Data backup
- Secure data transfer options for laboratory system integrations like LIMS and ELN

Balances can ensure 21 CFR part 11 compliance through:

- Technical control features
- Full user management capabilities including access control with personalized user and role management
- Customizable password and login security measures
- Electronic signatures tied to confirmation by password entry
- Comprehensive audit trail features
- Full traceability to tamper-protected raw data saved on the balance in immutable records
- Effective, secure connections to IT systems
- Maintains integrity of exported data, verifiable with software integrated mechanisms

Planning for future needs

Lab workflows and processes evolve over time as throughput changes, new workflows are developed, or protocols are retired. Needing new features often means having to purchase a new balance.

Upgradeable or modular hardware and software for balances allow more flexible use, providing investment security.

Cubis® II Ultra-High Resolution

A new generation of premium modular balances

The modern balance design offers flexible solutions to these challenges. The new Cubis® II Ultra-High Resolution adapts to changing lab conditions, allows disassembly for simplified cleaning, and is modular for future upgrades for software and hardware.

Engineering upgrades compensate for changes in temperature, humidity, and air flow, as well as static and magnetic interference to ensure measurement stability.

- Draft shield designs minimize electrostatic and disturbances by drafts
  - Optional inner draft shield
  - Conductive glass coating
- Nose generation monolithic weighing system
- Intelligent temperature management
  - Optional climate module to track environmental conditions
- Lockable built-in stirrer
- Non-magnetic titanium weighing pans and sample holders

Software-guided cleaning processes simplify cleaning with both basic and advanced options.

- Intuitive, tool-free disassembly and assembly
  - Removable display, baseplate, weighing pan, draft shields, and front glass panel
- Cleaning kit with helpful tools
- Detailed guides with users through each step with clear illustrations
- Built-in contamination prevention design, e.g. base plate with ISO-KL retention volume
- Cleaning and maintenance app
  - Helps support compliance with optional electronic signature

Full integration with LIMS and IT systems via connectors facilitates fully connected workflows.

Data integrity compliance is supported directly from the balance, which ensures correct recording, archival, and sharing of data.

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Application Note

Keywords or phrases:
Pipetting, contamination, cross-contamination, sample preparation, filter tips, sterile tips

How to Avoid Contamination in Pipetting

Introduction

Preventing contamination in pipetting is paramount to achieving reliable results. It requires identification of the potential contamination mechanisms in order that they can all be addressed.

Aerosols, suspensions of solid or liquid particles in a gas, are formed in many laboratory activities such as pipetting with air displacement pipettes, and aerosols are the major contamination source in pipetting. They may transfer into the pipette body when unfiltered pipette tips are used and consequently contaminate subsequent samples. A slow and careful pipetting rhythm helps minimize aerosol formation.

This paper addresses the three contamination types that originate from pipetting: pipette-to-sample contamination, sample-to-pipette contamination, and sample-to-sample contamination.

Pipette-to-Sample Contamination
This type of contamination occurs when a contaminated pipette or pipette tip contaminates the sample.

Pipette tips are available in multiple purity grades from most manufacturers. Purity grades can be divided into three categories:

- No purity certification
- Certified free of contaminants like DNase, RNase, and endotoxins
- Sterilized to be free of microbial life

Contaminants such as DNase, RNase, and endotoxins are difficult to remove by any sterilization method, so it is very important to prevent contamination during manufacturing. The absence of these contaminants is separately tested, usually by a third-party laboratory. Sterilization after manufacturing ensures that the tips do not contain any microbial life (bacteria, viruses etc.) when delivered to customers.

Pipette tips can also be a potential source of leachables – trace amounts of chemicals originating from materials or process equipment that can contaminate the samples. Examples of potential leachables are heavy metals, UV stabilizers, antioxidants, pigments, release agents, biocides, and surfactants. High quality tips manufactured from 100% virgin polypropylene in a high quality manufacturing facility do not contain leachables. It is recommended that you confirm this with the tip manufacturer. In daily laboratory work, pipette-to-sample contamination can be avoided by following these simple guidelines:

- Select a tip with the relevant purity class for your application.
- Use (sterilized) filter tips.
- Always change the pipette tip after each sample.
- Regularly autoclave, or disinfect, the pipette or the components that may come into contact with the sample.

Sample-to-Pipette Contamination

This type of contamination takes place when the pipetted liquid or aerosol particles from it enter the pipette body. To minimize the risk of sample-to-pipette contamination, the following precautions are recommended:

- Always release the pipette's push button slowly to prevent aerosol formation and uncontrolled liquid splashing within the pipette tip.
- Hold the pipette in a vertical position during pipetting and store the pipette in an upright position. This prevents liquids from running into the pipette body.
- Use filter tips to prevent aerosol transfer from the sample into the pipette body. Alternatively, filters can be used on pipette tip cones.

Sample-to-Sample Contamination

Sample-to-sample contamination (or carry-over contamination) occurs when aerosol or liquid residue from one sample is carried over to the next sample. This may take place, for example, when the same pipette tips are used multiple times. To avoid carry-over contamination:

- Use filter tips to prevent aerosol transfer from the sample into the pipette body, and again to the next sample.
- Always change the pipette tip after each sample.
- If you suspect pipette contamination, autoclave or disinfect the pipette according to the manufacturer's instructions.

Definitions:

Decontamination	Any activity that reduces microbial load to prevent contamination. Includes methods for sterilization, disinfection, and antisepsis.
Sterilization	The destruction of all microbial life, including bacterial endospores. Can be accomplished e.g. using steam, heating, chemicals, or radiation.
Autoclaving	Autoclaving (moist heat) is an efficient sterilization method for laboratories. A hot, pressurized, and saturated steam is applied to destroy microorganisms and decontaminate e.g. laboratory plastic and glassware. Exposure time and temperature are critical. Moreover, the steam needs to penetrate through the entire load to be efficient.
Disinfection	The elimination of virtually all pathogenic microorganisms (excluding bacterial endospores) and reduction of the microbial contamination to an acceptable level. A practical method for surface decontamination. The disinfectant (e.g. alcohols, phenolic compounds, halogens), concentration, and exposure time should be selected according to the assumed contamination type.
Antisepsis	The application of an antimicrobial chemical to living tissue to destroy microorganisms.
DNase	Powerful enzymes (nucleases) that degrade DNA by hydrolyzing it into short fragments. Even trace amounts of DNases can lead to low or no yields in DNA techniques such as PCR, or to degradation during DNA purification. Contamination sources: human contact, saliva, bacteria.
RNase	Powerful enzymes (nucleases) that catalyze the degradation of RNA into short fragments. Very stable enzymes that are difficult to remove. Contamination sources: oils from skin, as well as hair, tears, bacteria.
Endotoxins	Lipopolysaccharides, large molecules that are part of the outer membrane of Gram-negative bacteria such as E. coli, Salmonella, Shigella, Pseudomonas, and Haemophilus. Cause fever in humans and impair the growth of cell cultures. Are released into the environment when bacteria die and the cell wall is destroyed. Contamination sources: endotoxins are present wherever bacteria are able to grow, i.e. air, water, soil, skin, raw materials, any non-sterile environment.

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Simplifying Progress

A Guide to High Quality Laboratory Water

Knowledge is power when it comes to water purification systems

Introduction

Water is the most important laboratory reagent. It serves as the principal ingredient in the preparation of media, buffers, samples, dilution series, and blanks. It is also used to flush instruments, wash glassware and perform a range of routine cleaning procedures.

Given its wide use in virtually every life science and analytical application, having a reliable source of high-quality water that delivers the right volume and purity of water is a vital part of operating a lab.

This eBook will guide you on choosing the right water purification system for your laboratory, and describe the impurities found in water, different water standards, and methods of water purification. It will also guide you on purification methods and important standards, which must be considered when selecting a water system.

Topics covered:

- Impurities in water
- Lab water standards
- Application requirements
- Purification methods
- System configurations
- Choosing a system
- Sartorius solutions

Webinar: Ultrapure Water – The Basis for Reliable Laboratory Results

Impurities in Water

What's in your water and why does it matter?

Impurity	Example	Impact	
Inorganics	Calcium and magnesium salts, iron compounds, sodium salts, phosphates, nitrates	▪ Block DNA polymerases in PCR reactions ▪ Affect water conductivity and resistance ▪ Affect elemental and ion analysis	▪ Can cause cross reactions with reagents ▪ Can cause interference with protein interations ▪ Can cause scaling on membrane filter modules
Organics	Tannins, fats, oils, detergents	▪ Lead to background fluorescence	▪ Increase baseline noise in HPLC or LC/MS ▪ Cross-react in cell culture and blotting experiments
Particulates	Sand, silt, rock, pipe work debris, and colloids	▪ Obstruct/clog instrument lines	▪ Clog membrane-based filter modules ▪ Hinder valves, fittings, injectors
Microorganisms	Bacteria, such as Staphylococcus and Pseudomonas	▪ Release endotoxins and nucleases ▪ Nucleases impact downstream assays like PCR, ELISA, immunoblotting	▪ Endotoxins are toxic to mammalian cell cultures and can prevent other sensitive processes ▪ Bacteria can create biofilms
Dissolved gases	Nitrogen, oxygen, carbon dioxide	▪ Produce bubbles that interfere with spectrophotometric measurements or microfluidic channels	▪ CO_2 can decrease resin lifetime ▪ Causes bubbles

Lab Water Standards

Defining quality for laboratory water

Laboratory water is categorized based on its purity: ranging from lower quality to higher quality. Depending on the standard, the names and specifications can differ.

Water standards for different laboratory applications are set by regulatory bodies, such as American Society for Testing and Materials (ASTM) International, The International Organization for Standardization (ISO), The Clinical and Laboratory Standards Institute – Clinical Laboratory Reagent Water (CLSI-CLRW), and The International Pharmacopeia (including USP, EP and JP). The ASTM International standard is one of the most common standards for laboratory water.

The table below shows examples of general parameters for water quality, but the actual requirements for a specific application can vary. In general, Type 1 water is used for highly critical and/or sensitive applications, while Type 2 water satisfies less critical and/or sensitive applications. The Arium® ultrapure water purification systems meet or exceed the ASTM International criteria for Type 1 water.

Parameter	Type IV	Type III***	Type II**	Type I*
Resistivity (MΩ-cm)	> 0.2	> 0.25	> 1.0	> 18.0
Conductivity (µS / cm)	< 5.0	< 4.0	< 1.0	0.055
TOC (ppb)	no limit	< 200	< 50	< 50
Sodium (µg/L)	50	10	5	1
Chloride (µg/L)	50	10	5	1

* 0.2µm membrane filter is required
** prepared by destillation
*** 0.45µm membrane filter is required

Water Academy: Become a Lab Water Expert

Application Requirements

Choose the water quality that meets your needs

Some laboratory applications require higher purity water than others. For example, the water used to wash glassware and fill water baths does not need to be as pure as the water used in sensitive analytical techniques like an HPLC. It is important to choose a water purification system that meets the needs of your intended application(s). The table below shows application examples for each type of water.

Type 3: Primary Grade, Pure or RO Water	Type 2: General or Pure Water	Type 1: Ultrapure Water
▪ Glassware washing and rinsing ▪ Feed water to laboratory instruments (dishwashers, autoclaves, ice machines, stills) ▪ Feeding Type 1 water systems *Note:* Generally, Type 2 can be used in place of Type 3 water, but not the other way around (Type 3 water is never a replacement for Type 2 water).	▪ General laboratory use ▪ Preparation of media, buffers and pH solutions ▪ Flame AAS ▪ ELISA ▪ Glassware washing and rinsing ▪ Feed water to laboratory instruments (hydrogen generators, incubators, dishwashers) ▪ Histology ▪ Colorimetry ▪ Spectrophotometry ▪ Titrators ▪ Feeding Type 1 water systems	▪ Preparation of media, buffer and pH solutions ▪ HPLC, LCMS, ICP-MS, ▪ ICP-OES, AAS, GC, IC, MALDI ▪ Molecular biology (PCR, sequencing) ▪ TOC analysis ▪ Cell culture media ▪ Blotting ▪ Electrochemistry ▪ Immunohistochemistry ▪ Electrophoresis

Application Note: Ultrapure Water for HPLC Analysis

Application Guide: Lab Water Applications A to Z

Purification Methods

Getting pure water is a multistep process

Generating high-quality laboratory water is a multistep process. Water purification instruments, like the Arium® Systems, perform these steps automatically, making pure water readily accessible. Learn about the different purification methods and how they are combined to produce Type 1, Type 2, and Type 3 water.

External Pre-Treament

- Depth Filters
- Activated Carbon

Type 3 Water

- Activated Carbon
- Depth Filters
- Reverse Osmosis (RO)

Type 2 Water

- Activated Carbon
- Depth Filters
- Reverse Osmosis (RO)
- Electrodeionization / Ion Exchange

Type 1 Water

- (Activated Carbon +) Ion Exchange
- Membrane filtration
- UV (optional for Analytical applications)
- Ultrafiltration (optional for Life Science applications)

More Information (click to expand)

- Activated Carbon
- Depth Filters
- Reverse Osmosis (RO)
- Ion Exchange
- Electrodeionization (EDI)
- UV Oxidation
- Ultrafiltration
- Final Membrane Filtration

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Activated Carbon

It is often used in pre-treatment cartridges and in the final water polishing step. The process adsorbs and removes organic contaminants, such as radicals, through a diffusion-controlled process.

Pros	Cons
Removes chlorines and significantly reduces organics (measured as TOC, total organic carbon).	Requires combination technology with UV lamp for maximum TOC removal.

More Information (click to expand)

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Depth Filters

Microporous 5 µm depth filters create a physical barrier that trap particulates.

Pros	Cons
Is easy to operate and maintain. Removes over 98% of suspended solids.	Does not remove dissolved inorganics, organics, or pyrogens.

More Information (click to expand)

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Reverse Osmosis (RO)

Water is forced through a semi-permeable membrane against the osmotic pressure to remove bacteria, ions, dissolved organics, and other small molecules. Type 3 water for daily laboratory applications can be produced using RO membranes with systems like the Arium® Advance RO.

Pros	Cons
Removes a broad range of impurities. It is economical and easy to maintain. Removes organic 95%, particles, bacteria 98%, ions 98%.	Removes the majority of ions, but very small ions can still pass through. Membrane filtration reduces the flow rate - tank needed as intermediate storage solution.

More Information (click to expand)

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Ion Exchange

Ion exchange resins remove ions from water and replace them with H+ and OH- ions.

Pros	Cons
Provides water resistivity binding all negative or positive charged molecules in water up to 18.2 MΩ-cm.	Does not remove molecules without charge, like microorganisms, particulates, and organics. Requires pre-treated feed water.

More Information (click to expand)

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Electrodeionization (EDI)

Uses a current to pull ions through a semi-permeable membrane.

Pros	Cons
Provides water resistivity of 5-15 MΩ-cm. Resins are continuously regenerated, so an EDI stack does not have to be exchanged like a cartridge.	Does not provide water resistivity of 18.2 MΩ-cm. Requires pre-treated feed water. Is CO_2 sensitive.

More Information (click to expand)

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UV Oxidation

Irradiation with UV light at 185 and 254 nm breaks down organic contaminants and ionizes the molecules.

Pros	Cons
Oxidizes dissolved organic components for sensitive analytic applications to < 2 ppb TOC.	Does not remove ions, particulates, and colloids. May require pre-treated feed water.

More Information (click to expand)

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Ultrafiltration

Uses a porous cross-flow membrane filter (pore size 1-10 nm) to filter out a range of impurities based on size. The Arium® systems offer two different ultrafiltration solutions: an integrated option or an external end-point ultrafilter.

Pros	Cons
Removes colloids, microorganisms, particulates, enzymes, and endotoxins. Is efficient and easy to use. Integrated cross-flow filters have a self-cleaning effect on the membrane.	May require pre-treated feed water. Dead-end filters require frequent changing.

More Information (click to expand)

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Final Membrane Filtration

Membrane filters are often used at the outlet of water purification systems as a last-step protection and sterile filtration.

Pros	Cons
Removes all impurities larger than the pore size. Sterilized and integrity-tested 0.2 µm filters can be used for sterile filtration.	Dead-end filters require frequent changing.

More Information (click to expand)

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Water Academy: Become a Lab Water Expert

System Configurations

Centralized or point-of-use?

Laboratory water purification systems can be configured in two ways: centralized or point-of-use. A centralized system provides water to an entire facility, while point-of-use systems are dedicated to one laboratory or application.

Centralized systems simplify maintenance and reduce overall costs. However, it is difficult to control the quality of the treated water or get point-of-use quality information. A centralized system is an efficient way to feed pretreated water to a building or a complete laboratory, and the water quality may be adequate for laboratory devices that require Type 2 pure water, or for general tasks like rinsing.

A point-of-use system is purchased and housed in a laboratory. Systems can be qualified (IQ/OQ). It provides complete control of maintenance and access to information about water quality and, labs requiring Type 1 ultrapure water can use a final polisher, like the Arium® Mini Essential or Arium® Pro, to treat water sourced from a centralized system.

Brochure: Arium® Mini – Compact Ultrapure Water Systems

Brochure: Arium® Water Purification Systems

Choosing a System

Key considerations when selecting a water system

A water purification system is one of the vital investments you make when building a laboratory. Water purification systems come in many different sizes and capabilities. When choosing a system, it helps to have a good understanding of water impurities in your feedwater and how they might affect your experiments. Talking to a Sartorius laboratory water expert is a great place to start.

Additional Information (click to expand)

- Application
- Volume Needs
- Water Storage
- Operation
- Maintenance
- Feedwater
- Space
- Cost
- Connectivity

Brochure: Arium® Mini – Compact Ultrapure Water Systems

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- Connectivity

Application

The water purification system you select must meet the needs of your intended application. If you require different types of water, combined systems like the Mini Plus and Comfort I or II that offer two different water qualities from one system are a convenient, space-saving option.

Lab Water Applications A to Z

Brochure: Arium® Mini – Compact Ultrapure Water Systems

Brochure: Arium® Water Purification Systems

Choosing a System

Key considerations when selecting a water system

A water purification system is one the vital investments you make when building a laboratory. Water purification systems come in many different sizes and capabilities. When choosing a system, it helps to have a good understanding of water impurities in your feedwater and how they might affect your experiments. Talking to a Sartorius laboratory water expert is a great place to start.

Additional Information (click to expand)

- Application
- Volume Needs
- Water Storage
- Operation
- Maintenance
- Feedwater
- Space
- Cost
- Connectivity

Volume Needs

Consider the daily water usage in your lab when selecting a water system. Select a system that slightly exceeds your daily water requirements so it can handle unexpected overages. However, a significantly oversized system is not recommended as it requires more space and runs the risk of microbial contamination if not used constantly.

Lab Water Applications A to Z

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Water Storage

Water purification systems that include membrane filtration technologies, such as RO and EDI modules, have a reduced flow rate. To compensate for this, intermediate storage of pretreated water, such as the Arium® Bagtank technology, provides generous water volume, flow rate and pressure when in use.

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Brochure: Arium® Water Purification Systems

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Operation

Usability and efficiency features, like an easy-to-use touch screen display, are important selection criteria for a water purification system. Different functionalities like Favorites, Volume-Controlled and/or Time-Controlled dispensing options also streamline dispensing. Arium® Systems offer these features in addition to a remote dispenser Smart Station for both ultrapure and pure water.

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Maintenance

Water systems require regular cleaning and maintenance to provide reliable performance. For Arium® systems with a storage reservoir, the Bagtank technology vastly simplifies cleaning compared to a tanked system. Entrusting these tasks to the manufacturer's technical services experts help to prolong instrument lifetime, while freeing up the lab technician's time to focus on other tasks.

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Feedwater

The water feeding the purification system must meet the required instrument specifications to ensure you are getting the right purity of water. Some combined water systems can work directly with tap water, but if you already have a reliable source of Type 2 or Type 3 feed water, then a final polisher might be all you need for Type 1 ultrapure water.

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Space

Instrument systems with flexible installation help manage limitations around space in the laboratory. The Arium® systems, for example, offer more compact designs in addition to table-top, wall-mount, and under/inside workbench installation options.

Another space-saving option available with the Arium® systems is the Smart Station. It allows for installing multiple remote dispensing points using flexible tubing that pulls ultrapure water from the main system. These satellite dispensing points require much less space compared to a full system.

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Cost

In addition to the cost of the instrument itself, you must consider the cost of accessories, pre-treatment requirements, and consumables (e.g., replacement cartridges). Service contracts are an optional cost, however professional maintenance extends the lifetime of your system and prevents downtime.

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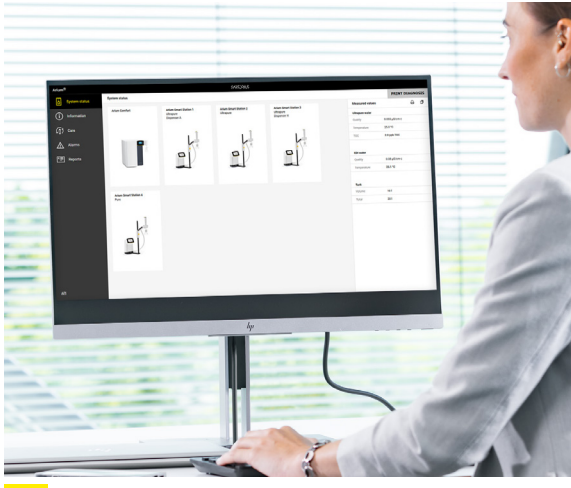
Connectivity

In the regulated laboratory environment, data monitoring and documentation for lab water are important. You can use a connected printer or a SD-card to retrieve data from most systems. It is also possible to connect our Arium® Smart Station either via ethernet or USB-C to collect and monitor the required data.



Brochure: Arium® Mini – Compact Ultrapure Water Systems

Brochure: Arium® Water Purification Systems

Sartorius Solutions

Compact, innovative water purification systems

Our Arium® laboratory-grade water purification systems feature an inspiring, application-oriented design. Perform your workflows faster and more reliably, while ensuring cost-efficient operation over the long term. All instruments offer flexible solutions as they can be adapted to your requirements.

Ultrapure Water Systems

A wide range of modular-designed systems for producing Type I ultrapure water for life science, chromatography, mass spectrometry and other applications.

Explore the Systems +

Pure Water Systems

High-quality Type 2 water for buffer and media preparation with EDI technology and convenient Bagtank technology.

Explore the Systems +

Reverse Osmosis Pure Water Systems

Type 3 water for standard laboratory applications with a speed of up to 24 L/hr.

Explore the Systems +

Combined Water Systems

Pre-treatment and final polishing purification technologies in one system give you flexibility.

Explore the Systems +

Arium® Smart Station

A flexible and remote solution for dispensing ultrapure and pure water where you need it.

Learn More +

Arium® Bagtank

Exchangeable, closed-system bags for storing purified water prevent contamination and simplify maintenance.

Learn More +

Questions? Contact a Sartorius Lab Water Expert

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Application Note

Keywords or phrases:
Syringe Filter, Protein Adsorption, mAb, RFP, RuBisCo, Design of Experiments (DoE)

How to Increase Recovery at Critical Protein Samples: Impact of Syringe Filter Membrane, Volume and pH

Abstract

Protein loss during sample preparation can be an obstacle to reliable product quantitation in biological, biotechnological and biopharmaceutical settings. We compared four membranes typically used as part of syringe filters for sample preparation. In a design of experiments approach we quantified the recovery of four model proteins under different sample conditions and found that membranes composed of cellulose acetate or polyethersulfone adsorbed on average less than 5% of protein analyte. Even when only 0.5 mL sample with 0.01 g L^{-1} protein was filtered, the recovery was ~90% with these membranes. In contrast, nylon or polyvinylidene difluoride-based membranes exhibited adsorption of more than 30% of product under these conditions. Furthermore, adsorption was dependent on sample properties like pH which can facilitate a fine tuning of the sample conditions to improve product recovery during preparation.

Find out more: sartorius.com/en/products/lab-filtration-purification/syringe-filters

Introduction

Biopharmaceutical samples are often prepared from feedstocks containing insoluble particles like cell debris or protein aggregates and therefore require a solid-liquid separation before analysis to protect analytical instruments. Because separation by centrifugation requires a difference in density between solid and liquid phase, sample filtration can be advantageous and membrane filters offer absolute particle retention. However, filter membranes can adsorb analytes like proteins and thereby distort the results of the subsequent analyses. It is therefore important to select filter membranes with a minimal tendency to protein adsorption. But the latter does not only depend on the membrane type, yet is also affected by the sample and protein properties, like pH and surface charge respectively, as well as the specific handling steps including sample volume per unit filter area. Identifying conditions suitable to achieve minimal analyte loss can thus be a complex multi parameter problem with a work load that would be prohibitively high, especially for early development and screening approaches. We have therefore selected four typical syringe filter membranes and quantified the recovery of four model proteins including two different antibodies under various sample conditions representative for many biological, biotechnological and biopharmaceutical applications. The design of experiments (DoE) approach we used may provide guidance as to which conditions and membranes can help to minimize analyte loss during sample preparation.

Materials and Methods

Four model proteins were used to study protein adsorption to filter membranes (Table 1).

A split-plot I-optimal design with 120 runs containing four numerical and two categorical factors (Table 2) was set up to investigate protein binding to different membranes of syringe filters by a mixed linear-quadratic model. The numerical factor levels were selected based on typical sample conditions, for example in-process-controls during biopharmaceutical production. Proteins were dissolved in phosphate buffer (10 mmol L^{-1}, pH 5.5 or pH 7.5) containing 140 mmol L^{-1} (15 mS cm^{-1}) or 550 mmol L^{-1} (50 mS cm^{-1}) of sodium chloride according to the DoE approach. Sample preparation was carried out in glass containers and protein solutions were loaded to membrane filters using polypropylene syringes. Filtrates were collected in glass containers and filtration was performed at 22° C.

Table 1: Model proteins used for filter membrane testing

Protein name [-]	Protein type [-]	Molecular mass (monomer) [kDa]	Isoelectric point (pI) [-]	Oligomeric state	Purity [-]
DsRed	Red fluorescent protein (RFP)	27.15	7.4	4	0.84
Adalimumab	Monoclonal antibody (mAb1)	145.4	8.4	1[c]	>0.97
M12	Monoclonal antibody (mAb2)	144.8	7.9	1[c]	>0.97
RuBisCO[a]	Enzyme	52.9/20.3[b]	6.6	16[d]	0.92

a. Ribulose-1,5-bisphosphate carboxylase/oxygenase; b. values for large and small subunit respectively; c. composed of two heavy and two covalently linked heavy and light chains; d. composed of 8 small and 8 large subunits that are non-covalently attached.

RFP was diluted in 0.9% m/v sodium chloride and quantified by fluorescence spectroscopy with excitation at 559 nm and emission at 585 nm in black 96-well plates with a 7 mm measurement height and 50 flashes per sample using an EnSpire (Perkin Elmer) multimode plate reader. RuBisCO containing 10-µL samples were analyzed at 220 nm by ultra-high performance size exclusion chromatography (UHPSEC) using an Ultimate 3000 (Thermo Fischer Scientific). Proteins were separated isocratically on an Acquity UPLC Protein BEH SEC Column, 20 nm, 1.7 µm, 4.6 × 150 mm with 50 mmol L^{-1} sodium dihydrogen phosphate, 250 mmol L^{-1} sodium chloride, pH 6.8 at a column temperature of 30° C and a flow rate of 0.2 mL min^{-1}.

Monoclonal antibody samples of M12 and Adalimumab were analyzed by surface plasmon resonance (SPR) spectroscopy using a Biacore T200 (GE Healthcare). Samples were diluted and analyzed in 0.01 mol L^{-1} HEPES, 0.15 mol L^{-1} sodium chloride, 3 mmol L^{-1} EDTA and 0.005% v/v polysorbate-20 and loaded to a Protein A functionalized chip surface at 22° C with 0.03 mL min^{-1} and a contact time of 180 s. Injections of 45 µL 0.03 mol L^{-1} hydrochloric acid were used for surface regeneration.

Results and Discussion

A statistical experimental design (DoE) was used to quantify the binding of four model proteins to four different types of syringe filter membranes (all with a pore size of 0.2 µm), frequently used for sample preparation, for example in the context of in-process controls. The highest protein recovery of >98% was observed for a cellulose acetate (CA) membrane (Minisart® NML, Table 3) which was insignificantly higher than the average recovery achieved with a polyethersulfon (PES) membrane (Minisart® High Flow) (two-sided t-test with 0.05 alpha level). Also, both membranes exhibited a 3 to 8-fold lower standard deviation compared to a nylon or a polyvinylidene difluoride membrane, indicating that high recoveries were achieved with these membranes even for varying sample conditions and target proteins (Table 2).

When analyzing the DoE, sample volume and especially protein concentration had the strongest effects on protein recovery and the latter increased with higher concentrations and volumes (Figure 1). These observations were in good agreement with a saturation model for protein adsorption to surfaces, for example a Langmuir model. In such a model, a given surface will bind a certain absolute quantity of protein and accordingly the (relative) recovery increases as sample volume and concentration increase. Therefore, large volumes and high concentrations can reduce the percentage of product loss during sample preparation using syringe filters.

Table 2: Summary of the DoE setup used to study protein adsorption to filter membranes

Factor	Unit	Type	Level
Conductivity	mS cm^{-1}	Numeric	15; 50
pH	-	Numeric	5.5; 7.5
Protein concentration	g L^{-1}	Numeric	0.01; 0.10; 1.00
Specific sample volume	mL cm^{-2}	Numeric	0.5; 5.0
Protein	-	Categoric	[see Table 1]
Membrane	-	Categoric	[see Table 3]

a. Ribulose-1,5-bisphosphate carboxylase/oxygenase; b. values for large and small subunit respectively; c. composed of two heavy and two covalently linked heavy and light chains; d. composed of 8 small and 8 large subunits that are non-covalently attached.

The membrane type had a relevant effect as well and membranes composed of CA or PES exhibited substantially less protein adsorption (>95% recovery) compared to counterparts made of nylon or polyvinylidene difluoride (PVDF), especially when exposed to low product concentrations and sample volumes (<75% recovery) (Figure 1). Importantly, the recovery achieved with CA and PES membranes was largely independent of protein, sample conditions and handling, implying that a fine tuning may not be necessary for each new product to be investigated. Therefore, CA or PES-based membranes can help to limit product loss during sample preparation for analysis if a target protein is scarce. The pH-effect was strongly protein specific. For example, no substantial pH effect was observed for mAb1 at pH 5.5 (0.01 g L^{-1}, 0.5 mL cm^{-2}) but a recovery of only ~60% was observed for RuBisCO even when Minisart® NML was used under the same conditions. However, the low recovery of RuBisCO was linked to a known low-pH instability of the protein and therefore unlikely an effect of membrane adsorption.

Whereas the conductivity did not exhibit a significant influence on recovery within the parameter space investigated in this study, a salinity below 15 mS cm^{-1} or above 50 mS cm^{-1} may cause product losses as it can affect protein solubility and may trigger protein aggregation. The resulting aggregates in turn may interact with the membrane or, depending on their size, can be sterically retained by the latter. Therefore, care should be taken if conditions outside the reported parameter space are used.

Conclusion

Most sample manipulation or preparation is associated with some product loss. However, analytics during process development or monitoring require that such losses are kept to a minimum so that reliable results can be obtained. Minimal product loss during sample preparation can be achieved over a wide range of conditions by selecting an adequate filter membrane. For example, ~90% of product was recovered using Minisart® NML (CA) or Minisart® High Flow (PES) filter membranes even with sample volumes and concentrations as little as 0.5 mL cm^{-2} and 0.01 g L^{-1} respectively. The product recovery may be further improved by fine tuning the sample conditions for an individual product, e.g. by selecting a proper pH value. In contrast, if protein binding is beneficial for sample preparation, nylon-based membranes such as Minisart® NY can be used instead.

Table 3: Properties of 0.2 µm pore size filters and average protein recovery after filtration in dependence of membrane type. RFP, mAb1, mAb2 and RuBisCO samples were in a 5.5–7.5 pH range, conductivities of 15 or 50 mS cm^{-1}, concentrations between 0.01 and 1.00 g L^{-1} and loadings of 0.5 or 5.0 mL sample per cm^2 membrane area

Filter name [-]	Membrane type [-]	Housing material [-]	Filter area [cm^2]	Average recovery [%][a]	n
Minisart® NML	Cellulose acetate (CA)	Methacrylate butadiene styrene (MBS)	6.2	98.4 ± 7.4	15
Minisart® High Flow	Polyethersulfon (PES)	Methacrylate butadiene styrene (MBS)	6.2	98.2 ± 5.3	18
Minisart® NY	Nylon (NY)	Polypropylene (PP)	4.8	59.7 ± 41.4	20
Standard filter	Polyvinylidene difluoride (PVDF)	Polypropylene (PP)	4.2	81.7 ± 27.4	17

a. The variability is indicated as the standard deviation.

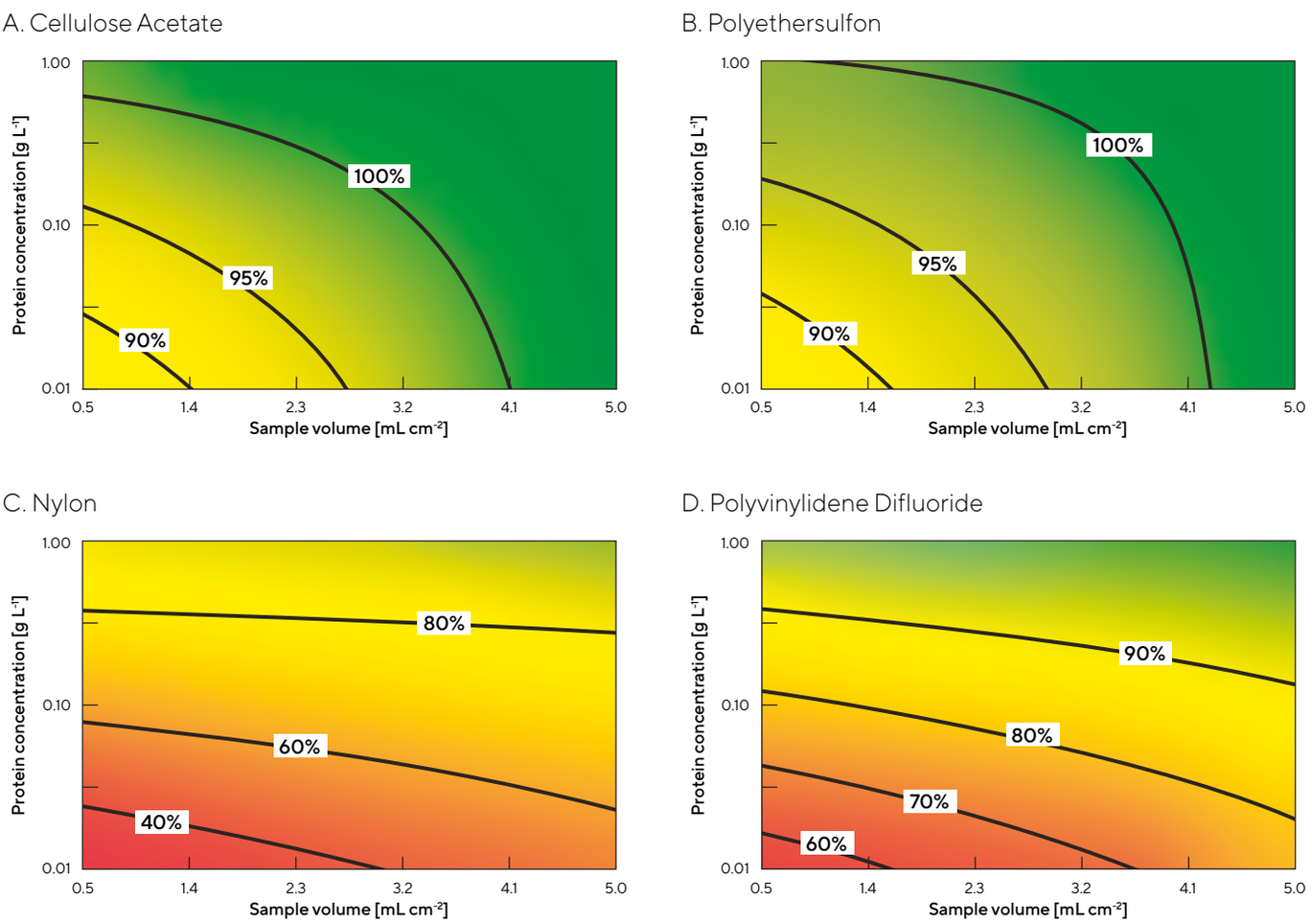

Figure 1: Average protein recovery with membrane-based syringe filters. Recovery was averaged over proteins RFP, mAb1, mAb2 and RuBisCO for a conductivity of 32.5 mS cm^{-1} at pH 6.5 using cellulose acetate (A), polyethersulfon (B), nylon (C) and polyvinylidene difluoride (D) membranes.

Acknowledgements

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