

asertain[®]

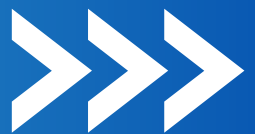
VALIDATION SERVICES

**Ensure Safety, Identity, Strength, Purity
and Quality of Your Product**

About mdi

Advanced Microdevices (**mdi**) is a highly vertically integrated company offering purification, separation, and fluid management solutions for the healthcare sector. It offers customization, rapid prototyping, and productionization of consumables for critical applications in biopharmaceuticals, pharmaceuticals, immunodiagnostics, and life science research.

making a difference
with innovation.





VALIDATION SERVICES

Since 2008, mdi has been a trusted partner to the pharmaceutical and biopharma industries, providing asertain® validation services that support the regulatory approval of drug products. Our extensive experience spans a wide range of formulations, including conventional injectables, ophthalmic drugs, oncological treatments, emulsions, and novel drug delivery systems (NDDS) such as liposomal and depot formulations (solvent phase). We also specialize in validating specialty pharmaceuticals and biopharmaceuticals including monoclonal antibodies (mAbs), recombinant proteins and plasma proteins.

mdi's asertain® validation services are tailored to meet specific customer requirements while ensuring alignment with regulatory expectations. These services facilitate validation of critical process components such as sterilizing-grade filters or complete single use systems (SUS) in contact with process fluids such as media, buffers, and drug substance–drug product (DS–DP).



OUR SERVICES | 5

Filter Validation Services

- Microbial Retention Validation Studies
 - Viability Studies
 - Bacterial Challenge Test
- Establishing Product Wetted Integrity Test Specifications
- Physicochemical Compatibility Studies
- Extractable Studies
- Adsorption Studies
- Throughput Study (Sizing & Selection for process efficiency)

Single Use Systems Validation Services

- Physicochemical Compatibility Studies
- Adsorption Studies

Extractables & Leachables Studies

- Advanced Extractable Studies and Leachable Studies
- Toxicological Assessment

OUR PROCESS | 19

REGULATORY COMPLIANCE | 20

WHY CHOOSE mdi | 21





asertain[®]

FILTER VALIDATION

SERVICES



Filter Validation Services

MICROBIAL RETENTION VALIDATION STUDIES

Our microbial retention studies qualify the filter under test to repeatedly produce a sterile filtrate with the drug product under simulated worst case process conditions.

The drug product or simulant is inoculated with the challenge organism at $>1 \times 10^7$ viable organisms/cm² of filter area and the test is performed on filters from three different lots, with at least one having a pre-filtration physical integrity test value at/or near the filter manufacturer specified limit.

This involves establishing the viability of the test organism in the drug product and testing the filter for bacterial retention test under simulated process conditions.

Viability Studies

It establishes whether the drug product is bactericidal to the test organism under simulated process conditions of temperature and contact time. This in turn helps establish the test methodology for the bacterial challenge/retention studies.



Bacterial Challenge Test

For non-bactericidal drug products the filter is challenged with the test organism suspended in drug product.

For bactericidal products viability studies are carried out with modified formulation, modified process conditions, or in product surrogate. In such cases, filter preconditioning with the product under worst case process conditions is carried out followed by bacterial challenge test with modified formulation/process under which test organism viability has been established.



Filter Validation Services

ESTABLISHING PRODUCT WETTED INTEGRITY TEST SPECIFICATIONS

Conducting a filter integrity test for sterilizing grade filters, used in drug product sterilization, is a crucial aspect of sterile drug product manufacturing. The product itself serves as the most appropriate wetting fluid. Specifications for product-wetted integrity tests become particularly valuable when Pre-use Post Sterilization Integrity Testing (PUPSIT) is part of the process.

Variations in test gas solubility, diffusion constants, and the surface tension of the wetting fluid often lead to differences between product-wetted integrity test values and those obtained with a reference fluid. It is crucial to avoid mixing process fluid with the reference wetting fluid, as product residues or interactions between the liquids may prevent complete and stable wetting of the filter membrane. This can result in either a false negative, potentially causing the loss of an entire production batch or a false positive that will compromise patient safety.



In asertain® filter validation, the product-wetted bubble point value and diffusion flow value are determined. This validation is conducted using three lots of filters, with three filters from each lot. Factors such as filter sterilization conditions, test gas, and process conditions are simulated.

The bubble point value obtained using the product as the wetting fluid is compared with the bubble point value using the filter manufacturer's recommended reference wetting fluid on the same membrane to establish product-wetted specifications. The product-wetted bubble point limit is then calculated. Additionally, the diffusion flow value is determined by identifying the test pressure, and then diffusion flow test limit is calculated.

Filter Validation Services

PHYSICOCHEMICAL COMPATIBILITY STUDIES

The filter's characteristics must be compatible with the fluid and remain unaffected by the product being filtered. Ensuring the filter's compatibility with the product is crucial.

Chemical compatibility testing involves the entire device and depends upon fluid, filtration temperature, and contact time. Common physicochemical compatibility tests include integrity testing, flow rate testing, visual checks, thickness testing of the membrane, filter media, support layers, and O-rings, as well as weight testing of these components before and after exposure to the test product under process conditions.

The filter is exposed to the process fluid for a specified period under pre-determined conditions that include, simulated sterilization condition of filter, exposure times exceeding the maximum process time and temperature exceeding maximum process temperature.



Physicochemical compatibility tests ensure that the selected filter is suitable for the filtration / sterilization of process fluid under specified process conditions.



Filter Validation Services

EXTRACTABLE STUDIES

The “Extractable study” is an essential part of filter validation in the pharmaceutical and biopharmaceutical industries. Extractable study under asertain® filter validation ensures that the filters used in the manufacturing processes, particularly those for sterile products, do not release leachables above the regulatory specified limits into the product.



An extractable study is designed to identify and quantify the chemical compounds that may leach from a filter under exaggerated conditions, such as extreme pH, temperature, and solvent conditions. These compounds are referred to as “extractables.”

The main purpose of an extractable study in filter validation is to assess the potential risk that filtration system poses to product purity, safety, identity, quality, and efficacy.

Regulatory bodies across the globe require an extractable study as part of the validation process to ensure that the manufacturing process does not introduce contaminants into the product.

In asertain® filter validation program, the filter is subjected to exaggerated conditions to mimic potential worst-case scenarios. This could include using solvents, high temperatures, or extreme pH values that the filter might encounter during the production process. The filter is exposed to these conditions for a specific period as defined, and the extraction medium is collected and analysed.

The NVR of filter extract is estimated and analysed by technique such as FTIR and RP HPLC.

[mdi also offers Advanced Extractables & Leachables Studies as well as Toxicological Assesment. Refer Page 16](#)



Filter Validation Services

ADSORPTION STUDIES

Adsorption is a fundamental surface phenomenon where molecules from drug product components, such as therapeutic proteins, oligonucleotides, APIs, preservatives, antioxidants, and surfactants, bind to the surface of a membrane. This can affect the product's composition and concentration.

The loss of expensive drug products due to adsorption represents a significant cost that must be minimized. During the filtration process, yield reductions from non-specific adsorptions onto filters can lead to decreased production capacity, directly impacting market value. Even milligram losses from non-specific adsorption can accumulate to unacceptable levels over a year of production. Thus, it is crucial to evaluate individual membrane polymers and filter designs to minimize yield loss as much as possible.



During filter validation, adsorption tests are conducted on a small scale to determine the level of adsorption of drug product components on the filter. A Filter Saturation Curve is used, measuring the concentration of the filtrate as a function of the volume filtered per unit area of the filter.

It is critical that filters are selected to minimize adsorption and loss of product components. Laboratory scale filter tests are used to generate adsorption profiles to help with filter selections and process qualification.



Filter Validation Services

THROUGHPUT STUDY (SIZING & SELECTION FOR PROCESS EFFICIENCY)

Filter throughput capacity depends on factors such as porosity, pore size, nonspecific adsorption, pore shape, filtration area, and contamination load in the process fluid. A filter throughput study measures the total volume that can be filtered through the effective filtration area under defined process conditions. The objective is to determine the appropriate size of a prefilter or sterilizing grade filter for the complete filtration of a given batch of process fluid.



A throughput study is conducted under constant pressure to determine the flow rate decay pattern over time and the maximum volume that can be filtered through a test device. This information is then used to determine the appropriate filter size for a given batch size and process time during scale-up.





asertain[®]

SINGLE USE SYSTEMS VALIDATION SERVICES



Single Use Systems Validation Services

PHYSICOCHEMICAL COMPATIBILITY STUDIES

Single use assemblies are highly customized fluid management systems used in manufacture of biopharmaceuticals. These systems must be compatible with the fluid in contact and must remain unaffected in terms of their integrity and other functional aspects.

Depending upon the process requirements, single use assemblies incorporate a wide range of single use components such as bags, tubing, filling needles, fittings, connectors etc. with different materials of construction.

Therefore each component needs to be tested individually to establish physico-chemical compatibility with the contact fluid under simulated worst case conditions of actual use such as contact time, pressure, temperature etc.



A variety of tests related to integrity, dimensions, fitment, pressure resistance, visual inspection, hardness, volume accuracy, flow rates etc. are performed on single use components to be validated before and after exposure to the process fluid.



Single Use Systems Validation Services

ADSORPTION STUDIES

Adsorption of process fluid components to the surface within the fluid pathway of a single use system may impact critical biopharmaceutical manufacturing steps such as cell growth resulting in low product titre, downstream purification, and drug substance concentration. It may also affect label claim values of drug product components such as therapeutic proteins, oligonucleotides, preservatives, antioxidants, and surfactants.

Losses due to these interactions with SUS components are increased exponentially in case of high value drug products. Thus, it is important to evaluate individual single use components with specific drug products to minimize adsorption.



During adsorption studies, tests are conducted on individual single use components or miniaturized single use assemblies under simulated worst case conditions of actual use such as contact time and temperature.

These studies help design the most suitable single use systems for minimum impact.





asertain®

Extractables & Leachables

STUDIES



E & L Studies

ADVANCED EXTRACTABLES & LEACHABLES STUDIES

Establishing process specific extractable profile of the single use component is a pre-requisite for establishing the need for conducting leachable studies. This requires a detailed identification and quantification of volatile, semi-volatile and non-volatile organic compounds under simulated process conditions. Toxicity evaluation of the extractable profile based on the safety concern threshold (SCT) established from patient daily exposure (maximum dosage) helps establish whether the toxicity risk level is acceptable or not. In case the risk is unacceptable, a leachable study with the drug product is required.

MDI offers to facilitate the risk assessment in compliance with Biophorum Operations Group (BPOG) Best Practices Guide For Evaluating Leachables Risk From Polymeric Single Use Systems Used In Biopharmaceutical Manufacturing.



GC-MS/MS

In order to do so, process specific Advanced Extractables Studies are conducted on model solvent streams selected on the basis of their ability to simulate the extraction abilities of different drug components. These studies are carried under simulated worst case process conditions. A toxicological assessment of identified extractable compounds is required to establish target compounds (with concentrations higher than permissible daily exposure limits) for a Leachable Study.



E & L Studies

ADVANCED EXTRACTABLES & LEACHABLES STUDIES (continued)

These studies require a detailed understanding of the process fluid and the process conditions encountered by the fluid contact single use component. Based on the component type, application and process conditions, a well thought out study design to assess the volatile, semi-volatile and non-volatile compounds, is proposed.



Q-TOF LC-MS/MS

The study design includes a draft study plan with detailed methodology.

MDI provides miniaturized test components that truly represent the single use process components in terms of materials of construction and fabrication processes, and meet the study requirement of volume to surface area ratio.

These studies are designed to simulate actual process conditions such as temperature, contact time, volume to surface area ratio etc. through component preconditioning.



Advanced Extractables Studies as well as Leachable Studies are conducted at state-of-the-art MDI analytical laboratories with calibrated equipment using validated methods such as:

- Head Space Gas Chromatography Mass Spectroscopy (HS-GC-MS) to analyze volatile organic compounds.
- Automatic Liquid Sampler Gas Chromatography Mass Spectroscopy (ALS-GC-MS/MS) to analyze semi volatile organic compounds.
- Quadrupole Time of Flight Liquid Chromatography Mass Spectroscopy (QTOF-LC-MS) to analyze non-volatile organic compounds.
- Inductively coupled plasma mass spectrometry (ICP-MS) to analyze elemental impurity.

E & L Studies

TOXICOLOGICAL ASSESSMENT

A toxicological evaluation of the extractables profile for impact assessment of potential leachables, and if required, of leachable compounds is carried out to establish the potential toxicological risk to final drug product safety.

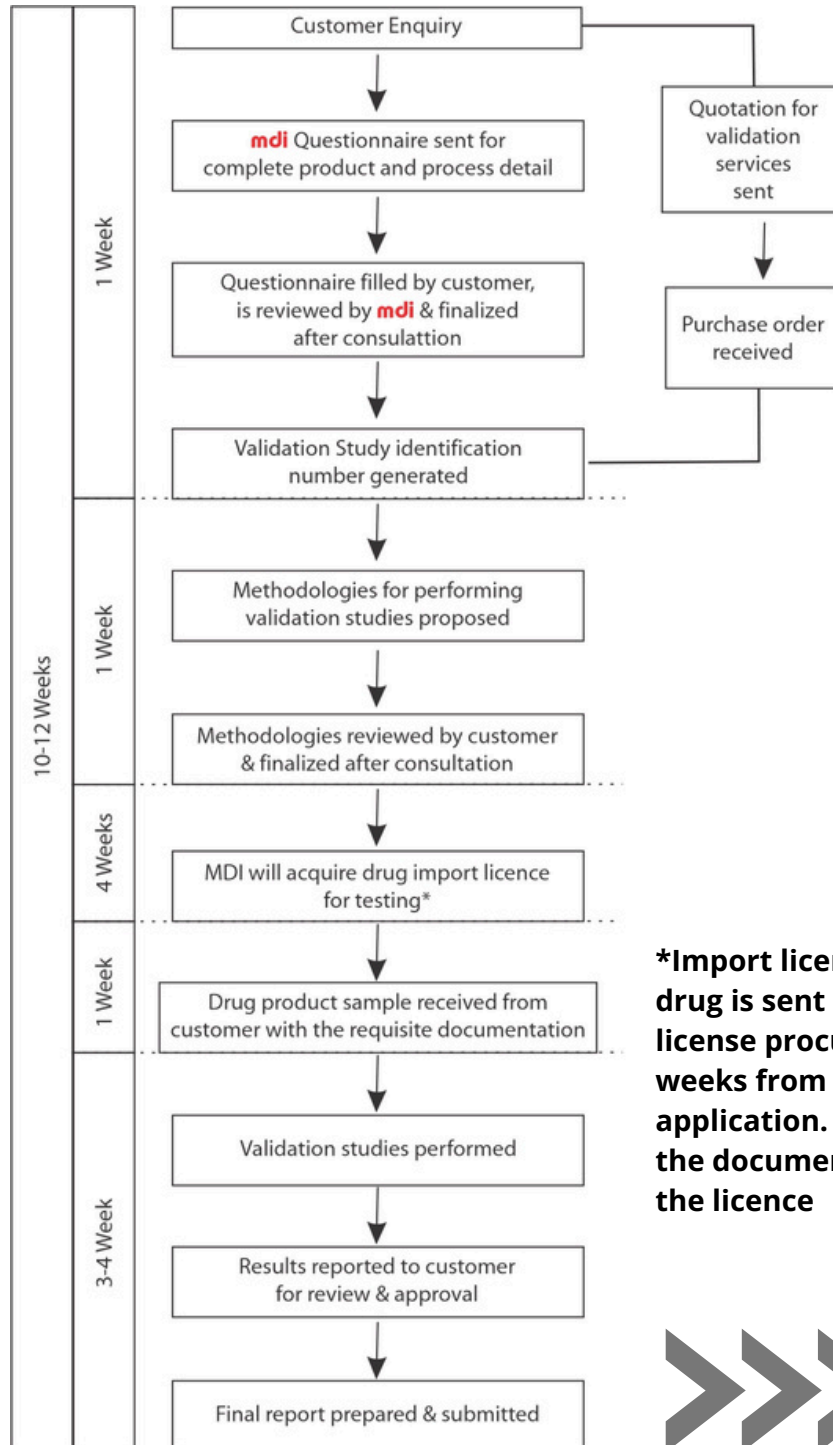
An in-silico assessment is carried out as per Cramer's Classifications. Based on this assessment, the compounds are reclassified as per PQRI and accordingly the PQRI specified threshold levels are applied.



All organic compounds are also verified against various databases.



Our Process



***Import licence is required only in case the drug is sent from outside India. The import license procurement takes approximately 4 weeks from the date of filing of the licence application. mdt can provide information on the documentation required for the filing of the licence**



Regulatory Compliance

mdi asertain® validation services are fully compliant with key global regulatory and industry guidelines. Our processes are designed to meet the most stringent expectations for sterilizing-grade filter validation and single-use component assessment in pharmaceutical and biopharmaceutical manufacturing.

Compliance Includes:

- USFDA – Guidance for Industry: Sterile Drug Products Produced by Aseptic Processing — Current Good Manufacturing Practice
- European Union – Volume 4: EU Guidelines for Good Manufacturing Practice for Medicinal Products for Human and Veterinary Use, Annex 1 (2022)
- EMA – Guideline on the Sterilization of the Medicinal Product, Active Substance, Excipient and Primary Container (EMA/ CHMP/ CVMP/ QWP/ 850374/2015)
- ISO 13408-2 – Aseptic Processing of Healthcare Products – Part 2: Sterilizing Filtration
- PDA Technical Report No. 26 – Sterilizing Filtration of Liquids
- BioPhorum – Best Practices Guide for Extractable Testing of Polymeric Single-Use Components in Biopharmaceutical Manufacturing
- USP <665> – Plastic Components and Systems Used to Manufacture Pharmaceutical and Biopharmaceutical Drug Substances and Products

These guidelines provide comprehensive direction on the validation of sterilizing-grade filters and the qualification of components to ensure sterility, safety, and regulatory readiness throughout the drug manufacturing process.



Why Choose mdi

Unique advantages of mdi asertain Validation Services

- State-of-the-art Laboratories: Ensuring high accuracy and reliable data for compliance and quality assurance.
- Rapid Study Execution: Fast turnaround times to help accelerate your development and approval process.
- Expertise in E/L & Toxicological Assessments: Extensive in-house extractables library, enabling the identification of all extracts with minimum unknowns.
- Cost Efficiency: Affordable validation services without compromising on quality or reliability.



Advanced Microdevices Pvt. Ltd.

20-21, Industrial Area, Ambala Cantt-133001, INDIA

Email: info@mdimbrane.com

Tel: +91-171-2699290, +91-9896394509

MDI Membrane Technologies INC

75 Utley Drive STE 103

Camp Hill, Pennsylvania 17011

United States of America

www.mdimembrane.com

Updated: July 7, 2025