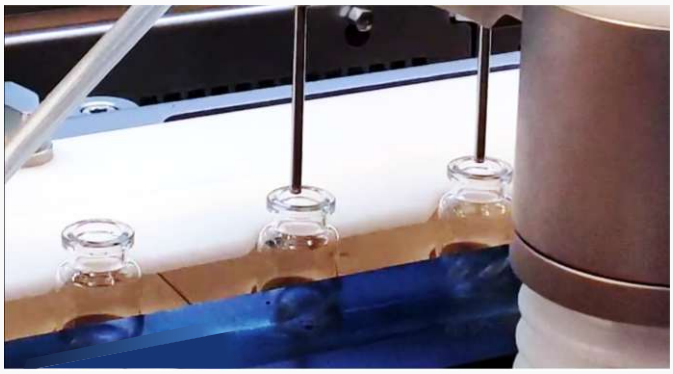
mdi
Membrane Technologies

Disposable Single Use Filling Lines

The current therapeutic healthcare is becoming more and more focused on highly potent, high value drugs from both the biopharmaceutical as well as pharmaceutical industry. This has resulted in a continuous stream of new drug products with smaller lot sizes, requiring quick turn around times and thereby challenging the existing reusable fill finish systems with time and man power consuming cleaning and sterilization processes.

mdi disposable single-use filling lines offer customized solutions for final fill of drug products, overcoming flexibility and productivity constraints associated with traditional fill and finish systems.

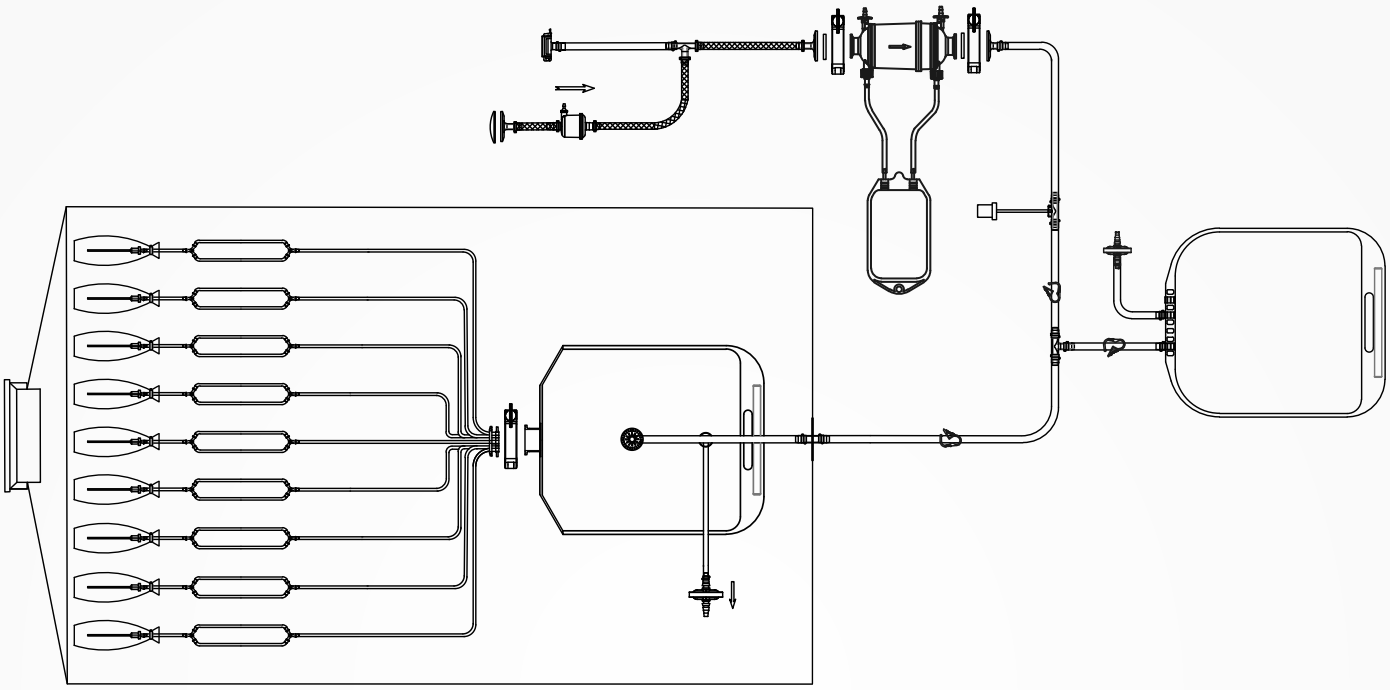


These ready to use, gamma sterilized filling assemblies are designed to not only ensure regulatory compliance but also enhance product and operator safety.

mdi disposable single-use final fill assemblies ensure:

- Quick turnaround time
- Product and operator safety
- Reduced risk of cross contamination
- No cleaning validation
- Increased flexibility and productivity

Disposable Single Use Filling Lines



Filling line with AseptiSac Bags with Beta Port

mdi single use filling lines are customized to suit new as well as existing fill and finish systems. These are designed to comply with regulatory requirements such as “Final sterile filtration should be carried out as close as possible to the filling point” and “The integrity of the sterilized filter should be verified before use and should be confirmed immediately after use by an appropriate method such as a bubble point, diffusive flow or pressure hold test” (European Union Current Good Manufacturing Practices).

However, combining both these within an Isolator/RABS* system becomes quite challenging.

Disposable Filling Lines for Isolator/RABS

These ready to use gamma sterilized filling lines are also available housed within a specially designed *AseptiSac* bag with Beta Port for transfer into and out of an Isolator or RABS.

These assemblies are pre-validated, pre-assembled, pre-sterilized systems with bags, tubings, connectors, filters and filling needles, placed inside a beta port bag for easy andsecure insertion and removal around the aseptic filling system.

The beta port bags come with a special port which connects the sterilizing filters with the filling lines, making it convenient for the user to conduct PUPSIT (Pre-use/Post Sterilization Integrity Testing).

Customization

mdi works closely with the process owners to understand their functional as well as regulatory requirements. A technical feasibility of the required design is established based on available components and an initial drawing is proposed. Product prototyping and final approval leads to user specific filling line realization.

Customization may include but is not limited to:

- Bag size and ports
- Filter MOC, size and pore size
- Tubing length, lumen and thickness
- Different filling needle lumen for different fill volumes
- Filling needle hub connections with hose barb or female luer lock

*Restricted Access Barrier System

Disposable Single Use Filling Lines

Critical components in Disposable Filling Lines

mdi manufactures some of the most critical components in-house for disposable filling lines. These components undergo a stringent component incorporation regimen to ensure regulatory as well as functional compliance.

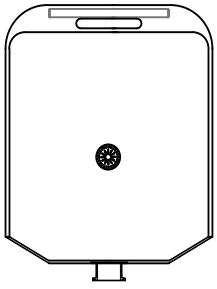
Sterilizing Grade Membrane Filters

mdi capsule filters with PES and hydrophilic PVDF membranes are available in different pore sizes, sizes and end connections for sterile filtration of drug products. **mdi** also offers filter validation services with specific drug products in compliance with international regulatory requirements.

mdi also offers hydrophobic PVDF membrane capsule filters for air/gas filtration applications.

Click here to know more.

Storage and Transfer Bags



mdi *AseptiBag* Gold storage and transfer bags are made with multilayered film validated for high barrier properties such as Co_2, O_2 and water vapours. This protects the drug product from oxidation, change in pH and change in concentration.

The ULDPE contact layer ensures very low extractables.

Click here to know more.

Filling Needles

mdi Acufil single use filling needles offer flexibility as these come in different sizes (1.6mm I.D - 5.4 mm ID) with different hub options (female luer connection or hose barb connections).

These are validated for accurate volume filling and no drip formation.

Click here to know more.

Quikonnect Quick Connectors

mdi QuiKonnect gamma irradiatable Polycarbonate Quick Connectors provides reliable and easy connectivity in critical aseptic process steps in the manufacture of pharmaceuticals and biopharmaceuticals.

Click here to know more.

Beta Bags

mdi Acufil disposable filling lines comes with AseptiSac beta bags for isolators. These are available with a special port for attaching sterilizing grade filtration assemblies to the disposable filling line from outside, to facilitate easy pre-use post-sterilization integrity testing (PUPSIT) of filters.

50 mm 9 Port Manifold

The 9 Port Manifold with 50 mm sanitary flange connection for multiple filling lines.

AseptiFit PP Fittings

A wide range of gamma stable fittings such as cross connections, T connections, Y connections and reducers to support various plumbing requirements within these customized filling lines.

Disposable Single Use Filling Lines

Quality Assurance

mdi single use filling lines are well designed products with in-built quality assurance. ISO-9001 Certified Quality Management System, careful selection of raw materials, validated production processes and testing procedures based on international standards and guidelines such as CFR, PDA, and ASTM, ensures manufacture of consistently high quality assemblies.

36 Acre Campus

Validation

Validation at **mdi** is an integral part of product and process development. As per Bio-Process Systems Alliance (BPSA) guidelines and standards committee document and component quality test matrices for single use systems, a wide range of physical, chemical, biological, and functional tests are to be conducted to qualify and validate various product specifications and ensure compliance.

Since **mdi** single use filling lines are used in biopharmaceutical processes, all critical components used in these assemblies have been validated to provide detailed evidence of compliance with regulatory as well critical process requirements with regard to sterility, bioburden, bacterial endotoxins,biosafety, extractables, product integrity, packaging and transportation. These validations have been designed based on various regulatory and industry standards and guidelines such as USP, ISO, ASTM and CFR.

GC-MS-MS

QTOF-LC-MS

Extractables

mdi has strong analytical abilities with in-house state of the art analytical instrumentation such as HS-GCMS, GCMS, LCMS, TOC Analyzer along with well qualified and trained manpower to deeply characterize different SUS components for volatile, semi-volatile and non-volatile extractables with multiple extraction media under different conditions of time and temperature.

The extractables study on filling line components is performed as per **BioPhorum Best Practices Guide for Extractable Testing of Polyemric Single-Use Components used in Biopharmaceutical Manufacturing**.

Disposable Single Use Filling Lines

Bacterial Endotoxin

Aqueous extracts exhibit <0.25 EU/ml as established by Limulus Amebocyte Lysate (LAL) Test as per USP <85>.

Particulate Matter

mdi Filling line comply with USP <788> test for particulate matter in injections.

Biosafety

Single use filling lines passes Biological Reactivity test, In-Vivo, as per USP <88> for Class VI plastics

TSE BSE Free

mdi Acufil single use filling lines are free from BSE and TSE transmitters, and fulfill the requirements laid down in the "Note for Guidance EMEA/410/01, rev. 03".

Sterility Assurance

mdi Acufil single use filling lines are sterilized by gamma irradiation to provide a sterility assurance level of 10^{-6}. The sterilization process has been validated as per ISO 11137-2 which includes dose verification, dose mapping and quarterly dose audits.

The sterilization dose of 25 kGy has been substantiated through careful definition of the test samples, bio-burden testing of multiple lots of the selected test samples, calculation of verification dose and sterility testing.

Single Use Assembly Manufacturing

mdi quality management system emphasizes on quality by design along with end product testing. Robust processes are developed for product manufacturing and are continuously monitored to ensure that the products meet their predetermined specifications and lot to lot reproducibility is ensured.

mdi single use filling lines are produced by trained personnel in validated ISO class 7 facilities using validated production processes.

ISO Class 7 Manufacturing Areas

Employee hygiene, gowning and continuous monitoring of clean room environment are an essential part of these processes.

Each lot has well compiled batch manufacturing records (BMR) that ensure complete traceability of raw materials, machines, in-process controls, personnel and quality control test data.

Quality assurance personnel carry out the final bath release after verification of complete batch manufacturing records.

Disposable Single Use Filling Lines

Quality Certification

mdi disposable single-use filling lines are supplied with a certificate of quality certifying compliance to product specifications as per regulatory as well as industry requirements.

Traceability: The lot number is mentioned on each **mdi** single use filling lines packing label to ensure complete traceability.

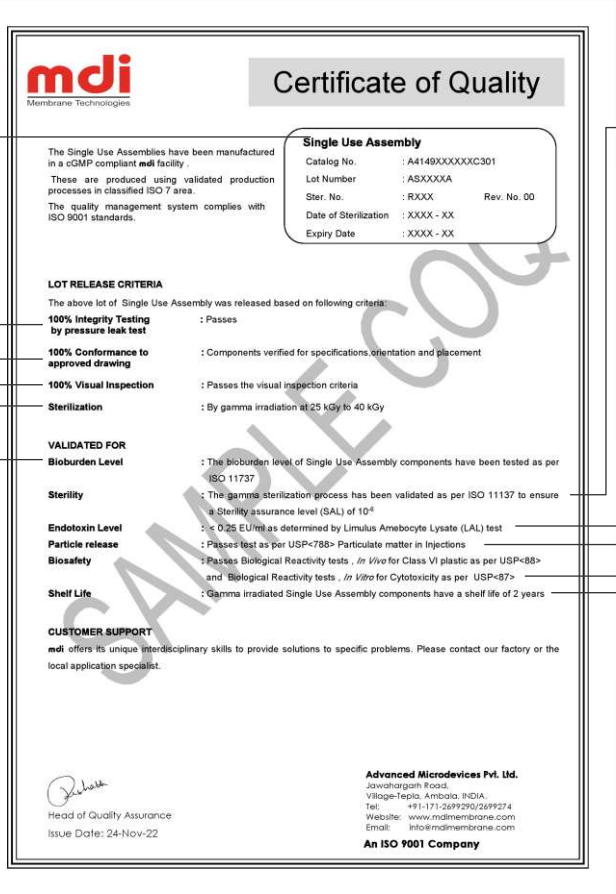
100% Integrity Testing by Pressure Leak test: Passes

100% Integrity Conformance to Approved Drawing: Component verified for specifications, orientation and placement

100% Visual Inspection: Passes the Visual Inspection criteria

Sterilization: By Gamma Irraidation at 25kGy to 40 kGy

Bioburden Level: The bioburden level of Single Use Assembly components have been tested as per ISO 11737



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Certificate of Quality

The Single Use Assemblies have been manufactured in a cGMP compliant **mdi** facility .
These are produced using validated production processes in classified ISO 7 area.
The quality management system complies with ISO 9001 standards.

Single Use Assembly

Catalog No.	: A4149XXXXXXC301
Lot Number	: ASXXXXA
Ster. No.	: RXXX Rev. No. 00
Date of Sterilization	: XXXX - XX
Expiry Date	: XXXX - XX

LOT RELEASE CRITERIA

The above lot of Single Use Assembly was released based on following criteria:

100% Integrity Testing by pressure leak test	: Passes
100% Conformance to approved drawing	: Components verified for specifications,orientation and placement
100% Visual Inspection	: Passes the visual inspection criteria
Sterilization	: By gamma irradiation at 25 kGy to 40 kGy

VALIDATED FOR

Bioburden Level	: The bioburden level of Single Use Assembly components have been tested as per ISO 11737
Sterility	: The gamma sterilization process has been validated as per ISO 11137 to ensure a Sterility assurance level (SAL) of 10^{-6}
Endotoxin Level	: < 0.25 EU/ml as determined by Limulus Amebocyte Lysate (LAL) test
Particle release	: Passes test as per USP<788> Particulate matter in Injections
Biosafety	: Passes Biological Reactivity tests , *In Vivo* for Class VI plastic as per USP<88> and Biological Reactivity tests , *In Vitro* for Cytotoxicity as per USP<87>
Shelf Life	: Gamma irradiated Single Use Assembly components have a shelf life of 2 years

CUSTOMER SUPPORT

mdi offers its unique interdisciplinary skills to provide solutions to specific problems. Please contact our factory or the local application specialist.

Head of Quality Assurance
Issue Date: 24-Nov-22

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An ISO 9001 Company

SAMPLE COC

Sterility: The gamma sterilization process has been validated as per ISO 11137 to ensure a Sterility assurance level (SAL) of 10^{-6}.

Endotoxin level: < 0.25 EU/ml as determined by Limulus Amebocyte Lysate (LAL) test

Particle Release: Passes test as per USP<788> Particulate matter in Injections.

Biosafety: Passes Biological Reactivity tests , *In Vivo* for Class VI plastic as per USP<88> and Biological Reactivity tests, *In Vitro* for Cytotoxicity as per USP<87>.

Shelf Life: Gamma irradiated Single Use Assembly components have a shelf life of 2 years

How to order: Product Realization

User Specified Filling Line Design Specifications

User process flow requirements such as working environment, volume range, temperature conditions, fluid pressure, size and number of connections, transfer lengths, sampling needs etc. are established

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Technical feasibility

Based on the above information and available components a technical feasibility of the filling line is done and an initial drawing of same is submitted for user approval

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Design approval

- User approval of filling line drawing
- Changes to finalize drawing, if required

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Finalized Single Use Filling Line

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