aranBiotech
SINGLE USE TECHNOLOGIES

Validation Guide

Contents

1. Product Overview

Liquid single-use bags are containers designed for the transfer and storage of liquids in cGMP biopharma manufacturing environments. Bags are available from 50 mL to 50 L, 2 to 4 ports, and can be customized with a variety of standard tubing and connections. The information in this validation guide summarizes the quality, properties and current testing of our standard chambers.

2. General Information

2.1 Quality Systems

Liquid single-Use bags manufactured under ISO 9001, ISO 13485 certified facilities in compliance with Current Good Manufacturing Practices (cGMPs) the production room is comply with ISO 14644, room classification, ISO 7.

2.2 Certificates of Conformance

Liquid single-use bags come with a certificate of conformance containing the following information: Product Name, Product Part number, Batch Number, Manufacturing Date, Expiry Date, Storage Condition, Manufacturing Date, Irradiation Range, Visual Inspection (100%), and Sterility

The certificate of conformance also contains information on product compliance with Product Conformity, Bag Conformity, Bag chamber leak test, Bag chamber burst test, Pressure test in water.

A sample Certificate of Conformance is available upon request.

3. Product Information

3.1 Shelf-Life

Standard liquid bags and custom liquid bags made of standard components have an expiration date of 30 months from the date of manufacture (pre and post irradiation). This shelf life is based on film aging tests and sterility claims.

3.2 Tubing

The standard liquid bag assembly configurations include line sets made from TPE or platinum-cured silicone tubing. All sizes use animal-derived component-free material and adhere to BPSA test and quality standards.

3.3 Ports

Our ports are specially engineered to offer high-integrity and improved flow for critical bioprocessing applications.

3.4 Sterility

Validation of the gamma irradiation for all single use system families is performed per ISO 11137-2 guideline. Products irradiated and released based on exposure to gammairradiation doses ranging from 25 to 40 kGy. Validation has determined that an irradiation dose of 25 to 40 kGy provides a minimum Sterility Assurance Level of 10^{-6} for product contact surfaces.Routine Dose Audit testing performed following ISO 11137 guideline.

3.5 Film Information

All liquid single-use bag chambers are made from Renolit 9101 Solmed Infuflex film. Renolit 9101 is a multilayer, coextruded barrier film with inert polyethylene fluid contact layer and internal EVOH oxygen barrier layer produced in a cGMP facility.

The film is free of animal-derived components, and has a low extractable/leachable profile, with data available upon request. The tables belowprovide specifics about the film's physical properties and biocompatibility.

Property	Typical Value Pre | Post Gamma	Method
Haze	7 | 7 %	ASTM D-1003
Clarity	97 | 97 %	ASTM D-1003
Transmittance	93 | 93 %	ASTM D-1003
Elongation at Break	370 | 350 %	ASTM D-882
Tensile Strength at Break	14 | 13 MPa	ASTM D-882
Elastic Modulus	250 | 270 MPa	ASTM D-882

Property	Typical Value Pre | Post Gamma	Method
Break at Cold Temperature	<-45 | <-45 °C	ISO 8570
Density	0.9 | 0.9 g/cm^3	ASTM D-792
Water Vapour Transmission Rate (23°C, 100% RH)	0.35 | 0.32 g/m^2/day	ASTM F-1249
O_2 Permeability (23°C, 0% RH)	<0.05 | <0.05 cm^3/m^2/day/bar	ASTM D-3985
CO_2 Permeability (23°C, 0% RH)	<0.2 | <0.2 cm^3/m^2/day/bar	ASTM F-2476

3.6 Film Biocompatibility Table

Method	Description
ISO 10993-4	Hemolysis
ISO 10993-5	Cytotoxicity
ISO 10993-6	Implantation
ISO 10993-10	Irritation and Sensitization
ISO 10993-11	Acute Systemic Toxicity
USP<85>	Bacterial Endotoxins – LAL
USP<87>	Biological Reactivity, in vitro
USP<88>	Biological Reactivity, in vivo, Class VI
USP<661.1>	Polyethylene Physiochemical Tests, Extractable Metals Plastic Additives Note: Exceeds TOC requirement because of EVOH. Statement of rationalization provided upon request.)
EP 3.1.5	Polyethylene with Additives for Containers for Parenteral Preparations and for Ophthalmic

3.7 Animal-Derived Component Free (TSE/BSE)

Standard single use system film that is Animal-Derived Component Free.

All direct product contact parts used in the single use system are animal-derived component free or in compliance with the European EMEA/410/01 Rev.3 and CPMP Guideline (CPMP/BWP/1230/98)

entitled “Note for Guidance for Minimizing the Risk of Transmitting Animal Spongiform EncephalopathyAgents via Medical Products” (TSE), including Bovine Spongiform Encephalopathy (BSE).

4. Single Use Design Testing

4.1 Summary

Liquid single-use system manufactured under ISO 9001 and ISO 13485 certified facilities in compliance with Current Good Manufacturing Practices (c'GMPs) as defined in CFR 21 Part 820.

The production area classification is ISO 7 according to ISO 14644-1.

Method	Description
Visual Inspection	Bags met the dimensional tolerances and requirements of engineering drawings.
Product Conformity	Technical Drawing compliance and Batch record review.
Bag Chamber Leak Test	Bags tolerated pressures of 6 PSI for 15 minutes without leakage.
Bag Chamber Burst Test	Bags tolerated pressures greater than 7 PSI without leaking.
Port Leak Test in Water	Bags filled with water at 4 PSI pressure without leaking.
Port Weld Seam Strengths	Peel tests were preformed on all welded seams (film-to-port).

4.2 Visual Inspection

100% articles were visually inspected relative to drawing for dimensional tolerance andseal quality. All articles met the product and drawing requirements.

4.3 Leak Test

Representative articles were filled with pressurized air in 6 PSI increments for 15 minutes without leakage. All articles passed the requirement of 6 PSI. No articles showed any signs of leakage.

4.4 Burst Test

Representative articles were filled with pressurized air in increasing 7 PSI increments until the bag burst or excessive growth was observed. All articles passed the requirement of 7 PSI.

4.5 Port Leak Test in Water

Representative assemblies (bags and port) prepared and filled with water. The assemblies then pressurized to 4 PSI. No signs of leakage identified in any assemblies.

4.6 Port Weld Seam Strengths

Peel tests were performed on all welded seams (film-to-port). All weld seam strengths met standard Single Use System Aran Biotech requirements according to our control methods for manufacturing all our single use systems sizes.

5. Quality Control

5.1 Introduction

Only the highest quality components are used in the manufacture of the Single Use System. Each component is given a unique part number and has a controlled material specification. In addition, we actively promote communication with vendors, conduct audits of vendors and maintain a vendor evaluation program.

5.2 Inspection

Incoming components are quarantined until they have met the approved component specification's criteria. During the inspection process, lot numbers and part numbers are recorded for traceability purposes. Once components have satisfied the requirements in the specification, they are released into inventory by QC personnel. In-process inspections and testing take place during the manufacturing process to ensure that each production is being manufactured to the approved specifications.

5.3 Lot Record Release and Certificate of Conformity

The production control process ensures traceability for each lot. The process control document becomes the stepwise manufacturing record, which physically accompanies the lot through manufacturing.

DHR: Device History Record contains all of the information and specifications needed to produce the final product from start to finish, including instructions for all manufacturing processes, drawings, documented specifications, and labeling and packaging requirements.

At the end of the production process, quality assurance reviews the lot record for completeness and correctness prior to the release of the lot. At this time a Certificate Of Conformity (COC) is issued.

Lot record review:

- Certificate of Conformity
- Bill of Materials
- Certificate of Irradiation
- Production quality inspections
- Production integrity testing
- Labels
- Deviations

Certificate of Conformity:

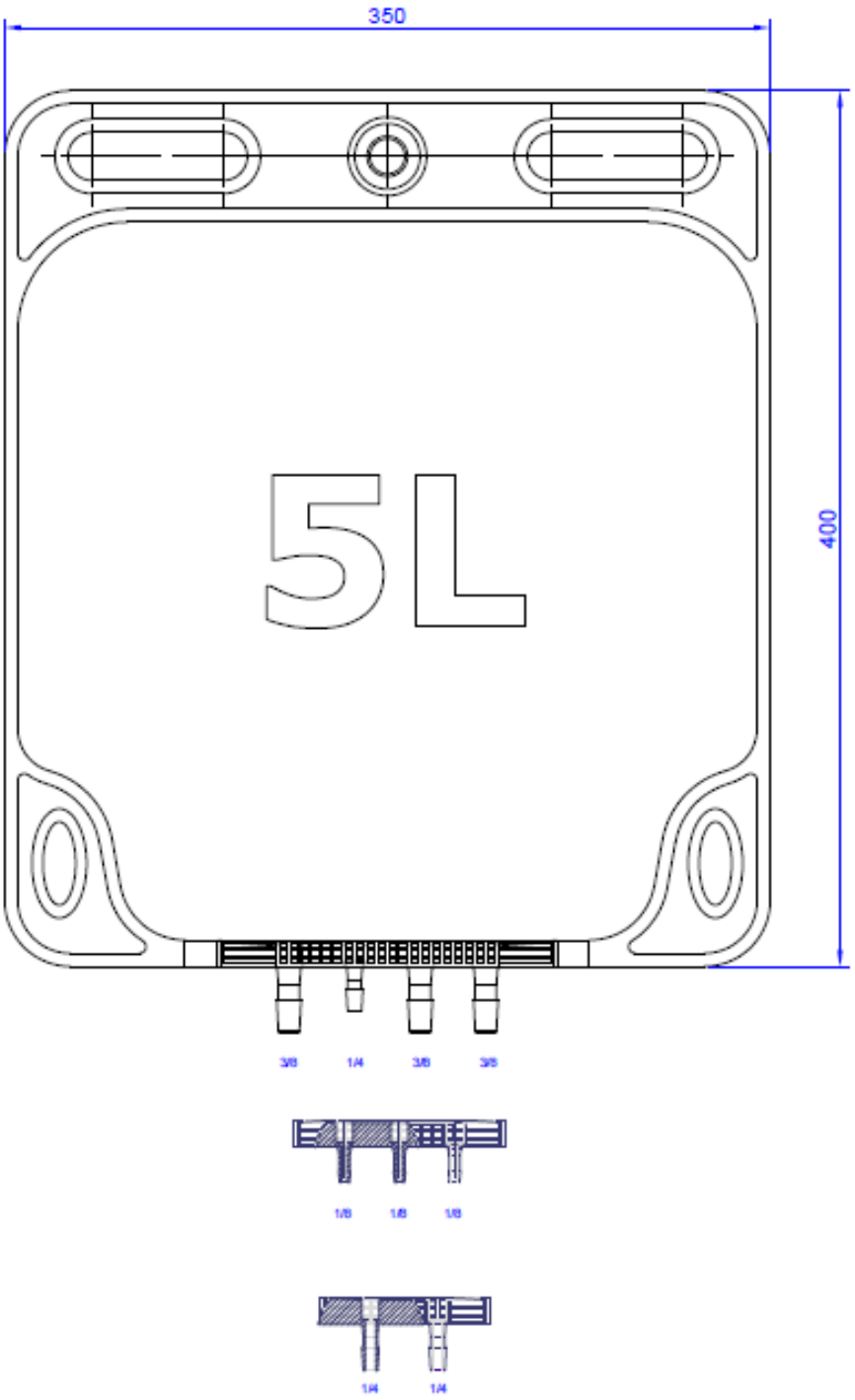
- Product name
- Catalog number
- Lot number
- Expiration date
- Irradiation dosage

6. Summary

Single use system covers longstanding commitment to quality as reflected in every single-use liquid bag. All bags are manufactured from high-quality materials and components under an ISO 9001 and ISO 13485 systems, in accordance with cGMPs, and comes with supporting quality documentation. Our routine testing of leak test, burst test, port weld test, and irradiation ensure the continued safety of our single-use system, and our extensive design testing instills confidence that each liquid single-use system will perform form as expected in cGMP-compliant biopharmaceutical processes.

7. Annexure

7.1 Figure: Single use system and optional ports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