ILC DOVER

Validation Guide

Liquid Single-Use Bags

BEYOND BOUNDARIES®

Contents

1. Product Overview 3

2. General Information 3

2.1 Quality Systems 3

2.2 Certificates of Conformance 3

3. Product Information 3

3.1 Shelf-Life 3

3.2 Tubing 3

3.3 USP<85> Endotoxin Testing 3

3.4 USP<788> Particulate Testing 4

3.5 Sterility 4

3.6 Film Information 4

3.7 Film Physical Properties Table 4

3.8 Film Biocompatibility Table 5

3.9 Animal-Derived Component Free (TSE/BSE) 5

4. Bag Design Testing 5

4.1 Summary 5

4.2 Visual Inspection 6

4.3 Volume Overage and Handling 6

4.4 Suspended Structural Capacity Test – 24 Hour Dwell 6

4.5 System Pressure Capability and Leakage 6

4.6 Drainage & Flow 6

4.7 Burst Test 6

4.8 Pinch Clamp Integrity with Head Pressure 6

5. Summary 7

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 are manufactured in ISO 9001 certified facilities in compliance with Current Good Manufacturing Practices (cGMPs) as defined in CFR 21 Part 820.

2.2 Certificates of Conformance

Liquid single-use bags come with a certificate of conformance containing the following information: ILC Part number, Customer Reference Number, Description, Quantity, Lot, Material, Thickness, Manufacturing Date, Expiration Date, Irradiation Range, Visual Inspection (100%), and Sterility

The certificate of conformance also contains information on product compliance with USP<85> Bacterial Endotoxin Test, USP<788> Particulate Matter in Injections Light Obscuration Count Test, and Renolit 9101 Film compliance with USP<661.1> (with TOC exemption), USP<85> Bacterial Endotoxins, USP<87> Biological Reactivity Test In Vitro, USP<88> Biological Reactivity Test In Vivo, and EP 3.1.5.

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 two years from the date of manufacture. This shelf life is based on film aging test and sterility claims.

3.2 Tubing

The standard liquid bag assembly configurations include linesets 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 USP<85> Endotoxin Testing

Endotoxin Validation was completed on representative 2D liquid bags. This validation included liquid bags in a range of sizes (50 mL to 200 L) across multiple lots. Samples were tested in accordance with USP Bacterial Endotoxin Test, USP<85>. All validation samples passed the USP requirement of ≤ 0.25 EU/mL (water for injection) as determined by the Limulus Amebocyte Lysate Test (LAL), Kinetic Chromogenic method.

Samples of representative products are routinely tested for the presence of endotoxin to confirm

consistent performance in accordance to USP<85> guidelines.

3.4 USP<788> Particulate Testing

Particulate Validation was completed on representative 2D Liquid bag samples. This validation included liquid bags in a range of sizes (50 mL to 200 L) across multiple lots. Testing of a 200 L Manifold was also completed as part of the validation. Samples were tested in accordance with USP<788>, Particulate Matter in Injections. All validation samples passed the requirements per USP<788>, Method 1 (Light Obscuration Count Test), Test 1A Criteria.

Samples of representative products are routinely tested for the presence of particulates to confirm consistent performance in accordance to USP<788> guidelines.

3.5 Sterility

Validation of the gamma irradiation for all ILC Dover bag product families is performed per ANSI/AAMI/ISO 11137-2 guidelines. Products are irradiated and released based on exposure to gamma irradiation doses ranging from 25 to 50 kGy. Validation has determined that an irradiation dose of 25 to 50 kGy provides a minimum Sterility Assurance Level of 10^{-6} for product contact surfaces. Routine Dose Audit testing is performed following ANSI/AAMI/ISO 11137 guidelines.

3.6 Film Information

All liquid single-use bag chambers are made from Renolit 9101 Solmed Infuflex film. Renolit 9101 is a 12.8 mil 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 extractables/leachables profile, with data available upon request. The tables below provides specifics around the film's physical properties and biocompatibility.

Property	**Typical Value** Pre I Post Gamma	**Method**
Haze	7 I 7 %	ASTM D-1003
Clarity	97 I 97 %	ASTM D-1003
Transmittance	93 I 93 %	ASTM D-1003
Elongation at Break	370 I 350 %	ASTM D-882
Tensile Strength at Break	14 I 13 MPa	ASTM D-882
Elastic Modulus	250 I 270 MPa	ASTM D-882
Break at Cold Temperature	<-45 I <-45 °C	ISO 8570
Density	0.9 I 0.9 g/cm^3	ASTM D-792
Water Vapor Transmission Rate (23°C, 100% RH)	0.35 I 0.32 g/m^2/day	ASTM F-1249
O_2 Permeability (23°C, 0% RH)	<0.05 I <0.05 cm^3/m^2/day/bar	ASTM D-3985
CO_2 Permeability (23°C, 0% RH)	<0.2 I <0.2 cm^3/m^2/day/bar	ASTM F-2476

3.8 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 Preparations

3.9 Animal-Derived Component Free (TSE/BSE)

Standard liquid bags use film that is Animal-Derived Component Free.

All direct product contact parts used in the 2D liquid bags 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 Encephalopathy Agents via Medical Products" (TSE), including Bovine Spongiform Encephalopathy (BSE).

4. Bag Design Testing

4.1 Summary

Liquid single-use bags are manufactured in ISO 9001 certified facilities in compliance with Current Good Manufacturing Practices (cGMPs) as defined in CFR 21 Part 820.

Method	Description
Visual Inspection	Bags met the dimensional tolerances and requirements of engineering drawings.
Volume Overage & Handling	Bags tolerated the nominal volumes with a 1.2x factor of safety.
Suspended Structural Capacity Test – 24 Hour Dwell	Bags tolerated being filled by 1.2x their nominal volume and hung for 24 hours without any signs of structural failure.

Method	Description
System Pressure Capability & Leakage	Bags and tubing tolerated pressures of 2 PSI without leakage.
Drainage & Flow	Bag drained 95% of contents (by mass) under free flow and 99% of contents (by mass) with manipulation.
Burst Test	Bags tolerated pressures greater than 2 PSI without leaking.
Pinch Clamp Integrity with Head Pressure	Bags tolerated pinch clamp at 2 PSI pressure without leaking.

4.2 Visual Inspection

Representative articles were visually inspected relative to drawing for dimensional tolerance and seal quality. All articles met the product and drawing requirements.

4.3 Volume Overage and Handling

Representative chambers were tested to ensure they can accommodate 1.2 times the nominal volume. All chambers tested accommodated the volume.

4.4 Suspended Structural Capacity Test – 24 Hour Dwell

The articles from "Volume Overage and Handling" testing were hung from their handle for 24 hours and then evaluated for any signs of structural failure. No articles showed any signs of structural failure.

4.5 System Pressure Capability and Leakage

Representative assemblies (bags and tubing) were prepared and filled with water. The assemblies were then pressurized to 2 PSI and all connections were flexed 90 degrees while checking for any signs of leakage. No signs of leakage were identified in any assemblies.

4.6 Drainage & Flow

A representative article was filled to the nominal volume, hung, and then allowed to drain by gravity without and with manipulation. The test article drained at least 95% of contents by mass under free flow and at least 99% of contents by mass with manipulation.

4.7 Burst Test

Representative articles were filled with pressurized water in increasing 0.25 PSI increments until the bag burst or excessive growth was observed. All articles passed the requirement of 2 PSI.

4.8 Pinch Clamp Integrity with Head Pressure

Representative articles were pinch clamped on one tubing, filled with water and pressurized to 2 PSI water, then checked for any leaks. The tests were then repeated by clamping the opposite end and re-pressurizing. No articles showed any signs of leakage.

5. Summary

ILC Dover's longstanding commitment to quality is reflected in every single-use liquid bag. All bags are manufactured from high-quality materials and components under an ISO 9001 system, in accordance with cGMPs, and comes with supporting quality documentation. Our routine testing of endotoxin, particulate, and irradiation ensure the continued safety of our bags, and our extensive design testing instills confidence that each liquid single-use bags bag will perform as expected in cGMP-compliant biopharmaceutical processes.

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