SEAMLESS BIO
HIGH PERFORMANCE

VALIDATION & COMPLIANCE GUIDE

Single-Use 2D & 3D Bioprocess Bags

Material compliance, sterilisation, validation results and extractables data — for supplier qualification and audits.

Document	**SB-SUS-VG-01 · Revision 01 · November 2026**
Products	**Single-use 2D bioprocess bags (50 mL – 50 L) and 3D bioprocess bags (50 – 5,000 L), incl. tubing, ports, connectors and fittings**
Fluid-contact material	**Multilayer PE/EVOH film, 0.325 mm, ULDPE contact layer**
Supplied by	**SeamlessBio GmbH, Passau (DE) · Seamless Bio GmbH, Münchenstein (CH)**
Manufactured by	**Certified manufacturing partner (ISO 9001:2015 · ISO 13485:2016), ISO Class 7 cleanroom, in-house gamma irradiation**
Intended use	**Biopharmaceutical, biotechnology, diagnostics and R&D fluid handling**

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1 Scope & product configuration

This guide applies to **2D single-use bags** used for solution preparation, storage and transfer, and to **3D single-use bags** used for larger-volume preparation, storage and process integration. Covered components: multilayer film, heat-sealed seams and welds, ports, tubing, connectors and fittings. Customer-specific assemblies are defined by an approved technical drawing.

2 Applicable standards

QUALITY & GMP

- ISO 9001 · ISO 13485
- EU GMP (sections applicable to single-use systems)
- ICH Q9 quality risk management

PHYSICAL & MECHANICAL

- ASTM D882 tensile · D1003 haze/transmittance · D792 density
- ASTM D4169 drop / distribution · F88 seal strength
- ASTM F1929 dye penetration · F2095 pressure decay
- ASTM F1249 WVTR · D3985 OTR

CHEMICAL & EXTRACTABLES

- USP <661>, <661.1>, <661.2>
- USP <665> · <1663> extractables · <1664> leachables
- ISO 10993-18 chemical characterisation
- Ph. Eur. 3.1.5 · 5.20 · USP <232>/<233>

BIOLOGICAL SAFETY & STERILISATION

- USP <85>, <87>, <88>
- ISO 10993-4, -5, -6, -10, -11
- ISO 11137 radiation sterilisation · ISO 13004
- ISO 11737 bioburden & sterility

3 Material compliance

Topic	Statement
Substances	No medicinal substances, blood derivatives, plant tissues or derivatives, allergens (e.g. gluten, lactose), melamine, TNPP, SVHC, conflict minerals or constituents of concern per ISO/TS 21726, 5.3.
Animal origin (TSE/BSE)	No substances of human or animal origin (EMEA/CPMP/1230/98); TSE/BSE-free per EC 999/2001 and EMA/410/01 rev. 3.
Residual solvents	Not part of the formulation and not used in manufacturing (ICH Q3C, Ph. Eur. 5.4, USP <467>).
GMO	No ingredients within the scope of Dir. 2001/18/EC and Reg. 1830/2003.
PFAS & flame retardants	Not used and not intentionally incorporated, including precursors.
Latex & thiuram	No natural rubber latex or thiuram used — including packaging and shipping materials.
Nitrosamines	Not used and not intentionally incorporated.
Plasticisers	No phthalates, plasticisers, fillers or flexibilisers intentionally added. Resin complies with 21 CFR 177.1520.
Other	REACH and RoHS compliant · DNase/RNase-free · BPA-free

4 Manufacturing & packaging

Bags are manufactured and packed in an ISO Class 7 cleanroom under an ISO 9001 / ISO 13485 quality system with full lot traceability. Dimensions and bill of materials are verified against the approved drawing for every order.

PRIMARY & SECONDARY PACKAGING

- Individually double-packed in cleanroom-grade LDPE bags
- Inner and outer bag heat-sealed
- Cartons 3–5 ply corrugated, sealed and labelled

UNIT LABEL

- Part number and description
- Lot number and quantity
- Expiry date
- Sterilisation indicator (where applicable)

Shelf life and packaging performance are supported by accelerated ageing studies at accredited third-party laboratories (ASTM F1980).

5 Sterilisation

Item	Details
Method	Gamma irradiation, in-house
Validation	ISO 11137 · dose substantiation per ISO 13004 (VDmax25); customer-specific dose validation on request
Sterility assurance level	SAL 10^{-6} — satisfactory dose verification, no growth observed
Routine dose range	25–40 kGy
Film radiation tolerance	Qualified for gamma doses up to 50 kGy (film manufacturer statement)
Bioburden	ISO 11737
Endotoxin	LAL, kinetic chromogenic assay per ISO 11737-3 / USP <85>; limit ≤ 0.01 EU/mL

6 Pharmacopoeia & biocompatibility (fluid-contact film)

PHARMACOPOEIA

- Ph. Eur. 3.1.5 — polyethylene with additives for containers for parenteral and ophthalmic preparations; metals per Ph. Eur. 5.20
- USP <661.1> plastic materials of construction
- USP <85> bacterial endotoxins
- USP <87> in vitro and <88> in vivo, Class VI

ISO 10993 BIOCOMPATIBILITY

- -4 haemolysis
- -5 cytotoxicity (also tested before each film batch release)
- -6 intramuscular implantation
- -10 intracutaneous irritation and sensitisation (Kligman)
- -11 acute systemic toxicity

7 Food contact & migration

Regulation	Result
EU 10/2011 — overall migration	EN 1186, simulants A (10 % ethanol), B (3 % acetic acid) and D2 (vegetable oil), condition OM2 (10 days, 40 °C): all results within the 10 mg/dm² limit
USA — 21 CFR	Food contact substances per 21 CFR; resin per 21 CFR 177.1520 olefin polymers
Bisphenol A	Not used and not knowingly present as impurity (21 CFR 175 restrictions)
Scope	2D bags 50 mL – 50 L · 3D bags 50 – 5,000 L

8 Validation strategy (IQ / OQ / PQ)

IQ

Equipment ready. Calibration of tensile testers, pressure testers, balances and measuring devices; test fixtures verified.

OQ

Methods repeatable. Integrity, mechanical and functional tests run under defined conditions; repeatability confirmed.

PQ

Product consistent. Representative bag sizes and configurations tested across representative production lots.

Acceptance: all samples comply with the defined acceptance criteria. IQ/OQ/PQ protocols and reports, raw data, calibration certificates and deviation/CAPA records are retained by the manufacturer.

9 Validation tests & results

Test	Purpose	Standard	Result
Leak (bubble emission)	Gross leaks in body, seams, ports	ASTM E515 / F2096	No bubbles under pressure
Connection firmness	Security of tubing and ports	Internal	No dropout, 15 N axial for 15 s
Heat-seal strength	Strength of sealed joints	ASTM F88	> 50 N/15 mm, no separation
Tensile / elongation	Film strength and ductility	ASTM D882	Meets film specification
Drop test	Handling and transport stress	ASTM D4169	No rupture or leakage
Unsupported hold	Long-term integrity without support	Internal	1,000 L and 2,000 L: no leakage after 90 days
Weight loss	Evaporation / permeation	Internal	No significant change, 30 days RT
Water vapour permeability	WVTR of bag film	ASTM F1249	Within applicable limits
Insoluble particles	Particulate release	USP <788>	≥ 5, ≥ 10, ≥ 25 µm within limits
Pressure decay	Micro-leaks in sealed cavity	ASTM F2095	Pressure drop ≤ 10 %
Dye penetration	Seal continuity	ASTM F1929	No dye penetration
Freeze–thaw	Low-temperature suitability	Internal	Repeated cycles to -80 °C, no leakage or seal failure

10 Extractables study

An extractables profile of bags made from the fluid-contact film was generated following the BioPhorum (BPOG) standardised extractables protocol. The study was performed by an external contract laboratory under cGMP (21 CFR 210/211). It supports USP <665> and gives you the basis for a leachables risk assessment.

Parameter	Study design
Test articles	Bags from 2 film lots, gamma-irradiated at 42.1–47.7 kGy (worst case)
Extraction fluids	50 % ethanol · 1 % polysorbate 80 · 5 M NaCl · 0.5 M NaOH · 0.1 M H_3PO_4 · deionised water
Time points	T0 (room temperature) · 24 h · 21 days · 70 days at 40 °C
Surface / volume	6 cm²/mL · 48 bags in total (2 lots × 6 fluids × 4 time points)
Analytics	pH · TOC · ICP-MS (trace elements) · HS-GC-MS/FID · GC-MS/FID · LC-UV/MS
Reporting threshold	Organics 0.1 µg/mL (0.02 µg/cm²); identification levels unidentified / tentative / confident / confirmed

Key findings

BULK CHEMISTRY

- pH shift vs. control in 0.5 M NaOH and 0.1 M H_3PO_4 below 0.1 units at all time points
- TOC (control-subtracted) in 0.5 M NaOH at most ~1.1 µg/cm² after 21–70 days
- pH changes in DI water and PS-80 mainly from CO_2 uptake and PS-80 hydrolysis (also seen in controls)

ELEMENTS & ORGANICS

- Trace elements mostly < 0.002 µg/cm²; silicon up to 0.027 µg/cm² (0.5 M NaOH); sodium 0.88 µg/cm² in 1 % PS-80 only
- No trace elements detected in 5 M NaCl
- Carboxylic acids (C5–C7) seen in 0.5 M NaOH; hexadecanoic and octadecanoic acid also present in controls, therefore not listed as extractables

The 70-day condition is the most challenging and is used for maximum estimated concentrations. Complete aggregated tables of organic extractables and metal ions are part of the full report, available on request (NDA if required).

11 Lot release & traceability

Every delivery comes with a lot-specific Certificate of Analysis listing batch number, volume, product description, material, production and expiry date.

Release test	Limit	Result reported
Particle count, USP <788>	≥ 10 µm: 12 particles/mL · ≥ 25 µm: 2 particles/mL	Compliant with USP <788>
Sterility assurance, ISO 11137	Satisfactory dose verification, no growth	SAL 10^{-6} achieved
Endotoxin / pyrogen, ISO 11737-3	≤ 0.01 EU/mL	Endotoxin / pyrogen-free

The CoA also confirms: material per 21 CFR 177.1520; USP <88> Class VI, <87> and <661.1>; BSE/TSE statement; latex-free statement; ISO 11137-validated irradiation process; LAL method (kinetic chromogenic).

Lot number structure

10-digit lot number plus 3-digit serial number. The lot number encodes volume, container type, material, year, production serial number and month, so that every unit can be traced back to its manufacturing records in the event of a non-conformity.

12 Documentation & disclaimer

AVAILABLE ON REQUEST

- Lot-specific Certificate of Analysis
- Radiation processing certificate
- Sterilisation validation report
- Extractables study report (BPOG)
- Film technical data sheet
- Declarations: migration (EU 10/2011), food contact, gamma compatibility, regulatory compliance
- Approved technical drawing per part number

DISCLAIMER

Statements in this guide are based on manufacturer and film supplier certifications, historical data and periodic representative testing. They are not specific to individual lots and do not imply routine batch-wise testing of finished products unless stated on the CoA.

The extractables study covers components typically used in custom assemblies and is not specific to a customer part number. It remains the responsibility of the user to confirm suitability for the intended process.

Prepared	Reviewed / approved	Date
SeamlessBio GmbH	Quality Assurance	November 2026

Need more for your audit? Send your supplier questionnaire to info@seamlessbio.de (Germany, +49 851 37932226) or info@seamlessbio.ch (Switzerland). We complete it together with our manufacturing partner and add the reports listed above.