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Statement

Object: Chemical compatibility study of selected Sartorius products

Dear Valued Customer,

Sartorius Stedim Biotech conducted a theoretical risk assessment and in-house and external functionality tests to assess the chemical compatibility (physical resistance) of select Sartorius Stedim Biotech (Sartorius) and 3rd Party single-use bioprocessing product contacting equipment to organic solvents. Table 1 lists the organic solvents used in the risk assessment, in-house studies and 3rd party studies.

Table 1: Solvents researched and tested in chemical compatibility study.

Solvent	Common Abbreviation	CAS No
N,N-dimethylacetamide	DMAc	127-19-5
Dimethyl sulfoxide	DMSO	67-68-5
N,N-dimethylformamide	DMF	68-12-2
Propylene glycol	PG	57-55-6
Acetonitrile	ACN	75-05-8
N-methyl-pyrrolidone	NMP	872-50-4

After theoretical risk assessment, the chemical compatibility of selected product contacting single-use equipment to Table 1 solvents was ensured by functionality testing after exposure to the solvents in Table 1 at concentrations of 100% and/or 20%, as applicable and described below.

Table 2 lists the fluid management and separation products that were tested with passing results after exposure to the solvents in Table 1 at 100% concentration at time zero and after accelerated aging (if applicable), their materials of construction, the experimental conditions and evaluation criteria.

Table 2: Single-use fluid management and separation bioprocessing equipment tested for chemical compatibility to 100% solvent with passing results.

Product	Material of construction	Test condition	Sterilization condition	Aging Condition	Evaluation Criteria	Results
Tubing	PharMed® BPT	Recirculation by peristaltic pump, 30 min, room temperature	Gamma irradiation	NA	Leakage, visual appearance	Passed
Tubing	TuFlux® TPE and C-Flex® 374	Recirculation by peristaltic pump, 1 hr, room temperature	Gamma irradiation	NA	Leakage, visual appearance	Passed ¹
Tubing	TuFlux® TPE	Immersion, 7 days, room temperature	Gamma irradiation and Autoclave	NA	Per ASTM D543-14: Standard practices for evaluating the resistance of plastics to chemical reagents	Passed ²
Sartopure® PP3 (Pre-filter)	Polypropylene, silicone	Recirculation at 3 Bar, 2 hrs, room temperature	Autoclave	Accelerated	Permeability, Burst pressure capsule housing	Passed
Sartofluor® 0.2 µm filter	Polypropylene, PTFE, EPDM	Recirculation at 3 Bar, 2 hrs, room temperature	Autoclave	Accelerated	Bubble point, burst pressure capsule housing	Passed
Bag port	LLDPE	Immersion, 2 hrs	Gamma irradiation	Accelerated	Traction, visual inspection	Passed
Bag port	HDPE	Immersion, 2 hrs	Gamma irradiation	Accelerated	Traction, visual inspection	Passed

¹ TuFlux® TPE and C-Flex® 374 achieved passing results for only DMSO and PG when recirculated by peristaltic pump.

² TuFlux® TPE did not achieve passing results for 100% DMAc and NMP after 7 day room temperature exposure. TuFlux® TPE may be acceptable for transfer of 100% DMAc and NMP for shorter exposure times, depending on the mechanical stress exerted on the tubing.

Table 3 lists the fluid management products that were tested with passing results after exposure to the solvents in Table 1 at 20% concentration (w/v in water) at time zero and after accelerated aging (if applicable), their materials of construction, the experimental conditions and evaluation criteria.

Table 3: Single-use fluid management bioprocessing equipment tested for chemical compatibility to 20% solvent with passing results.

Product	Material of construction	Test condition	Sterilization condition	Aging Condition	Evaluation Criteria	Results
Tubing	TuFlux® TPE	Immersion, 1 day, room temperature ¹	Gamma irradiation and Autoclave	NA	Per ASTM D543-14: Standard practices for evaluating the resistance of plastics to chemical reagents	Passed ¹
Tubing	TuFlux® SIL	Recirculation by Quattroflow pump, 24 hr, 20° C, 0.5 – 1 bar.	Gamma irradiation	Accelerated	Visual inspection, hardness, stickiness, color change, burst pressure	Passed
Tubing	Si(Pt) reinforced	Recirculation by Quattroflow pump, 24 hr, 20° C, 0.5 – 1 bar.	Gamma irradiation	Accelerated	Visual inspection, hardness, stickiness, color change, burst pressure	Passed
Tubing	C-Flex® 374	Recirculation by Quattroflow pump, 24 hr, 20° C, 0.5 – 1 bar.	Gamma irradiation	Accelerated	Visual inspection, hardness, stickiness, color change, burst pressure	Passed
Flexsafe® bag film	Polyethylene S80 contact layer	Immersion, 24 hrs, 40° C	Gamma irradiation	Accelerated	Traction, elongation at rupture, gelbo flex, air and water burst pressure, leakage	Passed

Product	Material of construction	Test condition	Sterilization condition	Aging Condition	Evaluation Criteria	Results
Flexel® bag film	Polyethylene S40-2 contact layer	Immersion, 24 hrs, 40° C	Gamma irradiation	Accelerated	Traction, elongation at rupture, gelbo flex, air burst pressure	Passed ²
Bag port	LLDPE	Immersion, 2 hrs, room temperature	Gamma irradiation	Accelerated	Traction, elongation at rupture	Passed
Bag port	HDPE	Immersion, 2 hrs, room temperature	Gamma irradiation	Accelerated	Traction, elongation at rupture	Passed
Flexel® and Flexsafe® welded components	Multiple	Immersion, 24 hrs, 40° C	Gamma irradiation	Accelerated	Traction, elongation at rupture	Passed
Magnetic mixer impeller with shield	HDPE/ PVDF/ Ceramic Beads	Immersion, 24 hrs, 40° C	Gamma irradiation	Accelerated	Visual inspection, roughness, ability to turn impeller	Passed
ProMixer® and small scale impeller, cup blades and body	HDPE/LLDPE	Immersion, 48 hrs, room temperature	NA	NA	Visual inspection, mechanical stability	Passed
Bag port: tri clamp 8"	HDPE	Immersion, 24 hrs, 40° C	Gamma irradiation	Accelerated	Visual inspection of clamp and gasket, roughness	Passed

Product	Material of construction	Test condition	Sterilization condition	Aging Condition	Evaluation Criteria	Results
Triclamp cap for 8" port	HDPE	Immersion, 24 hrs, 40° C	Gamma irradiation	Accelerated	Visual inspection, roughness	Passed
Triclamp gasket 8" port	Si(Pt)	Immersion, 24 hrs, 40° C	Gamma irradiation	Accelerated	Visual inspection, roughness	Passed
Thermowell port 3 mm ID	LLDPE	Immersion, 24 hrs, 40° C	Gamma irradiation	Accelerated	Leakage, visual inspection	Passed
Take one light	Stainless steel, platinum silicone, silicone	Immersion, 24 hrs, 40° C	Gamma irradiation	Accelerated	Multi-diffusion, septum tightness, permeability of septum tubing	Passed
Single-use pH Sensor	Glass membrane electrode with and without porous ZrO ₂ pin, polyethylene body	Immersion, 24 hrs, 40° C	Gamma irradiation	Real life	Slope, zero value	Passed
Single-use conductivity sensor	HDPE, ceramic, platinum	Immersion, 24 hrs, 40° C	Gamma irradiation	Real life	Cell constant	Passed

¹ TuFlux® TPE was only tested for 20% DMAc, NMP (because these two solvents were not recommended at 100% concentration after 7 day exposure) and DMF because they represent the most aggressive solvents listed in Table 1 per literature review. The remaining solvents listed in Table 1 were not tested.

² Flexel® bag film weld traction after accelerated aging did not meet acceptance criteria after exposure to NMP.

Flexel® bag film is not recommended for use with NMP solvent ≥ 20%. Flexel® bag film may be acceptable for use with NMP solutions < 20%

Table 4 lists the separation products that were tested with passing results after exposure to the solvents in Table 1 at 20% concentration (w/v in water unless noted otherwise) at time zero and after accelerated aging (if applicable), their materials of construction, the experimental conditions and evaluation criteria.

Table 4: Single-use separation bioprocessing equipment tested for chemical compatibility to 20% solvent with passing results.

Product	Material of construction	Solvent exposure condition	Sterilization condition	Aging Condition	Functional-ity Test/ Evaluation Criteria	Results
Sartobind® Q membrane	Functional-ized stabilized cellulose	20° C, 24 hrs (w/v in 20 mM Tris, pH 7.2)	Autoclave	Accelerated	Permeability, protein dynamic binding capacity	Passed
Sartobind® STIC membrane	Functional-ized stabilized cellulose	20° C, 24 hrs (w/v in 20 mM Tris, pH 7.2)	Autoclave	Accelerated	Permeability, protein dynamic binding capacity	Passed
Sartobind® S membrane	Functional-ized stabilized cellulose	20° C, 24 hrs (w/v in 10 mM potassium phosphate, pH 7.2)	Autoclave	Accelerated	Permeability, protein dynamic binding capacity	Passed
Sartobind® HIC membrane	Functional-ized stabilized cellulose	20° C, 24 hrs (w/v in 10 mM potassium phosphate, pH 7.2)	Autoclave	Accelerated	Permeability, protein dynamic binding capacity	Passed
Sartobind® Q 96 well plate	Polypropylene, polystyrene, silicon, functionalized stabilized cellulose	20° C, 24 hrs (w/v in 20 mM Tris, pH 7.2)	NA	NA	Tightness of wells/silicone gasket/holding frame, buffer permeability, homogenous coloration	Passed ¹
Sartobind® Q Pico device	Polypropylene, silicon, functionalized stabilized cellulose	20° C, 24 hrs (w/v in 20 mM Tris, pH 7.2)	NA	NA	Tightness, permeability	Passed
Sartobind® Q 75 mL capsule	Polypropylene, EPDM, functionalized stabilized cellulose	20° C, 24 hrs, recirculation at 3 bar (w/v in 20 mM Phosphate buffer)	Autoclave	Accelerated	Permeability, protein binding, burst pressure, diffusion	Passed

Product	Material of construction	Solvent exposure condition	Sterilization condition	Aging Condition	Functionality Test/ Evaluation Criteria	Results
Sartolon® 0.2 µm (Midicap®) filter	Nylon, polypropylene, EPDM	20° C, 24 hrs, recirculation at 3 bar	Autoclave	Accelerated	Diffusion, bubble point, burst pressure capsule housing	Passed
50cm ² 30 kDa Hydrosart® Sartocon Slice 50 E	Stabilized cellulose membrane, Silicone, Epoxide, Polypropylene ABS				Integrity, water flux, burst pressure	Passed ²
0.14m ² 30 kDa Hydrosart® self contained ECO	Stabilized cellulose membrane, PVDF, polypropylene, silicone, Polypropylene	20° C, 24 hrs, recirculation at 3 bar	Gamma irradiation	Accelerated	Permeate flow, diffusion	Passed

¹Coloration was inhomogeneous after exposure with 20% propylene glycol but tightness was not impacted.

² Hydrosart® Slice 50 is was only stable up to 10% ACN.

Table 5 lists the components of a single-use cross flow filtration loop that were tested with passing results after exposure to the solvents in Table 1 at 20% concentration (w/v in water) at time zero and after accelerated aging their materials of construction, the experimental conditions and evaluation criteria.

Table 5: Single-use crossflow filtration loop tested for chemical compatibility to 20% solvent with passing results.

Product	Material of construction	Solvent exposure condition	Sterilization condition	Aging Condition	Functionality Test/ Evaluation Criteria	Results
Single-use cross flow loop	Tubing ¹					
	Flow pipe sensor ½" (polybutylene terephthalate)	20° C, 24 hrs, recirculation at 0.5 - 1 bar	Gamma irradiation	Accelerated	Accurate flow rate, burst pressure	Passed
	Pressure sensor ½" (PBT)	20° C, 24 hrs, recirculation at 0.5 - 1 bar	Gamma irradiation	Accelerated	Accurate pressure, burst pressure	Passed
	GEMÜ valve (polypropylene, TPE)	20° C, 24 hrs, recirculation at 0.5 - 1 bar	Gamma irradiation	Accelerated	Closing behavior, burst pressure	Passed
	Quattraflo 1200 single-use pumphead (EPDM, polypropylene, TPV)	20° C, 24 hrs, recirculation at 0.5 - 1 bar	Gamma irradiation	Accelerated	Pump curve, leak tightness, permeability	Passed
	aseptic quick connector (polycarbonate, silicone, PES, PTFE)	20° C, 24 hrs, recirculation at 0.5 - 1 bar	Gamma irradiation	Accelerated	Burst pressure, Leak tight	Passed
	Hose barb connector (polypropylene)	20° C, 24 hrs, recirculation at 0.5 - 1 bar	Gamma irradiation	Accelerated	Visual inspection, hardness, stickiness, color change, weight	Passed
	Hose barb to 1.5" triclamp with gasket (polypropylene, silicone)	20° C, 24 hrs, recirculation at 0.5 - 1 bar	Gamma irradiation	Accelerated	Visual inspection, hardness, stickiness, color change, weight	Passed

¹Tubing is described in Table 3.

All analyzed components listed in Tables 2-5 passed our evaluation criteria. The physical strength of the materials and accuracy of single-use sensors was acceptable after solvent exposure at time zero and after accelerated aging (where applicable).

Our validation service and support team are available to assist in design and execution of customized chemical compatibility and extractable/ leachable studies under your process conditions. Please do not hesitate to contact us with further questions.

Sincerely,

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References

- (1) Memorandum Ref.: RDSME1508. Chemical Compatibility Assessment on plastics used in ADC applications.
- (2) Test Report: SAP Doc. No. 2489620. Trials chemical compatibility of tubes with DMAc, DMSO, DMF, PG, ACN and NMP under mechanical stress of a peristaltic pump.
- (3) ADC Chemical Compatibility Project Number PMO 1295
- (4) Validation guide TuFlux® TPE – Thermoplastic Elastomer Tubing
- (5) Extractables guide TuFlux® TPE
- (6) Validation guide for Flexsafe® Bags for Storage and Shipping
- (7) Test Report: SAP Doc. No. 2736686. Chemical Compatibility Trials Impeller Small Scale Mixing