

White Paper

Labtainer Pro BPC extractables profile

Introduction

Single-use technology (SUT) products are beneficial in the manufacturing of vaccines and biologics. Both the quality and purity of the materials chosen to produce Thermo Scientific™ BioProcess Containers (BPCs) are crucial to the purity and effectiveness of the final vaccines and biologics delivered to the market. It is important to analyze all materials that come in contact with process fluids to ensure that the best outcome is attained. With the introduction of the Thermo Scientific™ Labtainer™ Pro BPC, Thermo Fisher Scientific offers a compilation of the standard BPC assemblies for use in conjunction with other bioprocessing products.

The importance of extractables and leachables testing

The materials of construction selected and the processes and environments in which they are converted to BPCs impact the mechanical, physical, chemical, and biological characteristics of the finished BPC product. Because of this, the materials used in BPC construction is a critical element when deciding upon SUT products and suppliers. Several characteristics are important to the performance of BPCs, including biological compatibility, physical and mechanical properties, and extractables and leachables (E&L).

An **extractable** is any compound that migrates from a resin, material, component, or system when exposed to atypical conditions, such as extended incubation with

organic solvents at elevated temperatures, or at extreme pH. Extractables studies characterize the SUT product's materials of construction using these simulated worst-case conditions.

A **leachable** is any substance that migrates from in-process equipment or containers into the process liquid as a result of direct contact with a material, component, or system, under actual product-use conditions. Leachables studies characterize the SUT product's materials of construction under as-used conditions that are typical to bioproduction operations.

BioPhorum Operations Group (BPOG)

General requirements for E&L are already mandated by regulatory agencies. Biopharmaceutical companies must meet these requirements in demonstrating equipment suitability and GMP compliance, whether the equipment is of traditional design or single-use. However, due to the absence of specific regulatory requirements for extractables testing of SUT components, companies have developed SUT extractables testing methods based on their interpretation of regulatory requirements for existing testing methods for container-closure systems.

Since 2015, the BioPhorum Operations Group (BPOG)—a consortium of biopharmaceutical industry leaders—has focused on developing best practices for SUT and E&L workstreams. The BPOG has taken a leading role in enabling the adoption of SUT by stimulating collective

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industry discussions and providing common solutions to SUT challenges. Key deliverables already provided to the industry include establishing BPOG's extractables protocol, which has been implemented by many BPOG members, publishing a best practice guide on leachables, and developing refined user requirements, which are all aimed at advancing and improving SUT implementation.

As a BPOG member, Thermo Fisher Scientific is committed to providing customers with extractable test data. This section provides the BPOG extractables test protocol, and extractables test results for Thermo Scientific™ CX5-14 and Aegis™ 5-14 films, which are used in the construction of Labtainer Pro BPCs. Table 1 presents the BPOG extractables testing guidance.

Table 1. BPOG extractables testing guidance.

BPOG matrix	Solvents	Ratio of surface area (cm ²) to volume (mL)	Incubation	Time points	Assay	Reporting units	Sterilization
Mixing bags	Water for injection (WFI) 50% EtOH 0.1 M H ₃ PO ₄ 0.5 N NaOH 1% polysorbate-80 5 M NaCl	6:1	T ₀ 25°C, all else 40°C (on orbital shaker)	T ₀ , 24 hr, 21 days, 70 days	HPLC-PDA/MS GC-FID/MS HS-GC-FID/MS ICP/MS NVR analysis TOC pH	µm/cm ²	Gamma-irradiation at 50 ± 5 kGy, or steam sterilization at maximum time, temperature, number of cycles
Storage bags		6:1					
Bioreactor bags		6:1					
Tubing		6:1		T ₀ , 24 hr, 7 days		µm/cm and µm/cm ²	
Sterile filters		1(EFA):1		T ₀ , 24 hr, 21 days			
Process filters		1(EFA):1		T ₀ , 24 hr, 7 days		µm/cm ²	
Connectors		6:1		T ₀ , 24 hr, 21 days			
Sensors		6:1					

Time zero (T₀): incubation no longer than 30 minutes. EFA = Erythrofuransyladenine.

Labtainer Pro BPC films

Flexible container systems such as BPCs used in the Labtainer family of products consist of plastic films, ports, tubing, fittings, and end treatments. Performance of a specific container system in a particular application depends on the material and manufacturing quality, as well as the conditions and constraints imposed by the application. The integrity of stored contents depends primarily on the characteristics of the film—the largest component (product contact surface area) of any flexible container system.

For Labtainer Pro BPCs, Thermo Fisher Scientific offers two films that have been engineered specifically to meet the demands of the biopharmaceutical industry. The Aegis5-14 and CX5-14 films are single-web, five-layer coextruded films with an ultralow-density polyethylene (ULDPE) layer, an ethylene vinyl alcohol polymer (EVOH) gas/vapor barrier layer, and an outer polyester layer. The choice of film, and the processes and environments in which the film is converted into BPCs, shape the mechanical, physical, chemical, and biological characteristics of the film.

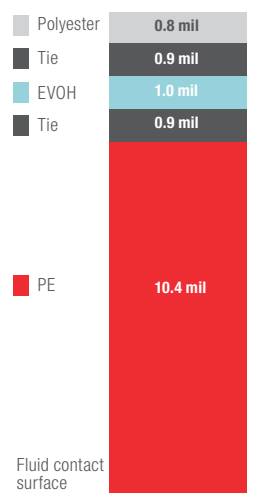


Figure 1. Cross-sectional structures and materials of construction of Aegis5-14 and CX5-14 films for Labtainer Pro BPCs

Figure 1 shows the cross-section structures and materials of construction of the films used to create the Labtainer Pro BPCs. Thermo Fisher Scientific has previously published extractables testing data for both the CX5-14 and Aegis5-14 films. This information is available to our customers upon request. Work is in progress to further identify extractables and leachables.

Table 2. Trace element extractables (maximum normalized concentration, $\mu\text{g}/\text{cm}^2$) at 40°C as measured by ICP-MS for CX5-14 and Aegis5-14 films.

Extraction solvent	Element	Results			
		30 min	24 hr	21 days	70 days
CX5-14 film, lot 1					
WFI	Copper	ND	ND	ND	0.0023
50% EtOH	Aluminum	0.077	ND	ND	ND
	Boron	ND	ND	ND	0.091
5 M NaCl	Phosphorus	ND	ND	0.14	0.54
	Rhodium	ND	ND	0.0070	ND
1% polysorbate-80	Titanium	0.033	ND	ND	ND
	Phosphorus	ND	ND	0.35	0.16
0.5 N NaOH	NA	ND	ND	ND	ND
0.1 M H_3PO_4	Selenium	ND	ND	0.014	ND
CX5-14 film, lot 2					
WFI	NA	ND	ND	ND	ND
50% EtOH	Boron	ND	ND	ND	0.10
	Phosphorus	ND	ND	ND	0.47
5 M NaCl	Rhodium	ND	ND	0.0070	ND
1% polysorbate-80	Aluminum	ND	ND	ND	0.017
	Magnesium	ND	ND	ND	0.034
	Phosphorus	ND	ND	ND	0.34
	Potassium	ND	ND	ND	0.01
0.5 N NaOH	Vanadium	ND	ND	ND	0.008
	Copper	0.008	0.007	ND	ND
0.1 M H_3PO_4	Aluminum	ND	ND	0.035	ND
	Selenium	ND	ND	0.014	ND

ND: not detected.

Table 2. (continued)

Extraction solvent	Element	Results			
		30 min	24 hr	21 days	70 days
Aegis5-14 film, lot 1					
WFI	Aluminum	ND	0.0026	ND	ND
	Copper	ND	ND	ND	0.0020
50% EtOH	Boron	ND	ND	ND	0.068
5 M NaCl	Rhodium	ND	ND	0.0070	ND
1% polysorbate-80	Aluminum	ND	ND	ND	0.017
	Magnesium	ND	ND	ND	0.033
	Phosphorus	ND	ND	ND	0.12
	Vanadium	ND	ND	ND	0.008
0.5 N NaOH	NA	ND	ND	ND	ND
0.1 M H ₃ PO ₄	Selenium	0.0074	0.0070	0.016	ND
Aegis5-14 film, lot 2					
WFI	Aluminum	ND	0.0028	ND	ND
	Copper	ND	ND	ND	ND
50% EtOH	Boron	ND	ND	ND	0.10
5 M NaCl	Aluminum	ND	ND	ND	ND
	Rhodium	ND	ND	0.0070	ND
1% polysorbate-80	Aluminum	ND	ND	ND	0.017
	Magnesium	ND	ND	ND	0.033
	Phosphorus	ND	ND	ND	0.12
	Vanadium	ND	ND	ND	0.008
0.5 N NaOH	Copper	0.0054	0.0074	ND	ND
0.1 M H ₃ PO ₄	Selenium	0.008	0.012	0.016	ND

ND: not detected.

Table 3. Volatile organic compound (VOC) results for CX5-14 film. The concentrations of the extracted compounds in different solvents are expressed in $\mu\text{g}/\text{cm}^2$.

Extraction solvent	Analyte	Results			
		30 min	24 hr	21 days	70 days
CX5-14 film, lot 1					
WFI	NA	ND	ND	ND	ND
50% EtOH	Unknown (RT = 1.27 min)	ND	ND	ND	0.0174
	Unknown (RT = 4.02 min)	ND	ND	ND	0.1290
	Unknown (RT = 4.91 min)	ND	ND	ND	0.0536
	Dimethylhexane isomer (RT = 6.1 min)	ND	0.0604	0.0662	ND
	Dimethylhexane isomer (RT = 6.2 min)	ND	0.0883	0.0542	ND
	Dimethylhexane isomer (RT = 6.7 min)	ND	0.0275	0.0275	ND
	1,3-di- <i>tert</i> -butylbenzene*	0.511	1.320	0.909	ND
	Unknown (RT = 10.8 min)	ND	ND	ND	0.0540
	Unknown (RT = 11.3 min)	ND	ND	ND	0.1590
	Unknown (RT = 14.3 min)	ND	ND	ND	0.0421
	Unknown (RT = 16.4 min)	ND	ND	ND	0.0177
	Unknown (RT = 17.5 min)	ND	ND	ND	0.0161*
	Unknown (RT = 20.3 min)	ND	ND	ND	0.0292
	Unknown (RT = 20.5 min)	ND	ND	ND	0.0200
Unknown (RT = 28.5 min)	ND	ND	ND	0.1360	
5 M NaCl	<i>tert</i> -butanol*	ND	1.97	1.78	ND
1% polysorbate-80	Dimethylhexane isomer (RT = 6.2 min)	ND	0.0256	0.0206	ND
	1,3-di- <i>tert</i> -butylbenzene*	0.134	0.327	0.269	ND
	Unknown (RT = 28.5 min)	ND	ND	ND	0.0883
0.5 N NaOH	NA	ND	ND	ND	ND
0.1 M H_3PO_4	<i>tert</i> -butanol*	ND	ND	2.47	ND

RT: retention time.

* Peak ID was confirmed by an authentic reference standard.

Table 3. (continued)

Extraction solvent	Analyte	Results			
		30 min	24 hr	21 days	70 days
CX5-14 film, lot 2					
WFI	NA	ND	ND	ND	ND
50% EtOH	Unknown (RT = 1.27 min)	ND	ND	ND	0.0188
	Unknown (RT = 4.02 min)	ND	ND	ND	0.1090
	Unknown (RT = 4.91 min)	ND	ND	ND	0.0546
	Dimethylhexane isomer (RT = 6.1 min)	ND	0.0561	0.0593	ND
	Dimethylhexane isomer (RT = 6.2 min)	ND	0.0100	0.0881	ND
	Dimethylhexane isomer (RT = 6.7 min)	ND	0.0306	0.0214	ND
	1,3-di- <i>tert</i> -butylbenzene*	0.544	1.310	0.928	ND
	Unknown (RT = 10.8 min)	ND	ND	ND	0.0813
	Unknown (RT = 11.3 min)	ND	ND	ND	0.2200
	Unknown (RT = 11.8 min)	ND	ND	ND	0.0205
	Unknown (RT = 14.3 min)	ND	ND	ND	0.0588
	Unknown (RT = 17.5 min)	ND	ND	ND	0.0177
	Unknown (RT = 20.2 min)	ND	ND	ND	0.0178
	Unknown (RT = 20.3 min)	ND	ND	ND	0.0353
	Unknown (RT = 20.5 min)	ND	ND	ND	0.0240
	Unknown (RT = 20.9 min)	ND	ND	ND	0.0164
Unknown (RT = 28.5 min)	ND	ND	ND	0.1390	
5 M NaCl	<i>tert</i> -butanol*	ND	2.17	1.80	ND
1% polysorbate-80	Dimethylhexane isomer (RT = 6.1 min)	ND	ND	ND	ND
	Dimethylhexane isomer (RT = 6.2 min)	ND	0.0284	ND	ND
	Dimethylhexane isomer (RT = 6.7 min)	ND	ND	ND	ND
	1,3-di- <i>tert</i> -butylbenzene*	0.142	0.326	0.292	ND
	Unknown (RT = 11.3 min)	ND	ND	ND	0.0185
	Unknown (RT = 28.5 min)	ND	ND	ND	0.0663
0.5 N NaOH	NA	ND	ND	ND	ND
0.1 M H ₃ PO ₄	<i>tert</i> -butanol*	ND	ND	2.38	ND

* Peak ID was confirmed by an authentic reference standard.

Table 4. VOC results for Aegis5-14 film. The maximum normalized concentration of the extracted compounds in different solvents is expressed in $\mu\text{g}/\text{cm}^2$.

Extraction solvent	Analyte	Results			
		30 min	24 hr	21 days	70 days
Aegis5-14 film, lot 1					
WFI	NA	ND	ND	ND	ND
50% EtOH	Unknown (RT = 5.28 min)	ND	ND	ND	0.0148
	Unknown (RT = 10.8 min)	ND	ND	ND	0.0337
	Unknown (RT = 11.3 min)	ND	ND	ND	0.0819
	Unknown (RT = 14.3 min)	ND	ND	ND	0.0192
	Unknown (RT = 16.4 min)	ND	ND	ND	0.0201
	Unknown (RT = 16.7 min)	ND	ND	ND	0.0204
	Unknown (RT = 17.2 min)	ND	ND	ND	0.0296
	Unknown (RT = 17.7 min)	ND	ND	ND	0.0168
5 M NaCl	NA	ND	ND	ND	ND
1% polysorbate-80	Unknown (RT = 10.2 min)	ND	ND	ND	0.0259
	Unknown (RT = 19.1 min)	ND	ND	ND	0.1110
	Unknown (RT = 22.4 min)	ND	ND	ND	0.0835
	Unknown (RT = 24.6 min)	ND	ND	ND	0.0639
	Unknown (RT = 26.5 min)	ND	ND	ND	0.0482
0.5 N NaOH	NA	ND	ND	ND	ND
0.1 M H_3PO_4	NA	ND	ND	ND	ND
Aegis5-14 film, lot 2					
WFI	NA	ND	ND	ND	ND
50% EtOH	Unknown (RT = 4.02 min)	ND	ND	ND	0.0296
	Unknown (RT = 4.91 min)	ND	ND	ND	0.0225
	Unknown (RT = 10.8 min)	ND	ND	ND	0.0235
	Unknown (RT = 11.3 min)	ND	ND	ND	0.0691
	Unknown (RT = 14.3 min)	ND	ND	ND	0.0138
	Unknown (RT = 16.4 min)	ND	ND	ND	0.0185
	Unknown (RT = 16.7 min)	ND	ND	ND	0.0252
	Unknown (RT = 17.2 min)	ND	ND	ND	0.0344
	Unknown (RT = 17.7 min)	ND	ND	ND	0.0217
5 M NaCl	NA	ND	ND	ND	ND
1% polysorbate-80	Unknown (RT = 10.2 min)	ND	ND	ND	0.0297
	Unknown (RT = 19.1 min)	ND	ND	ND	0.1150
	Unknown (RT = 22.4 min)	ND	ND	ND	0.0850
	Unknown (RT = 24.6 min)	ND	ND	ND	0.0651
	Unknown (RT = 26.5 min)	ND	ND	ND	0.0482
0.5 N NaOH	NA	ND	ND	ND	ND
0.1 M H_3PO_4	NA	ND	ND	ND	ND

Table 5. Semivolatile organic carbon (SVOC) results for CX5-14 film.

The maximum normalized concentration of the extracted compounds in different solvents is expressed in $\mu\text{g}/\text{cm}^2$.

Extraction solvent	Analyte	Results			
		30 min	24 hr	21 days	70 days
CX5-14 film, lot 1					
WFI	NA	ND	ND	ND	ND
50% EtOH	1,3-di- <i>tert</i> -butylbenzene*	0.122	0.384	0.381	0.295
	2,6-di- <i>tert</i> -butyl-benzoquinone	ND	ND	0.0583	0.0433
	Di- <i>tert</i> -butylphenol isomer	ND	ND	0.131	ND
	2,4-di- <i>tert</i> -butylphenol*	0.0560	0.395	0.884	1.06
	7,9-di- <i>tert</i> -butyl-1-oxaspiro(4,5) deca-6,9-diene-2,8-dione	ND	ND	ND	0.0278
	Unknown (RT = 22.7 min)	ND	0.0286	0.713	ND
	Unknown (RT = 23.8 min)	ND	ND	ND	0.0154
5 M NaCl	NA	ND	ND	ND	ND
1% polysorbate-80	1,3-di- <i>tert</i> -butylbenzene*	0.0490	0.123	0.125	0.109
	2,4-di- <i>tert</i> -butylphenol*	0.0291	0.586	0.783	1.10
	Unknown (RT = 22.7 min)	ND	0.0448	0.0364	ND
	7,9-di- <i>tert</i> -butyl-1-oxaspiro(4,5) deca-6,9-diene-2,8-dione	ND	ND	ND	0.0195
0.5 N NaOH	NA	0.0217	0.150	0.230	0.0812
0.1 M H ₃ PO ₄	NA	ND	ND	0.0159	ND
CX5-14 film, lot 2					
WFI	NA	ND	ND	ND	ND
50% EtOH	1,3-di- <i>tert</i> -butylbenzene*	0.149	0.339	0.344	0.258
	2,6-di- <i>tert</i> -butylbenzoquinone	ND	0.0566	0.0491	0.0405
	Di- <i>tert</i> -butylphenol isomer	ND	ND	0.122	ND
	2,4-di- <i>tert</i> -butylphenol*	0.0261	0.869	0.795	0.984
	7,9-di- <i>tert</i> -butyl-1-oxaspiro(4,5) deca-6,9-diene-2,8-dione	ND	ND	ND	0.0253
	Unknown (RT = 22.7 min)	ND	0.0397	0.0591	ND
	Unknown (RT = 23.8 min)	ND	ND	ND	0.0190
5 M NaCl	NA	ND	ND	ND	ND
1% polysorbate-80	1,3-di- <i>tert</i> -butylbenzene*	0.0559	0.121	0.139	0.106
	2,4-di- <i>tert</i> -butylphenol*	0.0261	0.568	0.560	1.07
	Unknown (RT = 22.7 min)	ND	0.0459	0.0211	ND
0.5 N NaOH	2,4-di- <i>tert</i> -butylphenol*	0.0175	0.153	0.218	0.107
0.1 M H ₃ PO ₄	2,4-di- <i>tert</i> -butylphenol*	ND	ND	0.0103	ND

* Peak ID was confirmed by an authentic reference standard.

Port material

As a member of the BPOG, we have committed to customers to providing extractables testing on the components that “come into contact with product or process fluids” [4]. Per a customer request, we performed an extractables study on the Labtainer Pro BPC port based on the BPOG study guideline, Standardized Extractables Testing Protocol for Single-Use Systems in Biomanufacturing [4].

Table 6.1. Trace element extractables as measured by ICP-MS.

Extraction solvent	Replicate	Element	Results ($\mu\text{m}/\text{cm}^2$)		
			30 min	24 hr	21 days
WFI	1	NA	ND	ND	ND
	2	Silicon	0.012	ND	ND
0.1 M H_3PO_4	1	Aluminum	0.012	0.206	ND
	1	Calcium	ND	0.021	ND
	2	Iron	ND	ND	0.018
1% polysorbate-80	1	Zinc	0.006	0.009	0.029
	2	Zinc	0.006	0.009	0.009
50% EtOH	1	Zinc	ND	ND	ND
	1	Copper	ND	ND	0.021
	2	Zinc	ND	ND	0.006
0.5 N NaOH	1	Zinc	0.012	0.029	0.012
	1	Copper	ND	0.015	ND
	2	Zinc	0.009	0.012	0.006
	2	Copper	ND	0.009	ND
5 M NaCl	1	Magnesium	0.221	0.074	0.183
	1	Copper	ND	ND	0.021
	2	Magnesium	0.221	0.080	0.186
	2	Copper	ND	ND	0.015

Table 6.2. Conductivity results.

Extraction solvent	Replicate	Results ($\mu\text{S}/\text{cm}$)		
		30 min	24 hr	21 days
WFI	1	17.77	11.86	53.06
	2	11.88	16.49	76.75
0.1 M H_3PO_4	1	9,179.00	10,330.00	10,830.00
	2	9,314.00	10,330.00	10,240.00
1% polysorbate-80	1	10.02	13.54	196.80
	2	10.07	11.93	212.80
50% EtOH	1	24.13	10.32	28.91
	2	21.51	10.47	25.68
0.5 N NaOH	1	90,600	93,970	102,000
	2	92,770	95,900	101,800
5 M NaCl	1	236,000	241,900	249,300
	2	239,000	238,800	249,100

Table 6.3. pH results.

Extraction solvent	Replicate	Results		
		30 min	24 hr	21 days
WFI	1	4.88	4.70	4.11
	2	4.91	4.76	4.12
0.1 M H ₃ PO ₄	1	1.81	1.67	1.78
	2	1.71	1.73	1.84
1% polysorbate-80	1	6.08	5.86	3.19
	2	6.11	5.90	3.31
50% EtOH	1	5.17	4.76	4.23
	2	4.91	4.74	4.24
0.5 N NaOH	1	12.80	12.03	13.08
	2	12.88	12.08	13.09
5 M NaCl	1	6.97	5.85	4.13
	2	7.27	5.75	4.09

Table 6.4. Total organic carbon (TOC) results.

Extraction solvent	Replicate	Results (µm/cm ²)		
		30 min	24 hr	21 days
WFI	1	1.24	0.94	5.62
	2	4.20	0.58	5.94
0.1 M H ₃ PO ₄	1	7.42	4.72	7.16

Table 6.5. SVOC results.

Extraction solvent	Replicas	Analyte	Results (µm/cm ²)		
			30 min	24 hr	21 days
WFI	1	NA	ND	ND	ND
	2	NA	ND	ND	ND
0.1 M H ₃ PO ₄	1	NA	ND	ND	ND
	2	NA	ND	ND	ND
1% polysorbate-80	1	NA	ND	ND	ND
	2	NA	ND	ND	ND
50% EtOH	1	NA	ND	ND	ND
	2	NA	ND	ND	ND
0.5 N NaOH	1	NA	ND	ND	ND
	2	NA	ND	ND	ND
5 M NaCl	1	Unknown (RT = 17.07 min)	0.0002	ND	ND
	2	Unknown (RT = 17.07 min)	0.0008	ND	ND

Table 6.6. VOC results.

Extraction solvent	Replicate	Analyte	Results ($\mu\text{m}/\text{cm}^2$)		
			30 min	24 hr	21 days
WFI	1	Unknown (RT = 9.74 min)	ND	0.003	ND
	2	Unknown (RT = 9.74 min)	ND	0.003	ND
0.1 M H_3PO_4	1	Unknown (RT = 9.74 min)	ND	0.003	ND
	2	Unknown (RT = 9.74 min)	ND	0.003	ND
1% polysorbate-80	1	Unknown (RT = 4.75 min)	ND	0.003	ND
	1	Unknown (RT = 6.36 min)	0.003	ND	ND
	1	Unknown (RT = 8.00 min)	ND	0.012	ND
	1	Unknown (RT = 8.17 min)	ND	0.032	ND
	1	Unknown (RT = 8.60 min)	ND	0.012	ND
	1	Unknown (RT = 9.32 min)	ND	0.003	ND
	1	Unknown (RT = 10.58 min)	ND	0.009	ND
	1	Unknown (RT = 10.72 min)	ND	0.006	ND
	1	Unknown (RT = 11.01 min)	ND	0.006	ND
	1	Unknown (RT = 4.75 min)	ND	0.003	ND
	1	Unknown (RT = 8.00 min)	ND	0.015	ND
	1	Unknown (RT = 8.17 min)	ND	0.044	0.003
	1	Unknown (RT = 8.60 min)	ND	0.015	ND
	1	Unknown (RT = 9.32 min)	ND	0.006	ND
	1	Unknown (RT = 10.58 min)	ND	0.012	ND
	1	Unknown (RT = 10.72 min)	ND	0.009	ND
	1	Unknown (RT = 11.01 min)	ND	0.009	ND
50% EtOH	1	NA	ND	ND	ND
	2	NA	ND	ND	ND
0.5 N NaOH	1	Unknown (RT = 9.70 min)	ND	0.003	ND
	2	NA	ND	ND	ND
5 M NaCl	1	NA	ND	ND	ND
	2	NA	ND	ND	ND

6.7. Nonvolatile organic compound (NVOC) analysis by liquid chromatography/mass spectrometry/photodiode array (LC-MS/PDA).

Extraction solvent	Replicate	Analyte	Results ($\mu\text{m}/\text{cm}^2$)		
			30 min	24 hr	21 days
WFI	1	Unknown (RT = 1.26 min)	0.791	ND	ND
	NA	Unknown (RT = 1.77 min)	ND	0.183	ND
	NA	Unknown (RT = 2.77 min)	0.389	ND	ND
	NA	Unknown (RT = 15.58 min)	ND	1.286	ND
	2	Unknown (RT = 1.26 min)	0.540	ND	ND
	NA	Unknown (RT = 1.77 min)	ND	0.286	ND
	NA	Unknown (RT = 2.77 min)	0.540	ND	ND
	NA	Unknown (RT = 15.58 min)	ND	0.265	ND

Table 6.7. (continued)

Extraction solvent	Replicate	Analyte	Results ($\mu\text{m}/\text{cm}^2$)		
			30 min	24 hr	21 days
0.1 M H_3PO_4	1	Unknown (RT = 1.18 min)	1.047	ND	ND
	1	Unknown (RT = 1.53 min)	ND	0.183	ND
	1	Unknown (RT = 14.70 min)	0.540	ND	ND
	2	Unknown (RT = 1.18 min)	0.407	ND	ND
	2	Unknown (RT = 1.53 min)	17.525	ND	ND
	2	Unknown (RT = 14.70 min)	0.501	ND	ND
1% polysorbate-80	1	Unknown (RT = 14.51 min)	0.434	ND	5.386
	1	Unknown (RT = 14.72 min)	17.555	ND	1.186
	1	Unknown (RT = 15.43 min)	ND	ND	1.501
	1	Unknown (RT = 14.51 min)	ND	ND	3.891
	1	Unknown (RT = 14.72 min)	ND	ND	2.186
	1	Unknown (RT = 15.43 min)	ND	ND	8.782
50% EtOH	1	Unknown (RT = 1.27 min)	ND	ND	0.785
	1	Unknown (RT = 1.60 min)	ND	ND	0.457
	1	Unknown (RT = 2.06 min)	ND	ND	0.487
	1	Unknown (RT = 15.43 min)	ND	ND	1.823
	2	Unknown (RT = 1.27 min)	ND	ND	0.735
	2	Unknown (RT = 1.49 min)	ND	ND	0.425
	2	Unknown (RT = 1.60 min)	ND	ND	0.233
	2	Unknown (RT = 15.43 min)	ND	ND	1.298
0.5 N NaOH	1	Unknown (RT = 9.71 min)	1.584	ND	ND
	1	Unknown (RT = 12.97 min)	ND	ND	0.835
	2	Unknown (RT = 9.71 min)	1.088	ND	ND
	2	Unknown (RT = 12.97 min)	ND	ND	0.684
5 M NaCl	1	Unknown (RT = 1.62 min)	0.248	0.215	0.537
	1	Unknown (RT = 1.86 min)	ND	ND	0.481
	1	Unknown (RT = 2.30 min)	ND	ND	0.425
	2	Unknown (RT = 1.62 min)	0.354	0.363	0.201
	2	Unknown (RT = 1.86 min)	ND	ND	0.357
	2	Unknown (RT = 2.30 min)	ND	ND	0.808

Extraction testing strategies

Manufacturers of SUT products should perform an extractables assessment for all parts in direct contact with the system. Third-party suppliers who provide components specifically for SUT products (e.g., connectors and filters) should also generate supporting extractables testing data for the purpose of enabling end users to make informed risk-based decisions specifically for their application needs. This section characterizes extraction profiles for the tubing, film, and end treatments used in the manufacturing of Labtainer Pro products. The testing summaries provided below are from the relevant manufacturers; requests for any additional information should be directed to the relevant supplier.

Additional suppliers' extractables and leachables information

The vendors listed in Table 7 supply Thermo Fisher Scientific with components used in manufacturing the standard Labtainer Pro BPCs. Colder Products Company, Saint-Gobain, and Nordson Medical are each committed to providing customers with up-to-date extractables testing data. The table provides the appropriate contact information to request leachables and extractables data directly from the suppliers.

Table 7. Labtainer Pro BPC component information and corresponding suppliers.

Supplier	Part/component	Material	Contact information
Saint-Gobain	C-Flex™ 374 tubing	Thermoplastic elastomer (TPE)	North America +1 610-893-6000 SGNorthAmericaInfo@saint-gobain.com
Colder Products Company	<ul style="list-style-type: none"> AseptiQuik™ G connectors Sterile connectors MPC quick connectors MPX quick connectors 	Polycarbonate (white), USP class VI, ADCF	North America 1-800-444-2474 cpcworldwide.com/contact-us
Nordson Medical	<ul style="list-style-type: none"> Luer locks End plugs 	<ul style="list-style-type: none"> Polypropylene Luer locks (not including the Smartsite™) Polypropylene end plugs 	Global 1-888-404-5837 nordsonmedical.com/about/contact-us/
Thermo Fisher Scientific	<ul style="list-style-type: none"> CX5-14 Film Aegis5-14 Film 	<ul style="list-style-type: none"> Polyethylene (PE) Ethylene vinyl alcohol polymer (EVOH) gas/vapor barrier Polyester 	North America 1-866-356-0354 thermofisher.com/contactus
	Chamber ports	Low-density polyethylene (LDPE)	

Conclusion

Thermo Fisher Scientific has supplied BPCs to the biopharmaceutical industry for more than 20 years. The innovative Labtainer Pro family of products, manufactured from materials and components assessed per extractables testing profiles, provides improved flexibility and assurance in both upstream and downstream bioprocessing operations. Standard components for the Labtainer Pro BPCs have been tested by Thermo Fisher Scientific and their respective vendors, and we have compiled this comprehensive review of the extraction profiles for the entirety of the BPC product.

Thermo Fisher Scientific did not generate or verify the third-party studies and/or information in this document, and does not guarantee the results or testing methods of work done by the companies listed under "Tubing and Connector Manufacturers". Additionally, the information provided in this section of the document is a summary, and the full report for each company listed will need to be requested from the respective companies.

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