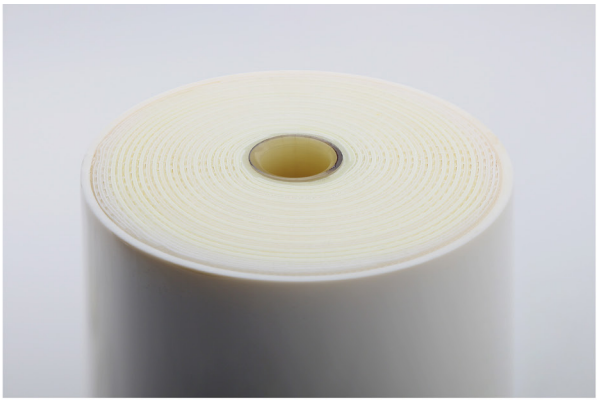
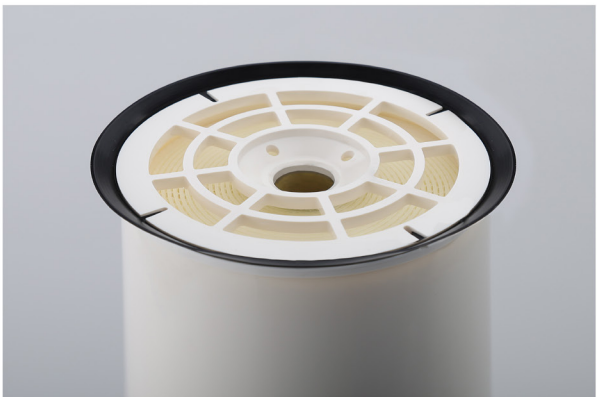
cobetter®
filtration

Validation Guide

Cobetter Consieve™ SC Spiral Cartridges







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I. Introduction

This Validation Guide provides information of Cobetter Consieve™[1] SC spiral cartridges, including test methods, performance and specifications related to pharmaceutical manufacturing process. This guide is designed as a reference for end user to validate Cobetter Consieve SC spiral cartridges to meet requirements of regulatory authorities within the pharmaceutical industry.

Quality Assurance

Cobetter establishes and continuously maintains the company's quality assurance system in accordance with the requirements of ISO® 9001:2015 quality management system and cGMP. All the products are manufactured under strict quality system to ensure stable and reliable quality.

Raw Material Control

Cobetter has established a rigorous supplier selection and periodic evaluation system. The core materials are selected from internationally renowned raw material suppliers and manage the suppliers hierarchically. The outsourced materials or components are inspected according to the company's internal control standards to ensure the quality of raw materials is stable and reliable.

Environment Management

The main manufacturing process of the Cobetter Consieve SC spiral cartridges is completed in the ISO Class 7 clean area, which ensures the cleanliness of the product and prevents pollution. The air purification system is confirmed and maintained regularly to ensure that the cleanliness of environment continuously meets the requirements of ISO Class 7. The suspended particles, sedimentation bacteria, temperature, humidity and differential pressure are monitored periodically to provide for a highly controlled clean environment.

Lot Release and Traceability

Cobetter Consieve SC spiral cartridges require 100% integrity test before delivery. The water flux and solute rejection of the membrane are sample tested.

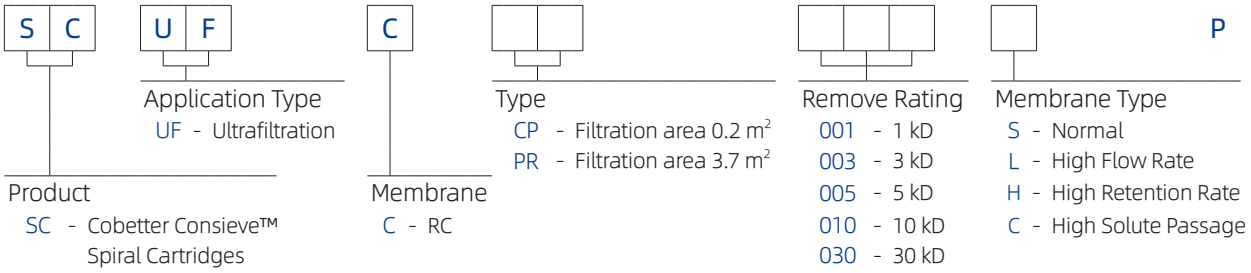
The product lot number of Cobetter Consieve SC spiral cartridges are engraved on the cartridges' side. Customers can also find the corresponding product lot number in the product label and quality certificate. The product can be traced from the whole process of raw materials, equipment, manufacturing process through the lot number.

1 Consieve is trademark of Cobetter Corporation.

II. Product Specifications

1. Catalogue Numbers Description

Cobetter Consieve™ SC Spiral Cartridges



2. Specifications

Cobetter Consieve™ SC Series CP Spiral Cartridge

Product	Consieve SC
Type	CP
Filtration Area	0.2 m^2
Size (Diameter × Length)	57.3 × 244 mm
Materials of Construction	
Membrane	Regenerated cellulose (RC)
Feed Screen	Polyethylene (PE)
Permeate Screen	Polypropylene (PP)
Outer Shell	Polysulfone (PSF)
Core	Polysulfone (PSF)
Encapsulant	Epoxy (EP)
Storage Solution	20% Ethyl alcohol and 20 - 22% glycerin
Air Diffusion @ 20 °C	≤ 20 mL/min @ 1 bar, water wetted
Bacterial Endotoxin	Flushing Fluid of cartridges after being flushed and sanitized by 0.1 M sodium hydroxide solution contains < 0.25 EU/mL as determined by *Amebocyte Lysate* , USP <85>.
USP <87> Cytotoxicity	Meet the requirement of USP <87> In Vitro Biological Reactivity Test.
USP <88> Biological Reactivity	Meet the criteria of the USP <88> Biological Reactivity Test for Class VI plastics.
Animal Derivative Content	Products do not contain animal derived components and are free from TSE risk.
Quality Assurance	These products are manufactured in a facility which adheres to ISO® 9001:2015 Practices.

Cobetter Consieve™ SC Series PR Spiral Cartridge

Product	Consieve SC
Type	PR
Filtration Area	3.7 m^2
Size (Diameter × Length)	96.7 × 652 mm
Materials of Construction	
Membrane	Regenerated cellulose (RC)
Feed Screen	Polyethylene (PE)
Permeate Screen	Polypropylene (PP)
Outer Shell	Polysulfone (PSF)
Core	Polysulfone (PSF)
Chevron Seal	EPDM
Encapsulant	Epoxy (EP)
Storage Solution	20% Ethyl alcohol and 20 - 22% glycerin
Air Diffusion @ 20 °C	≤ 370 mL/min @ 1 bar, water wetted
Bacterial Endotoxin	Flushing Fluid of cartridges after being flushed and sanitized by 0.1 M sodium hydroxide solution contains < 0.25 EU/mL as determined by *Amebocyte Lysate* , USP <85>.
USP <87> Cytotoxicity	Meet the requirement of USP <87> In Vitro Biological Reactivity Test.
USP <88> Biological Reactivity	Meet the criteria of the USP <88> Biological Reactivity Test for Class VI plastics.
Animal Derivative Content	Products do not contain animal derived components and are free from TSE risk.
Quality Assurance	These products are manufactured in a facility which adheres to ISO® 9001:2015 Practices.

III. Verification and Validation

1. Membrane

1.1. Membrane Water Flux

The purpose of membrane water flux test was to measure the membrane permeability. Membranes with high water permeability can increase the production throughput, thus shortening production time.

Summary of Method

Membrane water flux was measured in a stirred cell with clean purified water at 25 °C. RC membranes were tested at a certain transmembrane pressure (TMP).

Results

MWCO	TMP(bar)	Release Standard (mL/min/cm^2)	Average Water Flux (mL/min/cm^2)		
			Lot 1	Lot 2	Lot 3
1 kDS	3.8	0.04 - 0.06	0.042	0.046	0.042
3 kDH	3.8	0.03 - 0.05	0.042	0.044	0.040
3 kDS	3.8	0.04 - 0.08	0.074	0.079	0.077
3 kDL	3.8	0.08 - 0.12	0.092	0.098	0.096
3 kDC	3.8	0.10 - 0.15	0.116	0.115	0.118
5 kDS	3.8	0.12 - 0.20	0.142	0.131	0.128
10 kDH	3.8	0.20 - 0.30	0.260	0.252	0.240
10 kDS	3.8	0.30 - 0.60	0.524	0.499	0.513
30 kDS	3.8	0.75 - 2.00	1.941	1.978	1.905

Conclusion

The RC membrane of Cobetter Consieve SC spiral cartridges has a stable and acceptable water flux to ensure excellent filtration performance of cartridges.

1.2. Membrane Solute Passage

Membrane separation performance is greatly depended on solute passage or rejection. Membrane with low solute passage may lead to product leakage and a low product recovery. Each lot membrane is tested by quality control for solute rejection before membrane being released to spiral cartridge manufacturing, ensuring the cartridges will meet performance requirements.

Summary of Method

The solute passage test was to measure the ratio of the concentration of a given solute in the filtrate to the concentration of the original sample. RC membrane used Bacitracin, PVP, Lys and BSA as the test solute. Bacitracin, PVP, Lys and BSA concentrations are measured by spectrophotometer. All tests are conducted under standard test conditions with the results reported in the percentage of passages for a given solute passing through the membrane.

Test Standard

MWCO	TMP (bar)	Release Standard of Solute Passage (%)	
1 kDS	3.8	Bacitracin = 10 - 16%	–
3 kDH	3.8	–	PVP C17 < 3%
3 kDS	3.8	–	PVP C17 = 3 - 8%
3 kDL	3.8	–	PVP C17 < 5%
3 kDC	3.8	–	PVP C17 = 5 - 8%
5 kDS	3.8	Lys < 2%	PVP C17 = 8 - 15%
10 kDH	3.8	BSA < 1%	PVP C17 = 8 - 15%
10 kDS	3.8	BSA < 1%	PVP C17 = 50 - 80%
30 kDS	3.8	BSA < 2%	PVP K30 > 85%

Results

MWCO	Lot	Solute Passage (%)				
		Bacitracin (1.4 kD)	PVP C17 (8 kD)	Lys (14 kD)	PVP K30 (55 kD)	BSA (67 kD)
1 kDS	1	13.76	–	–	–	–
	2	13.65	–	–	–	–
	3	13.36	–	–	–	–
3 kDH	1	–	2.37	–	–	–
	2	–	2.27	–	–	–
	3	–	1.93	–	–	–
3 kDS	1	–	3.78	–	–	–
	2	–	3.84	–	–	–
	3	–	3.68	–	–	–
3 kDL	1	–	4.38	–	–	–
	2	–	4.45	–	–	–
	3	–	4.27	–	–	–
3 kDC	1	–	6.30	–	–	–
	2	–	6.54	–	–	–
	3	–	6.71	–	–	–
5 kDS	1	–	13.22	0.54	–	–
	2	–	13.65	0.48	–	–
	3	–	14.29	0.47	–	–
10 kDH	1	–	11.62	–	–	0.31
	2	–	11.79	–	–	0.23
	3	–	12.36	–	–	0.39
10 kDS	1	–	57.45	–	–	0.64
	2	–	59.15	–	–	0.47
	3	–	58.41	–	–	0.39
30 kDS	1	–	–	–	91.06	1.01
	2	–	–	–	88.82	1.08
	3	–	–	–	89.28	1.00

Conclusion

The RC membrane of Cobetter Consieve SC spiral cartridges has a stable and acceptable separation and retention ability to ensure excellent filtration performance of cartridges.

1.3. Membrane Protein Binding

Membranes are protein binding. Consequently, it is critical to quantify the binding capacity of a membrane and its potential impact on a process during the biopharmaceutical development stage. A membrane with a high protein binding capacity may lead to lower product recovery, reduced sample flux, and increased cleaning difficulty of the membrane.

Summary of Method

The purpose of the membrane protein binding test was to measure the amount of a protein bound to the tested membrane under specific conditions. Two proteins, BSA (pI 4.7, 67 kD) and lysozyme (pI 11.0, 14.4 kD), were utilized to measure static (soaking) protein binding capacity of the RC membrane of Cobetter Consieve SC spiral cartridges. The membrane discs were prewetted with buffer, and then soaked in a protein solution. After soaking step, the membrane discs were flushed three times to ensure unbound proteins removed. Proteins that remained on the membrane were analyzed using a protein test kit.

Results

BSA (μg/cm^2)	Lysozyme (μg/cm^2)
0.29	0.15

Conclusion

The RC membrane of Cobetter Consieve SC spiral cartridges has very low protein binding.

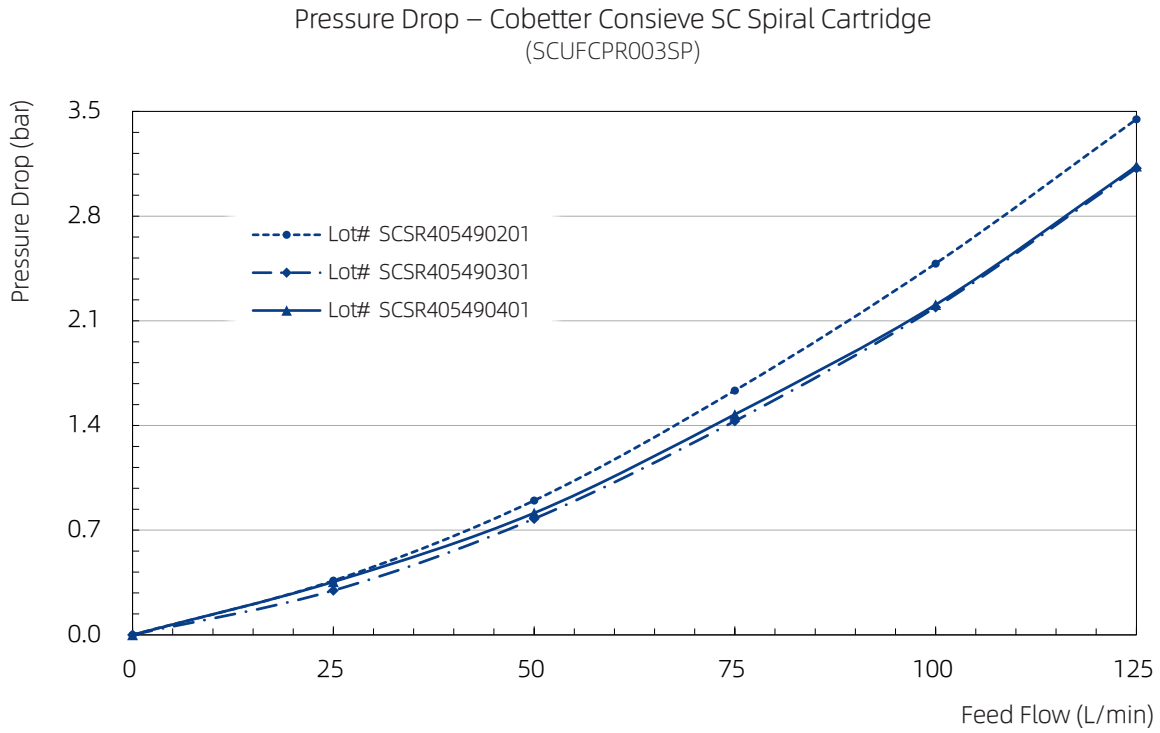
2. Pressure Drop

This test is mainly used to characterize the fluid resistance of the cartrdge. The flow resistance of the cartrdge should be controlled within a certain range, so as to ensure that the filtration performance remains relatively consistent.

Summary of Method

Cobetter Consieve SC spiral cartridges were installed in the test devices in the vertical orientation. Open retentate port and close permeate port, the cartridges were tested for pressure drop at the different inlet flow rates of 25 L/min, 50 L/min, 75 L/min, 100 L/min and 125 L/min.

Results



3. Filter Rinsing

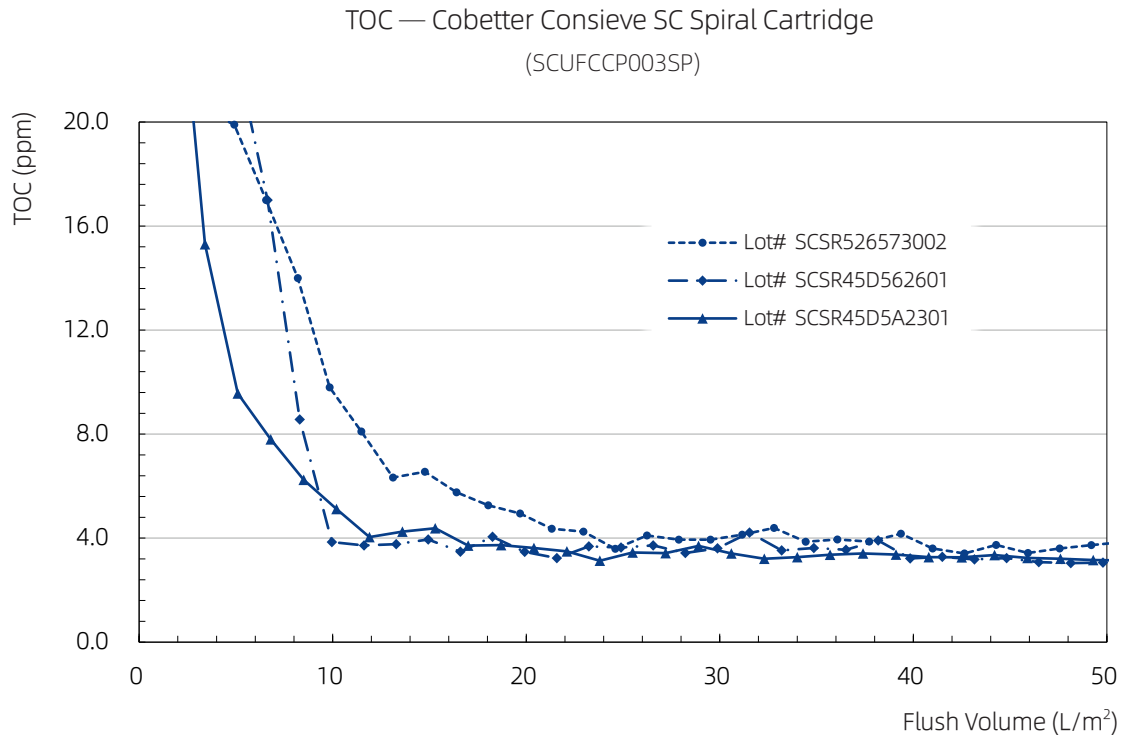
Cartridges must be thoroughly rinsed before use to ensure the cartridges storage solution removed and the level of extractables minimized. To help users develop an effective cartridges rinsing protocol, a study was conducted to outline the steps and conditions.

Summary of Method

Cobetter Consieve SC spiral cartridges were installed in the test devices. The cartridges were flushed with purified water for 5 min at the inlet flow rate of 10 L/min/m^2 and a TMP of 1.7 bar, with both retentate port and permeate port open. Next, the cartridges were circulated using 0.1 M NaOH solution for 30-60 minutes, controlling the TMP at 0.5-1 bar.

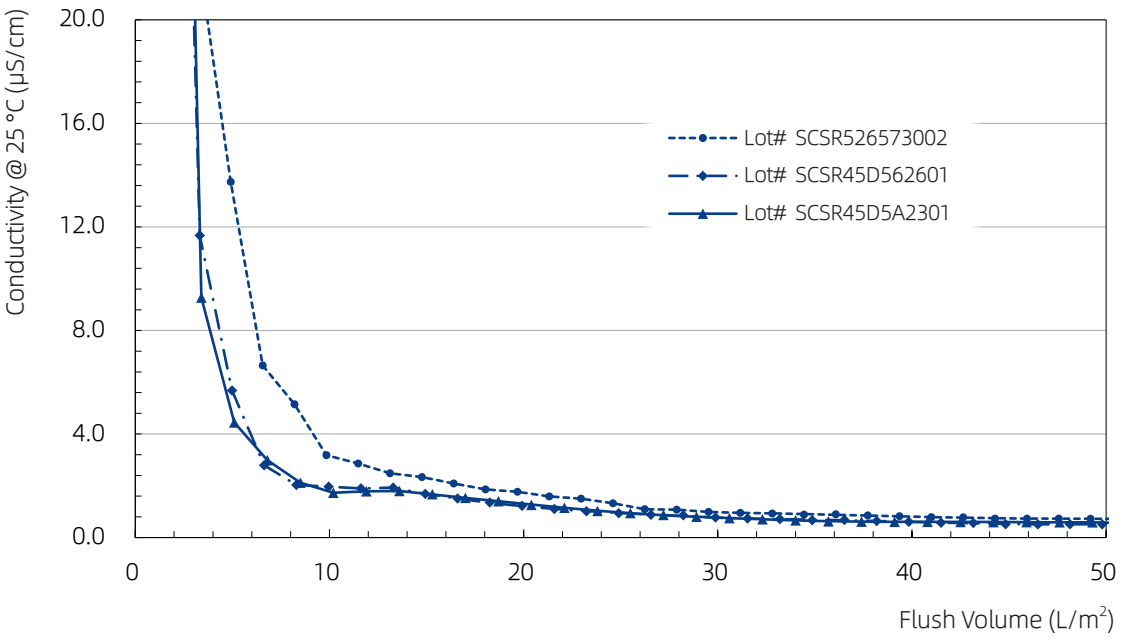
The cartridges were flushed with purified water at the inlet flow rate of 10 L/min/m^2 with a TMP of 1.7 bar. When the flushing volume at the retentate port reached 50 L/m^2, the retentate valve was closed slowly, and the TMP was maintained at 1.7 bar to continue flushing the permeate port. The total flushing volume at the permeate port was 50 L/m^2. The cartridge effluent was collected during the flushing process and analyzed for TOC, conductivity and pH.

Cobetter Consieve SC Spiral Cartridge (SCUFCCP003SP)



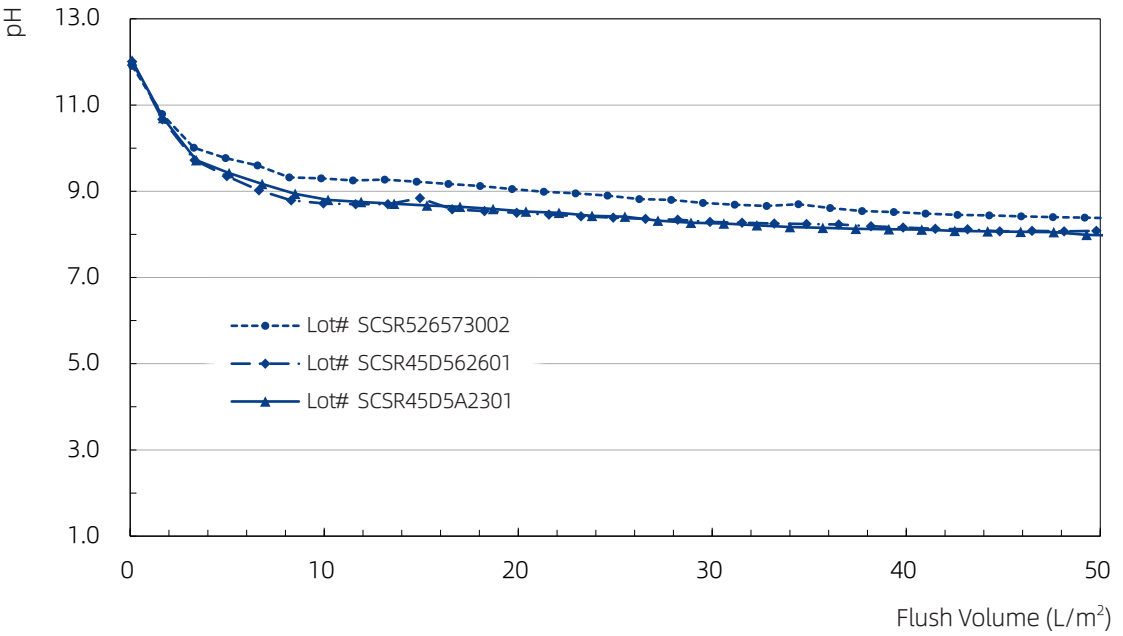
Conductivity — Cobetter Consieve SC Spiral Cartridge

(SCUFCCP003SP)



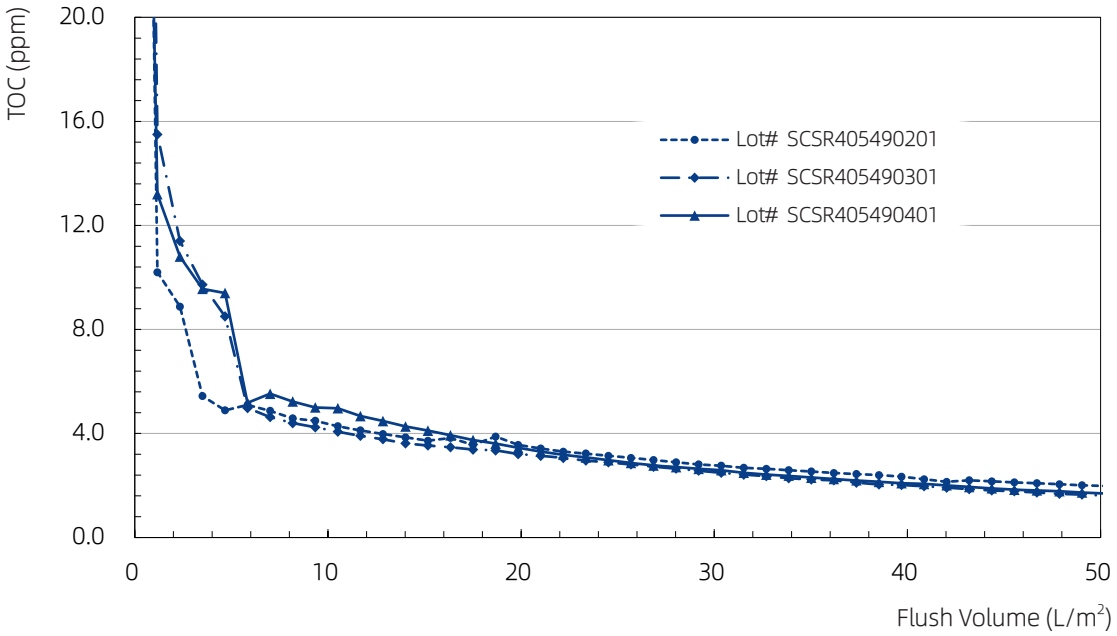
pH — Cobetter Consieve SC Spiral Cartridge

(SCUFCCP003SP)

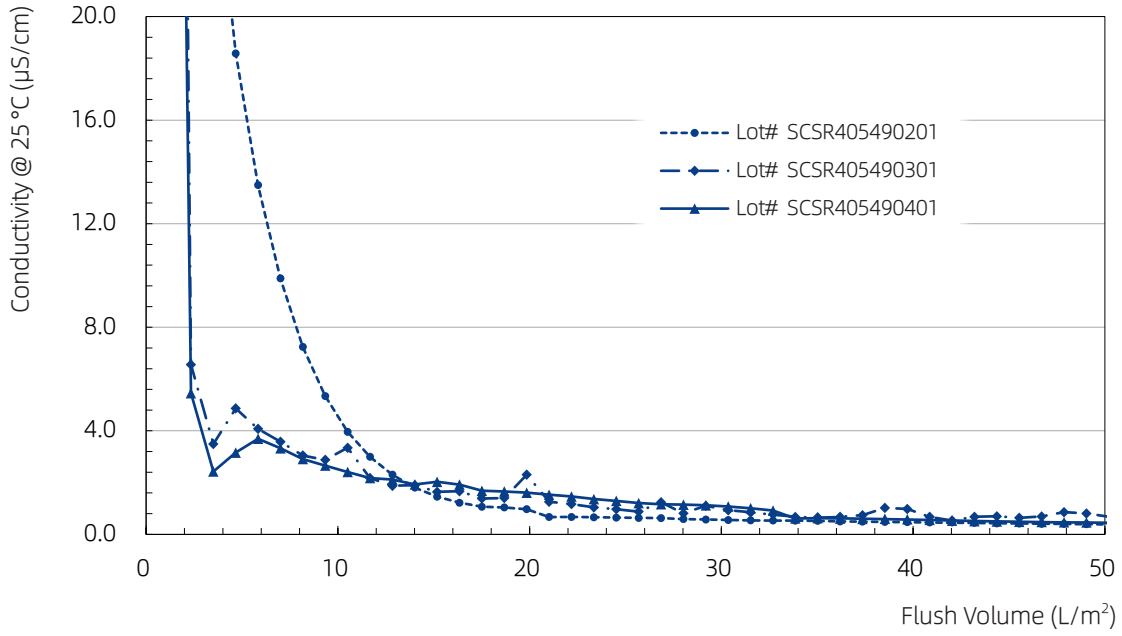


Cobetter Consieve SC Spiral Cartridge (SCUFCPR003SP)

TOC — Cobetter Consieve SC Spiral Cartridge
(SCUFCPR003SP)

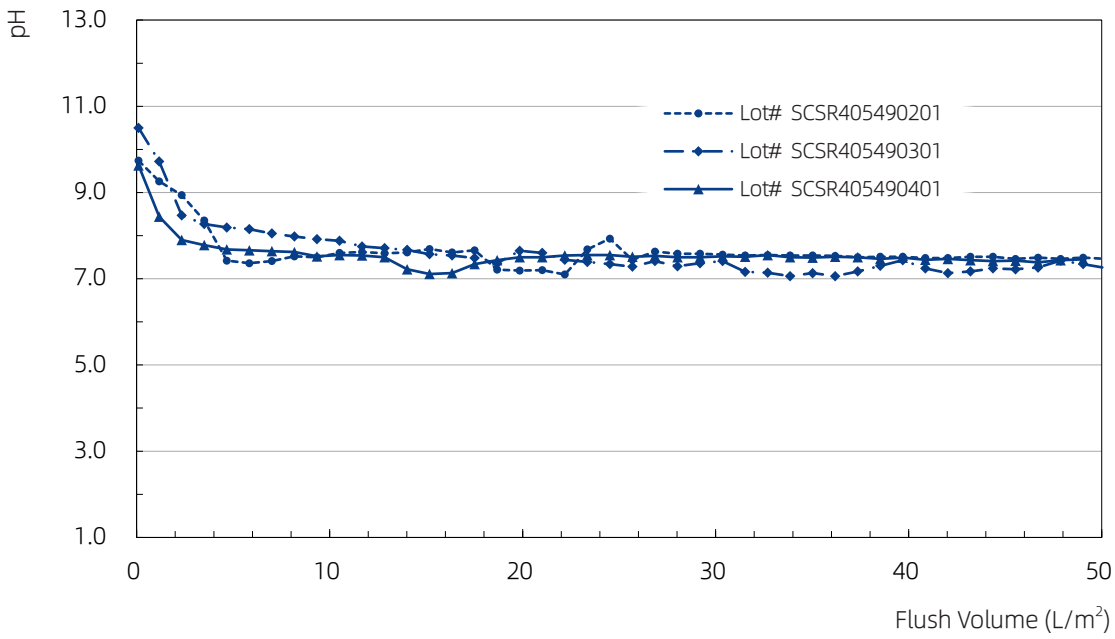


Conductivity — Cobetter Consieve SC Spiral Cartridge
(SCUFCPR003SP)



pH — Cobetter Consieve SC Spiral Cartridge

(SCUFCPR003SP)



4. Extractables

In order to ensure the safety of the product, it is very important to understand the contents of extractables leached from the cartridges. Two forms, non-volatile residue (NVR) and total organic carbon (TOC), were measured to evaluate the level of cartridges' extractables.

Summary of Method

Cobetter Consieve SC spiral cartridges were installed in the test devices. The cartridges were flushed with purified water for 5 min at the inlet flow rate of 10 L/min/m^2 and a TMP of 1.7 bar, with both retentate port and permeate port open. Next, the cartridges were circulated using 0.1 M NaOH solution for 30-60 minutes, controlling the TMP at 0.5-1 bar.

The cartridges were flushed with purified water at the inlet flow rate of 10 L/min/m^2 with a TMP of 1.7 bar. When the flushing volume at the retentate port reached 50 L/m^2, the retentate valve was closed slowly, and the TMP was maintained at 1.7 bar to continue flushing the permeate port. The total flushing volume at the permeate port was 50 L/m^2.

For the nonvolatile residue analysis, the cartridges were flushed and extracted using 25% ethanol 75% water solution or purified water for 24 hours at ambient room temperature.

For the total organic carbon analysis, the cartridges were flushed and then extracted using purified water for 24 hours at ambient room temperature.

At the same time, using purified water and 25% ethanol 75% water solution as a blank control for tests. Extraction solutions were sent out to an independent lab for analysis.

Purified Water Extraction Solution Results

Catalogue Number	Lot Number	NVR (mg/unit)	TOC (ppm)
SCUFCCP003SP	SCSR45D580601	0.6	18.2
	SCSR45D562601	0.9	23.5
	SCSR45D5A2301	0.6	21.7
SCUFCPR003SP	SCSR405490201	49.8	50.1
	SCSR405490301	58.8	30.9
	SCSR405490401	76.2	37.7

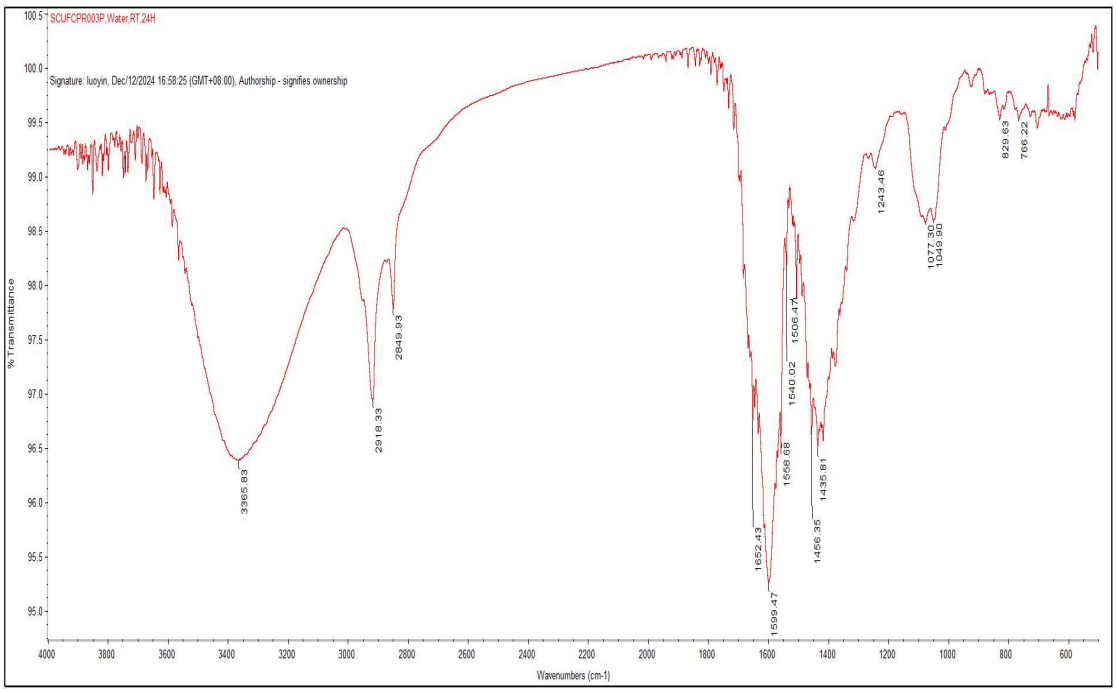
25% Ethanol Extraction Solution Results

Catalogue Number	Lot Number	NVR (mg/unit)
SCUFCCP003SP	SCSR526573002	1.2
	SCSR45D562601	0.6
	SCSR45D5A2301	0.9
SCUFCPR003SP	SCSR405490201	66.4
	SCSR405490301	30.6
	SCSR405490401	46.8

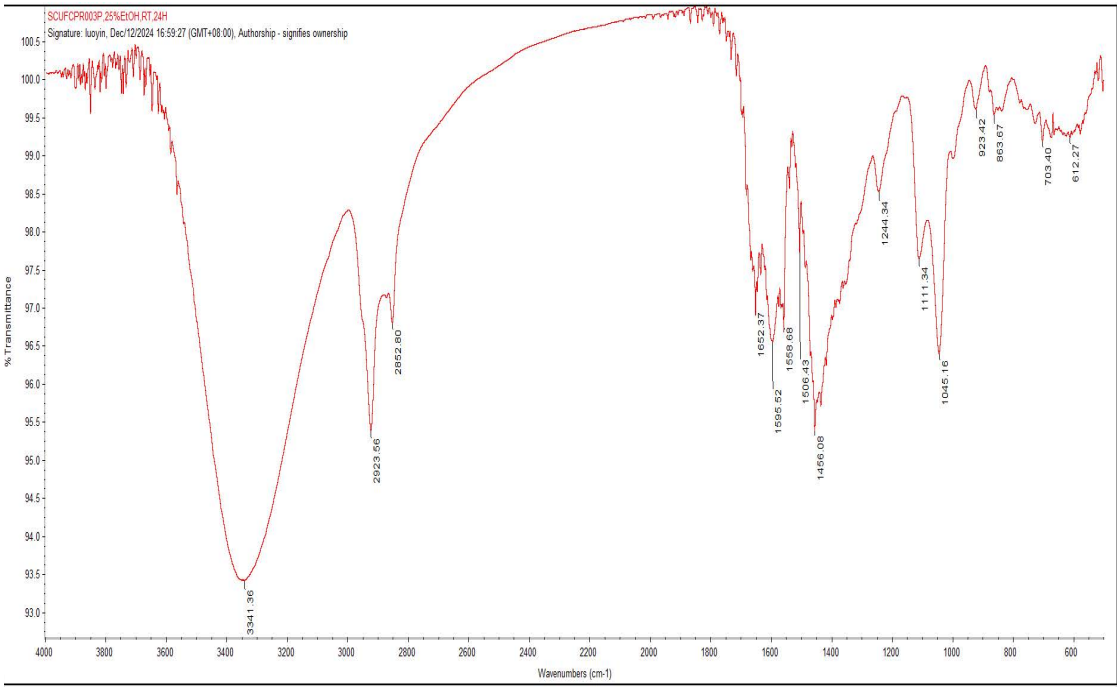
FTIR Analysis Results

Fourier transform infrared spectroscopy (FTIR) can analyze the characteristic absorption peaks of functional groups for the compounds in NVR and assist in the qualitative analysis of non-volatile residues. FTIR analysis results of NVR of purified water and 25% ethanol extraction solutions are shown below. The analysis results show that the main substance in NVR of purified water extraction solution 25% ethanol extraction solution is glycerin.

FTIR Spectrograms of NVR of Purified Water Extraction Solution



FTIR Spectrograms of NVR of 25% Ethanol Extraction Solution



Conclusion

The results indicate the extractable levels of the nonvolatile residue (NVR) and total organic carbon (TOC) for Cobetter Consieve SC spiral cartridge are at a relatively low level.

5. Particle Shedding

Summary of Method

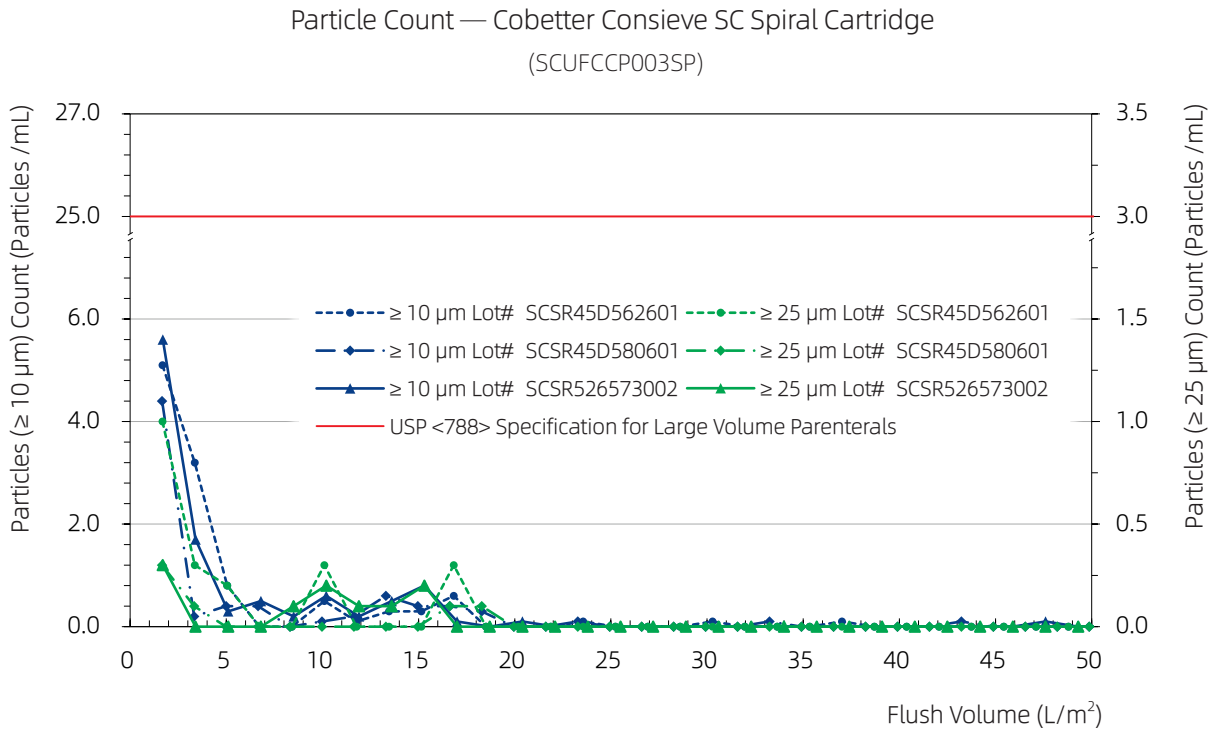
Cobetter Consieve SC spiral cartridges were installed in the test devices. The cartridges were flushed with purified water for 5 min at the inlet flow rate of 10 L/min/m^2 and a TMP of 1.7 bar, with both retentate port and permeate port open. Next, the cartridges were circulated using 0.1 M NaOH solution for 30-60 minutes, controlling the TMP at 0.5-1 bar.

The cartridges were flushed with purified water at the inlet flow rate of 10 L/min/m^2 with a TMP of 1.7 bar. When the flushing volume at the retentate port reached 50 L/m^2, the retentate valve was closed slowly, and the TMP was maintained at 1.7 bar to continue flushing the permeate port. The cartridge effluent was analyzed according to USP <788> Method 1 (light obscuration particle count test) for particle shedding.

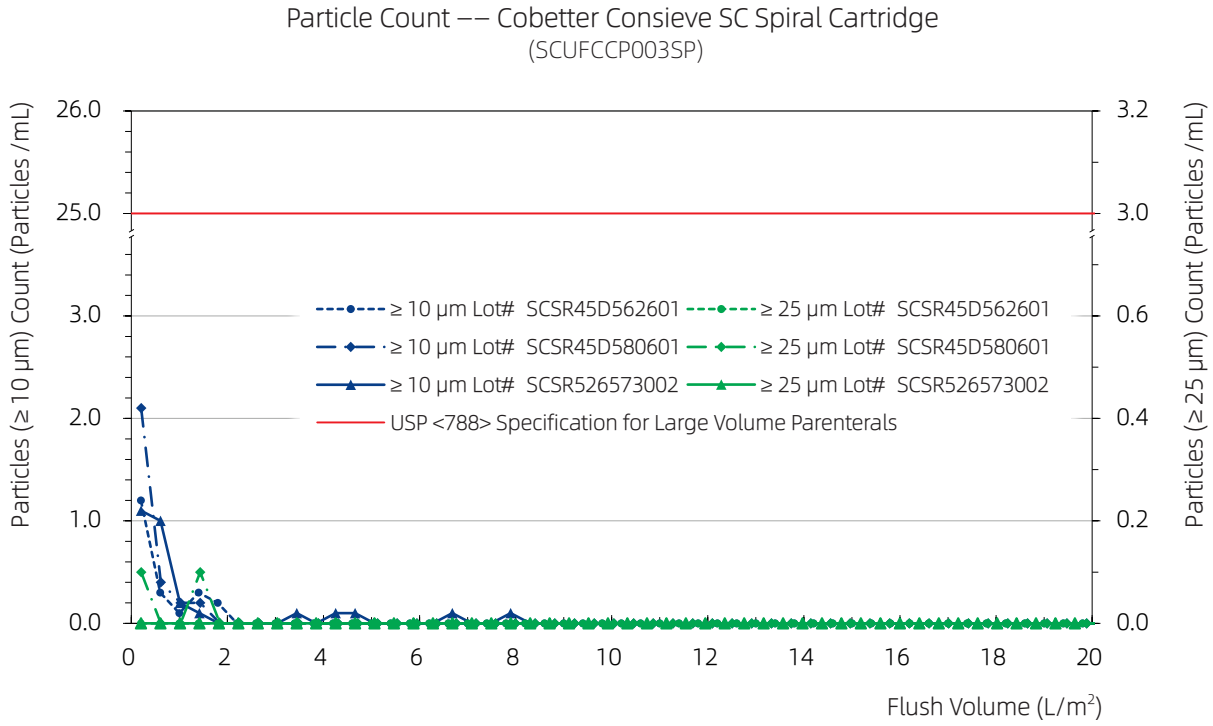
Particle Requirements for Large Volume Parenterals in USP <788>

Particle Size (μm)	Requirements
≥ 10	≤ 25 particles/mL
≥ 25	≤ 3 particles/mL

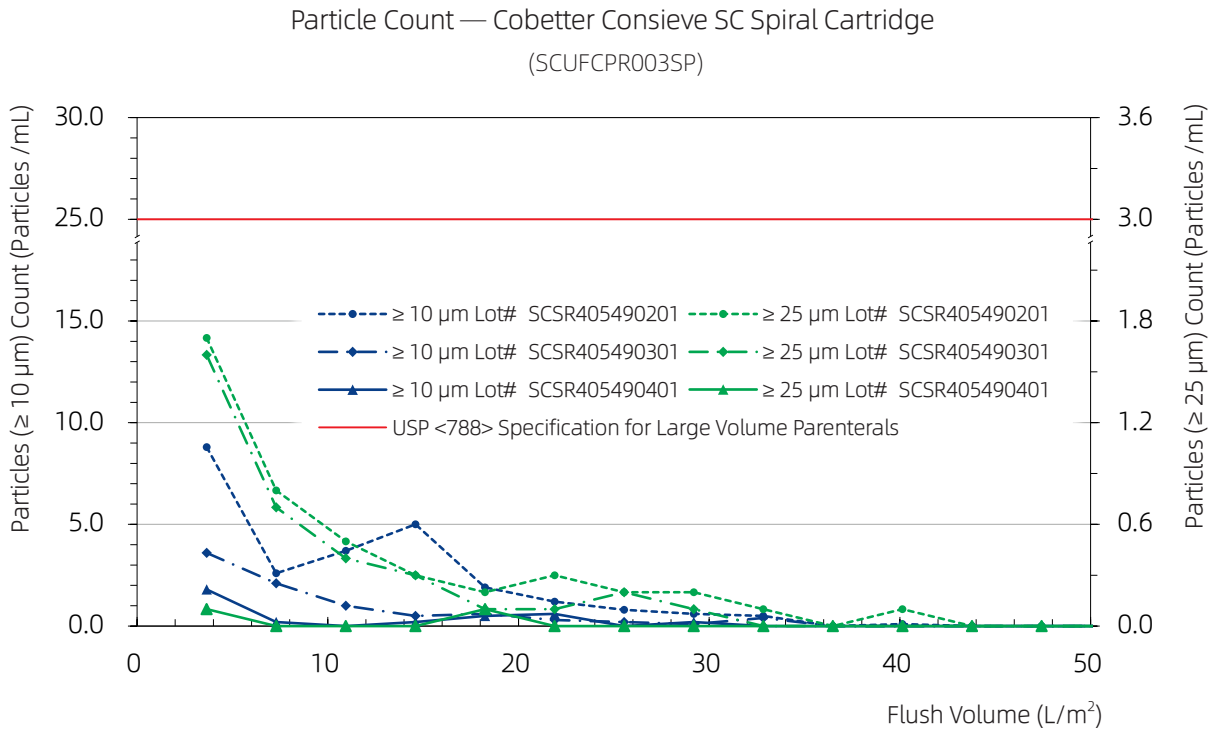
Cobetter Consieve SC Spiral Cartridge (SCUFCCP003SP) - Retentate Port



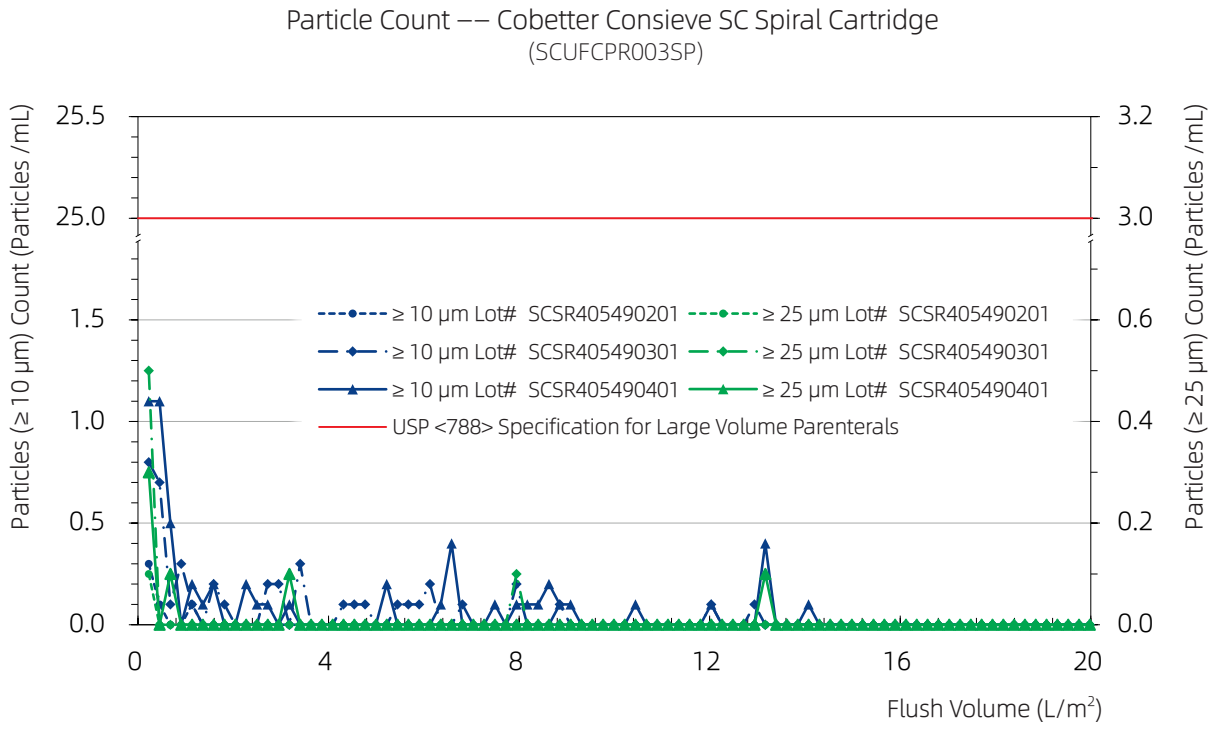
Cobetter Consieve SC Spiral Cartridge (SCUFCCP003SP) - Permeate Port



Cobetter Consieve SC Spiral Cartridge (SCUFCPR003SP) - Retentate Port



Cobetter Consieve SC Spiral Cartridge (SCUFCPR003SP) - Permeate Port



Conclusion

The particle count in the effluent of Cobetter Consieve SC spiral cartridge meets the requirements in USP <788> for large volume parenterals.

6. Non-fiber Releasing

Summary of Method

Cobetter Consieve SC spiral cartridges were installed in the test devices. The cartridges were flushed with purified water for 5 min at the inlet flow rate of 10 L/min/m^2 and a TMP of 1.7 bar, with both retentate port and permeate port open. Next, the cartridges were circulated using 0.1 M NaOH solution for 30-60 minutes, controlling the TMP at 0.5-1 bar.

The cartridges were flushed with purified water at the inlet flow rate of 10 L/min/m^2 with a TMP of 1.7 bar. When the flushing volume at the retentate port reached 50 L/m^2, the retentate valve was closed slowly, and the TMP was maintained at 1.7 bar to continue flushing the permeate port. The total flushing volume at the permeate port was 50 L/m^2.

The cartridge effluent was filtered through 0.8 μm black gridded disc filter to collect any fibers released from the cartridges. The disc filter was examined under 50x microscope for presence of any fibers.

Cobetter Consieve SC Spiral Cartridge

Catalogue Number	Lot Number	Number of Fibers in Effluent Retentate Port	Number of Fibers in Effluent Permeate Port
SCUFCCP003SP	SCSR45D580601	0	0
	SCSR45D562601	0	0
	SCSR45D5A2301	0	0
SCUFCPR003SP	SCSR405490201	0	0
	SCSR405490301	0	0
	SCSR405490401	0	0

Conclusion

Cobetter Consieve SC spiral cartridge meets the criteria for a “Non-fiber-releasing filter” as defined in 21 CFR 210.3 (b) (6).

7. Temperature and Pressure Resistance Test

Cartridges may work at higher pressure, higher temperature or lower temperature in the practical application process. The purpose of this test is to verify the temperature and pressure resistance of the cartridges.

7.1. High Temperature and High Pressure Resistance

Summary of Method

Cobetter Consieve SC series PR spiral cartridges were tested the water flux and integrity. The cartridges were cycled with purified water for 120 h at the conditions of 55-60 °C, TMP of 10 bar. The cartridges were tested for integrity and water flux after being circulated, water flux results of the cartridges were corrected to a temperature of 25 °C.

Cobetter Consieve SC series CP spiral cartridges were tested the water flux and integrity. The cartridges were cycled with purified water for 120 h at the conditions of 55-60 °C, TMP of 3 bar. The cartridges were tested for integrity and water flux after being circulated, water flux results of the cartridges were corrected to a temperature of 25 °C.

Results

Catalogue Number	Lot Number	Prior to Hydraulic Stress		Post Hydraulic Stress	
		Water Flux @1 bar (L/m^2/h)	Air Diffusion @ 1 bar (mL/min)	Water Flux @1 bar (L/m^2/h)	Air Diffusion @ 1 bar (mL/min)
SCUFCCP003SP	SCSR6165B1901	19.02	1.74	18.56	1.25
	SCSR6165B2601	18.46	1.88	18.04	1.46
	SCSR45D5B2201	18.00	1.36	18.62	1.91
SCUFCPR003LP	SCSR506531901	15.47	31.5	13.16	30.8
	SCSR506531801	15.69	22.8	13.67	26.6
	SCSR490831001	15.60	27.4	14.27	28.7

Conclusion

The water flux and integrity of the Cobetter Consieve SC spiral cartridge have no obvious changes after high temperature and high pressure test.

7.2. Low Temperature and High Pressure Resistance Test

Summary of Method

Cobetter Consieve SC spiral cartridges were tested the water flux and integrity. The cartridges were cycled with purified water for 48 h at the conditions of 2-8 °C, TMP of 4.1 bar. The cartridges were tested for integrity and water flux after being circulated, water flux results of the cartridges were corrected to a temperature of 25 °C.

Results

Catalogue Number	Lot Number	Prior to Hydraulic Stress		Post Hydraulic Stress	
		Water Flux @1 bar (L/m^2/h)	Air Diffusion @ 1 bar (mL/min)	Water Flux @1 bar (L/m^2/h)	Air Diffusion @ 1 bar (mL/min)
SCUFCPR003SP	SCSR405490201	15.61	16.3	15.54	24.8
	SCSR405490301	14.73	17.6	14.87	23.5
	SCSR405490401	14.50	22.3	15.33	19.5

Conclusion

The water flux and integrity of the Cobetter Consieve SC spiral cartridge have no obvious changes after low temperature and high pressure test.

8. Alkali Resistance Study

Sodium hydroxide is the most effective and commonly used reagent for cleaning, disinfection and depyrogenation in biological applications. The purpose of this test is to verify the alkali resistance of Cobetter Consieve SC spiral cartridges to sodium hydroxide solution.

Summary of Method

Cobetter Consieve SC spiral cartridges were tested the water flux and integrity. The cartridges were cycled with 0.1 M NaOH for 50 h at the conditions of 60 °C, TMP of 1 bar. The cartridges were flushed with purified water until the flushed solution was neutral and were tested for integrity and water flux after being circulated for 8 cycles (400 h). Water flux results of the cartridges were corrected to a temperature of 25 °C.

Results

Catalogue Number	Lot Number	Prior to Hydraulic Stress		Post Hydraulic Stress	
		Water Flux @1 bar ($L/m^2/h$)	Air Diffusion @ 1 bar (mL/min)	Water Flux @1 bar ($L/m^2/h$)	Air Diffusion @ 1 bar (mL/min)
SCUFCPR003SP	SCSR405490201	15.84	19.5	15.79	28.4
	SCSR405490301	14.78	15.4	14.64	23.2
	SCSR405490401	14.71	18.2	14.58	27.6

Conclusion

The water flux and integrity of the Cobetter Consieve SC spiral cartridge have no obvious changes after sodium hydroxide cycle test.

9. Pressure Pulse

Summary of Method

Cobetter Consieve SC spiral cartridges were tested the water flux and integrity. A air stress of 6.9 bar was applied to the cartridges for 3 seconds in the forward direction. After 3 seconds, the upstream pressure of the cartridges was instantly reduced to 0 bar for 3 seconds. The cartridges were tested for integrity and water flux after being circulated for 5000 cycles, water flux results of the cartridges were corrected to a temperature of 25 °C.

Results

Catalogue Number	Lot Number	Prior to Pressure Pulse		Post Pressure Pulse	
		Water Flux @1 bar (L/m^2/h)	Air Diffusion @ 1 bar (mL/min)	Water Flux @1 bar (L/m^2/h)	Air Diffusion @ 1 bar (mL/min)
SCUFCPR003SP	SCSR405490201	14.54	12.2	13.62	26.2
	SCSR405490301	14.88	18.6	13.91	18.4
	SCSR405490401	14.69	17.2	13.77	19.8

Conclusion

The water flux and integrity of the Cobetter Consieve SC spiral cartridge have no obvious changes after pressure pulse test.

10. Chemical Compatibility

The influence of chemicals on the cartridges is ought to be taken into consideration as using the incompatible chemicals may impact the spiral cartridge's materials of construction, bringing about poor spiral cartridge performance and impairing the spiral cartridge.

Summary of Method

The evaluation of chemical compatibility for cartridges were exposed to test chemicals for a period of time at specific temperature.

Results

Solvent	PH	Preservation Condition	Results
Phosphoric Acid, 0.1 M	1.61	23 °C / 28 days	Compatible
Citric Acid, 0.1 M	2.26	23 °C / 7 days	Compatible
Acetic Acid, 5%	2.46	23 °C / 7 days	Compatible
Ethanol, 50%	6.55	23 °C / 28 days	Compatible
Isopropyl Alcohol, 40%	6.51	23 °C / 7 days	Compatible
Sodium Dodecyl Sulfate (SDS), 0.01 M	6.01	23 °C / 7 days	Compatible
Triton-X 100, 0.01 M	5.98	23 °C / 7 days	Compatible
Dimethylsulfoxide (DMSO), 30%	5.20	23 °C / 28 days	Compatible
Dimethylacetamide (DMAC), 30%	5.21	23 °C / 28 days	Compatible
Dimethyl Formamide (DMF), 30%	6.42	23 °C / 28 days	Compatible
N-Methylpyrrolidone, 30%	8.36	23 °C / 7 days	Compatible
Carbamide, 8 M	9.43	23 °C / 28 days	Compatible
Acetonitrile, 60%	6.05	23 °C / 28 days	Compatible
Sodium Hydroxide, 0.1 M	12.97	23 °C / 28 days	Compatible
Sodium Hydroxide, 0.5 M	13.69	23 °C / 28 days	Compatible

Note: The pH value is a temperature-compensated measurement based on 25 °C. Due to factors such as instrument accuracy, solution preparation variations, and ambient temperature/humidity fluctuations, actual measured data may exhibit normal deviations within a reasonable range.

Conclusion

Cobetter Consieve SC spirals have a excellent compatibility with many common chemicals and can withstand a pH range of 2 to 13 under normal operating conditions. The chemical compatibility results under laboratory conditions are for reference only. It is recommended to verify the compatibility of the product with the spiral cartridges under actual process conditions before use.

11. Bacterial Endotoxins Test

Bacterial endotoxins test for Cobetter Consieve SC spiral cartridges was performed according to current USP <85> *BACTERIAL ENDOTOXINS TEST*. The Bacterial Endotoxins Test (*BET*) is a test to detect or quantify endotoxins from Gram-negative bacteria using *Amoebocyte lysate* from the horseshoe crab (*Limulus polyphemus* or *Tachypleus tridentatus*).

Summary of Method

Cobetter Consieve SC spiral cartridges were installed in the test devices. The cartridges were flushed with the non-pyrogenic ultrapure water (< 0.03 EU/mL) for 5 min at the inlet flow rate of 10 L/min/m^2 and a TMP of 1.7 bar, with both retentate port and permeate port open. Next, the cartridges were circulated using 0.1 M NaOH solution for 30-60 minutes, controlling the TMP at 0.5-1 bar.

The cartridges were flushed with the non-pyrogenic ultrapure water at the inlet flow rate of 10 L/min/m^2 with a TMP of 1.7 bar. When the flushing volume at the retentate port reached 50 L/m^2, the retentate valve was closed slowly, and the TMP was maintained at 1.7 bar to continue flushing the permeate port. The total flushing volume at the permeate port was 50 L/m^2.

At the end of flushing, samples were then taken from the retentate and the permeate ports and evaluated with the *Amebocyte Lysate* gel clot test.

Preparation of Solutions

	Solution	Endotoxin Concentration / Solution to Which Endotoxin Is Added	Number of Replicates
A	Sample solution	None / *Sample Solution*	2
B	Positive product control	2λ / *Sample Solution*	2
C	Positive control	2λ / *Water for BET*	2
D	Negative control	None / *Water for BET*	2

Prepare *Solution A* and the positive product control *Solution B* using Sample solution. The positive control *Solutions B* and *C* contain the *Standard Endotoxin Solution* at a concentration corresponding to twice the labeled lysate sensitivity. The negative control *Solution D* consists of *Water for BET*.

Incubate the reaction mixture at 37 ± 1 °C for 60 ± 2 min, avoiding vibration. To test the integrity of the gel, take each tube in turn directly from the incubator, and invert it through about 180° in one smooth motion. If a firm gel has formed that remains in place upon inversion, record the result as positive. A result is negative if an intact gel is not formed. The test is considered valid when both replicates of *Solutions B* and *C* are positive and those of *Solution D* are negative. When a negative result is found for both replicates of *Solution A*, the preparation under test complies with the test. When a positive result is found for both replicates of *Solution A*, the preparation under test does not comply with the test.

Results

Catalogue Number	Lot Number	Solution A	Solution B	Solution C	Solution D	Result (EU/mL)
SCUFCCP003SP	SCSR526573002	– –	+ +	+ +	– –	< 0.06
	SCSR45D562601	– –	+ +			< 0.06
	SCSR45D5A2301	– –	+ +			< 0.06
SCUFCPR003SP	SCSR405490201	– –	+ +	+ +	– –	< 0.06
	SCSR405490301	– –	+ +			< 0.06
	SCSR405490401	– –	+ +			< 0.06

Legend: '+' — A firm gel has formed that remains in place upon inversion, Positive.
'–' — An intact gel is not formed, Negative.

Conclusion

The flushing fluid of Cobetter Consieve SC spiral cartridge after being flushed and sanitized by 0.1 M sodium hydroxide solution contains < 0.25 EU/mL as determined by *Amebocyte Lysate,* meeting the requirements of USP monographs for *Sterile Water for Injection*.

12. Endotoxin Removal Test

The endotoxin content of Cobetter Consieve SC spiral cartridges itself is limited. The purpose of this test is to verify whether the removal of endotoxin by 0.1 M sodium hydroxide solution is effective through endotoxin challenge.

Summary of Method

Cobetter Consieve SC spiral cartridges were installed in the test devices. The cartridges were challenged with 5 L of solution containing endotoxin >1000 EU/mL at an inlet flow rate of 10 L/min/m^2 for 1 hour. Next, the cartridges were circulated using 0.1 M NaOH solution for 30 minutes, controlling the TMP at 0.5-1 bar.

The cartridges were flushed with the non-pyrogenic ultrapure water (< 0.03 EU/mL) at the inlet flow rate of 10 L/min/m^2 with a TMP of 1.7 bar. When the flushing volume at the retentate port reached 50 L/m^2, the retentate valve was closed slowly, and the TMP was maintained at 1.7 bar to continue flushing the permeate port. The total flushing volume at the permeate port was 50 L/m^2.

At the end of flushing, samples were then taken from the retentate and the permeate ports and evaluated with the *Amebocyte Lysate* gel clot test.

Preparation of Solutions

	Solution	Endotoxin Concentration / Solution to Which Endotoxin Is Added	Number of Replicates
A	Sample solution	None / *Sample Solution*	2
B	Positive product control	2λ / *Sample Solution*	2
C	Positive control	2λ / *Water for BET*	2
D	Negative control	None / *Water for BET*	2

Prepare *Solution A* and the positive product control *Solution B* using Sample solution. The positive control *Solutions B* and *C* contain the *Standard Endotoxin Solution* at a concentration corresponding to twice the labeled lysate sensitivity. The negative control *Solution D* consists of *Water for BET*.

Incubate the reaction mixture at 37 ± 1 °C for 60 ± 2 min, avoiding vibration. To test the integrity of the gel, take each tube in turn directly from the incubator, and invert it through about 180° in one smooth motion. If a firm gel has formed that remains in place upon inversion, record the result as positive. A result is negative if an intact gel is not formed. The test is considered valid when both replicates of *Solutions B* and *C* are positive and those of *Solution D* are negative. When a negative result is found for both replicates of *Solution A*, the preparation under test complies with the test. When a positive result is found for both replicates of *Solution A*, the preparation under test does not comply with the test.

Results

Catalogue Number	Lot Number	Solution				Result (EU/mL)
		A	B	C	D	
SCUFCPR003SP	SCSR405490201	– –	+ +	+ +	– –	< 0.06
	SCSR405490301	– –	+ +			< 0.06
	SCSR405490401	– –	+ +			< 0.06

Legend: '+' — A firm gel has formed that remains in place upon inversion, Positive.
'–' — An intact gel is not formed, Negative.

Conclusion

The bacterial endotoxin content of Cobetter Consieve SC spiral cartridge after being flushed and sanitized by 0.1 M sodium hydroxide solution meet the requirements of USP monographs for *Sterile Water for Injection.* 0.1 M sodium hydroxide solution is effective in removing endotoxin.

13. USP <87> Biological Reactivity Test, In Vitro

USP <87> *Biological Reactivity Test, In Vitro* is designed to determine the biological reactivity of mammalian cell cultures following contact with the elastomeric plastics and other polymeric materials with direct or indirect patient contact or of specific extracts prepared from the materials under test.

USP <87> Biological Reactivity Tests were performed on all components of Cobetter Consieve SC spiral cartridges to estimate the cytotoxicity. The tests were conducted in an accredited, independent laboratory following Good Laboratory Practices.

Conclusion

The component materials of Cobetter Consieve SC spiral cartridges were tested and meet the requirement of USP <87> *Biological Reactivity Test, In Vitro*.

EPINTEK

TEST RESULT CERTIFICATION

Sponsorl:	Hangzhou Cobetter Filtration Equipment Co., Ltd.	Technical initiation date:	2020-11-01
Address:	Zixia Village, Heshang Town, Xiaoshan District, Hangzhou, Zhejiang ,China	Technical completion date:	2020-11-06
		Report signature date:	2020-11-09
		Study number:	MED202010223-47

Test Article:	Regenerated cellulose ultrafiltration membrane	Study:	In Vitro Cytotoxicity Test-Elution Test
Lot#:	R028-01	Size:	About 0.1 m^2
Model:	RC-3KD	Ratio:	6 cm^2/ 1 mL
Physical State:	Solid	Vehicles:	Culture medium with 10% FBS
Color:	White	Temp/Time:	37°C, 72 h

1. REFERENCE:

USP 43- NF38 <87> BIOLOGICAL REACTIVITY TESTS, IN VITRO

2. GENERAL PROCEDURE:

The elution test was performed using L929 cell to evaluate the cytotoxicity of extract.
The eluates of the test material were performed in static conditions by immersing test material into medium culture and incubated at 37°C for 72 h. 2 mL of eluate of each test material were applied to the monolayer of L-929 and it was incubated at 37°C in atmosphere for 48 h.
After 48 h of incubation the cells culture were observed to evaluate the biological reaction.

3. RESULTS:

After incubated with extract for 48 h, the observed cytotoxicity grade was 2.

4. CONCLUSION:

The test article meet the requirement of In Vitro Cytotoxicity Test, USP 43- NF38 <87>.

5. AUTHORIZED PERSONNEL:

Alice Wang
Study Director

Bill Yu
QAU

* The brief report cannot be used for any purpose except test certificate. A complete test report that complies with the GLP specification is available upon request.

EPINTEK

TEST RESULT CERTIFICATION

Sponsor:	Hangzhou Cobetter Filtration Equipment Co., Ltd.	Test start date:	2023-05-17
		Test completion date:	2023-05-20
Address:	Cobetter Park, Heshang New Material Industrial Park, Xiaoshan District, Hangzhou 311265, China	Report completion date:	2023-06-02
		Study number:	SZB23040417C-47

Test Article:	Sealing Binder	Study:	In Vitro Cytotoxicity Test-Elution Test
Lot/Batch#:	321501	Size:	/
Model:	/	Ratio:	0.2 g / 1 mL
Physical State:	Solid	Vehicles:	Culture medium with 10% FBS
Color:	Yellow	Temp/Time:	37°C, 24 h

1. REFERENCE:

USP<87>, Official as of 01-Aug-2016 Biological Reactivity Tests, In Vitro

2. GENERAL PROCEDURE:

The elution test was performed using L929 cell to evaluate the cytotoxicity of extract.

The eluates of the test material were performed in static conditions by immersing test material into medium culture and incubated at 37°C for 24 h. 2 mL of eluate of each test material including extract (100%), blank control, positive control and negative control were applied to the monolayer of L929 and it was incubated at 37°C 5% CO_2 for 48 h.

After 48 h of incubation the cells culture were observed to evaluate the biological reaction.

3. RESULTS:

After incubated with extract for 48 h, the observed cytotoxicity grade was 1.

4. CONCLUSION:

The test article met the requirement of In Vitro Cytotoxicity Test, USP<87>.

5. AUTHORIZED PERSONNEL:

Laurel Li
Report Drafter

Amber Zhang
Study Director

* The brief report cannot be used for any purpose except test certificate. A complete test report that complies with the GLP specification is available upon request.

EPINTEK

TEST RESULT CERTIFICATION

Sponsor:	Hangzhou Cobetter Filtration Equipment Co., Ltd.	Test start date:	2024-12-09
Address:	Cobetter Park, Heshang New Material Industry Park, Xiaoshan District, Hangzhou City, Zhejiang Province	Test completion date:	2024-12-14
		Report completion date:	2024-12-25
		Study number:	SZB24110408B-047

Test Article:	Grid A	Study:	In Vitro Cytotoxicity Test-Elution Test
Test Article Material:	PE		
Lot/Batch#:	/	Size:	/
Model:	/	Ratio:	0.2 g / 1 mL
Physical State:	Solid	Vehicles:	MEM medium with 10% FBS
Color:	White	Temp/Time:	37°C, 72 h, 40 rpm

1. REFERENCE:

USP<87>, Official as of 01-Aug-2016 Biological Reactivity Tests, In Vitro

2. GENERAL PROCEDURE:

The elution test was performed using L929 cell to evaluate the cytotoxicity of extract.

The eluates of the test material were performed in static conditions by immersing test material into medium culture and incubated at 37℃ for 72 h. 2 mL of eluate of each test material including extract (100%), blank control, positive control and negative control were applied to the monolayer of L929 and it was incubated at 37℃ 5% CO_2 for 48 h.

After 48 h of incubation the cells culture were observed to evaluate the biological reaction.

3. RESULTS:

After incubated with extract for 48 h, the observed cytotoxicity grade was 1.

4. CONCLUSION:

Under the conditions of this study, the test article extract did not show a cytotoxic potential to L929 cells.

5. AUTHORIZED PERSONNEL:

杭州爵品质量技术服务有限公司 检验检测专用章

Youhan Fu

Youhan Fu
Report Drafter

Hulda Tan

Hulda Tan
Study Director

* The brief report cannot be used for any purpose except test certificate. A complete test report that complies with the GLP specification is available upon request.

EPINTEK

TEST RESULT CERTIFICATION

Sponsor:	Hangzhou Cobetter Filtration Equipment Co., Ltd.	Test start date:	2024-12-09
Address:	Cobetter Park, Heshang New Material Industry Park, Xiaoshan District, Hangzhou City, Zhejiang Province	Test completion date:	2024-12-14
		Report completion date:	2024-12-25
		Study number:	SZB24110408C-047

Test Article:	Grid B	Study:	In Vitro Cytotoxicity Test-Elution Test
Test Article Material:	PP		
Lot/Batch#:	/	Size:	/
Model:	/	Ratio:	0.2 g / 1 mL
Physical State:	Solid	Vehicles:	MEM medium with 10% FBS
Color:	White	Temp/Time:	37°C, 72 h, 40 rpm

1. REFERENCE:

USP<87>, Official as of 01-Aug-2016 Biological Reactivity Tests, In Vitro

2. GENERAL PROCEDURE:

The elution test was performed using L929 cell to evaluate the cytotoxicity of extract.

The eluates of the test material were performed in static conditions by immersing test material into medium culture and incubated at 37℃ for 72 h. 2 mL of eluate of each test material including extract (100%), blank control, positive control and negative control were applied to the monolayer of L929 and it was incubated at 37℃ 5% CO_2 for 48 h.

After 48 h of incubation the cells culture were observed to evaluate the biological reaction.

3. RESULTS:

After incubated with extract for 48 h, the observed cytotoxicity grade was 1.

4. CONCLUSION:

Under the conditions of this study, the test article extract did not show a cytotoxic potential to L929 cells.

5. AUTHORIZED PERSONNEL:

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EPINTEK

TEST RESULT CERTIFICATION

Sponsor:	Hangzhou Cobetter Filtration Equipment Co., Ltd.	Test start date:	2024-12-09
Address:	Cobetter Park, Heshang New Material Industry Park, Xiaoshan District, Hangzhou City, Zhejiang Province	Test completion date:	2024-12-14
		Report completion date:	2024-12-17
		Study number:	SZB24110408A-047

Test Article:	housing	Study:	In Vitro Cytotoxicity Test-Elution Test
Lot/Batch#:	/	Size:	/
Model:	/	Ratio:	0.2 g / 1 mL
Physical State:	Solid	Vehicles:	MEM medium with 10% FBS
Color:	White	Temp/Time:	37°C, 72 h, 40 rpm

1. REFERENCE:

USP<87>, Official as of 01-Aug-2016 Biological Reactivity Tests, In Vitro

2. GENERAL PROCEDURE:

The elution test was performed using L929 cell to evaluate the cytotoxicity of extract.

The eluates of the test material were performed in static conditions by immersing test material into medium culture and incubated at 37°C for 72 h. 2 mL of eluate of each test material including extract (100%), blank control, positive control and negative control were applied to the monolayer of L929 and it was incubated at 37°C 5% CO_2 for 48 h.

After 48 h of incubation the cells culture were observed to evaluate the biological reaction.

3. RESULTS:

After incubated with extract for 48 h, the observed cytotoxicity grade was 1.

4. CONCLUSION:

Under the conditions of this study, the test article extract did not show a cytotoxic potential to L929 cells.

5. AUTHORIZED PERSONNEL:

杭州烟品质量技术服务有限公司 检验检测专用章

Youhan Fu

Youhan Fu
Report Drafter

Hulda Tan

Hulda Tan
Study Director

* The brief report cannot be used for any purpose except test certificate. A complete test report that complies with the GLP specification is available upon request.

EPINTEK

TEST RESULT CERTIFICATION

Sponsor:	Hangzhou Cobetter Filtration Equipment Co., Ltd.	Test start date:	2024-12-09
Address:	Cobetter Park, Heshang New Material Industry Park, Xiaoshan District, Hangzhou City, Zhejiang Province	Test completion date:	2024-12-12
		Report completion date:	2024-12-17
		Study number:	SZB24110407C-047

Test Article:	EPDM O-ring	Study:	In Vitro Cytotoxicity Test-Elution Test
Lot/Batch#:	/	Size:	/
Model:	/	Ratio:	0.2 g / 1 mL
Physical State:	Solid	Vehicles:	MEM medium with 10% FBS
Color:	Black	Temp/Time:	37℃, 24 h, 40 rpm

1. REFERENCE:

USP<87>, Official as of 01-Aug-2016 Biological Reactivity Tests, In Vitro

2. GENERAL PROCEDURE:

The elution test was performed using L929 cell to evaluate the cytotoxicity of extract.

The eluates of the test material were performed in static conditions by immersing test material into medium culture and incubated at 37℃ for 24 h. 2 mL of eluate of each test material including extract (100%), blank control, positive control and negative control were applied to the monolayer of L929 and it was incubated at 37℃ 5% CO_2 for 48 h.

After 48 h of incubation the cells culture were observed to evaluate the biological reaction.

3. RESULTS:

After incubated with extract for 48 h, the observed cytotoxicity grade was 1.

4. CONCLUSION:

Under the conditions of this study, the test article extract did not show a cytotoxic potential to L929 cells.

5. AUTHORIZED PERSONNEL:

杭州熠品质量技术服务有限公司 检验检测专用章

Youhan Fu

Youhan Fu
Report Drafter

Hulda Tan

Hulda Tan
Study Director

* The brief report cannot be used for any purpose except test certificate. A complete test report that complies with the GLP specification is available upon request.

14. USP <88> Class VI Biological Reactivity Test, In Vivo

USP <88> *Biological Reactivity Test, In Vivo* is designed to determine the biological response of animals to elastomerics, plastics, and other polymeric material with direct or indirect patient contact, or by the injection of specific extracts prepared from the material under test.

USP <88> Class VI Biological Reactivity Tests were performed on all components of Cobetter Consieve SC spiral cartridges to estimate the biosafety. The tests were conducted in an accredited, independent laboratory following Good Laboratory Practices.

Summary of Method

The current USP <88> Class VI Plastics tests, including the following tests:

Procedure	Animal	Test Material
Systemic Injection Test	Mouse	• Extract of *Sample* in *Sodium Chloride Injection* • Extract of *Sample* in *1 in 20 Solution of Alcohol in Sodium Chloride Injection* • Extract of *Sample* in *Polyethylene Glycol 400* • Extract of *Sample* in *Vegetable Oil*
Intracutaneous Test	Rabbit or Guinea Pig	
Implantation Test	Rabbit	Implant strips of *Sample*

Conclusion

The component materials of Cobetter Consieve SC spiral cartridges meet the criteria of the USP <88> *Biological Reactivity Test* for Class VI plastics.

EPINTEK

TEST RESULT CERTIFICATION

Sponsor:	Hangzhou Cobetter Filtration Equipment Co., Ltd.	Technical initiation date:	2020-10-19
		Technical completion date:	2020-11-18
Address:	Daqiao Industrial Park, Heshang Town, Xiaoshan District, Hangzhou, Zhejiang, China	Report signature date:	2020-11-23
		Study Number:	MED202009207-11 MED202009207-17 MED202009207-27

Test Article:	Regenerated cellulose ultrafiltration membrane	Ratio:	6 cm^2: 1 mL
Lot#:	R021-01	Vehicles:	0.9% sodium chloride for injection（SC） Corn oil（CO） 1:20 Alcohol in SC（AL） Polyethylene glycol 400（PEG-400）
Physical State:	Solid		
Color:	White		
Study:	Biological Test for Plastics, Class VI	Temp/Time:	70°C for 24h

1. REFERENCE:

USP <88> BIOLOGICAL REACTIVITY TESTS, IN VIVO

2. GENERAL PROCEDURE:

The test article extraction and corresponding blank were injected systemically and intracutaneously in mice and rabbits, respectively. The injections were in the amounts and routes set forth by USP 42; including the further dilution of the extracts prepared with PEG-400. The animals were observed for signs of toxicity and skin reactivity for up to 72 hours post treatment. In addition, the test article components were implanted into the paravertebral musculature of rabbits for 1 week and observed for signs of hemorrhage, inflammation, necrosis, discoloration, and encapsulation, or infection.

3. RESULTS:

None of the mice injected with the test article extracts exhibited any signs of toxicity in the Systemic Injection Test. In addition, none of the rabbits injected intracutaneously with the test article extracts exhibited any signs of erythema, edema or clinical toxicity. In both the Systemic and intracutaneous Tests the controls were normal through 72 hours. Also, the implant sites exhibited no significant signs of hemorrhage, inflammation necrosis, discoloration, and encapsulation, or infection compared with the control sites.

4. CONCLUSION:

The test article meets the requirements of USP <88> for the Biological Test for Plastics, Class VI.

5. AUTHORIZED PERSONNEL:

Look Lu 2020-11-23
Look Lu (Study Director)

Bill Yu 2020-11-23
Bill Yu (Quality Assurance)

杭州品质量技术服务有限公司 检验检测专用章

* The brief report cannot be used for any purpose except test certificate. A complete test report that complies with the GLP specification is available upon request.

EPINTEK

TEST RESULT CERTIFICATION

Sponsor:	Hangzhou Cobetter Filtration Equipment Co., Ltd.	Test start date:	2023-05-28
		Test completion date:	2023-06-09
		Report completion date:	2023-06-17
Address:	Cobetter Park, Heshang New Material Industrial Park, Xiaoshan District, Hangzhou 311265, China	Study Number:	SZB23040417C-11 SZB23040417C-17 SZB23040417C-27

Test Article:	Sealing Binder	Ratio:	0.2 g / 1 mL
Lot#:	321501	Vehicles:	0.9% sodium chloride for injection (SC) Corn oil (CO) 1:20 Alcohol in SC (AL) Polyethylene glycol 400 (PEG-400)
Model/Size:	/		
Physical State:	Solid		
Color:	Yellow		
Study:	Biological Test for Plastics, Class VI	Temp/Time:	70°C, 24 h

1. **REFERENCE:**

   USP <88>, Official as of 01-Aug-2013 - BIOLOGICAL REACTIVITY TESTS, IN VIVO

2. **GENERAL PROCEDURE:**

   The test article extraction and corresponding blank were injected systemically and intracutaneously in mice and rabbits, respectively. The injections were in the amounts and routes set forth by USP 88; including the further dilution of the extracts prepared with PEG-400. The animals were observed for signs of toxicity and skin reactivity for up to 72 hours post treatment. In addition, the test article components were implanted into the paravertebral musculature of rabbits for 1 week and observed for signs of hemorrhage, inflammation, necrosis, discoloration, and encapsulation, or infection.

3. **RESULTS:**

   Within 72 h after injection, no abnormal toxicity of mice and erythema and edema of rabbit skin in the test and control were found. Meanwhile, there was no obvious bleeding, inflammation, necrosis, discoloration or infection were found at the test implant site and control implant site, and the thickness of fibrotic sac formation on both sides was similar.

4. **CONCLUSION:**

   The test article met the requirements of USP <88>, Official as of 01-Aug-2013 - BIOLOGICAL REACTIVITY TESTS, IN VIVO for the Biological Test for Plastics, Class VI.

5. **AUTHORIZED PERSONNEL:**

Colin Lu
Colin Lu
Report Drafter

Patryk Chen
Patryk Chen
Study Director

* The brief report cannot be used for any purpose except test certificate. A complete test report that complies with the GLP specification is available upon request.

TEST RESULT CERTIFICATION

Sponsor:	Hangzhou Cobetter Filtration Equipment Co., Ltd.	Test start date:	2024-12-10
		Test completion date:	2024-12-19
		Report completion date:	2024-12-23
Address:	Cobetter Park, Heshang New Material Industry Park, Xiaoshan District, Hangzhou City, Zhejiang Province	Study Number:	SZB24110408B-011 SZB24110408B-027 SZB24110408B-017

Test Article:	Grid A	Ratio:	0.2 g/mL
Lot#:	/	Vehicles:	0.9% sodium chloride for injection (SC) Sesame Oil (SO) 1:20 Alcohol in SC (AL) Polyethylene glycol 400 (PEG-400)
Model/Size:	/		
Physical State:	Solid		
Color:	white		
Test Article Material:	PE		
Study:	Biological Test for Plastics, Class VI	Temp/Time:	70℃ 24h 40 rpm

1. REFERENCE:

USP <88>, Official as of 01-Aug-2013 - BIOLOGICAL REACTIVITY TESTS, IN VIVO

2. GENERAL PROCEDURE:

The test article extraction and corresponding blank were injected systemically and intracutaneously in mice and rabbits, respectively. The injections were in the amounts and routes set forth by USP 88; including the further dilution of the extracts prepared with PEG-400. The animals were observed for signs of toxicity and skin reactivity for up to 72 hours post treatment. In addition, the test article components were implanted into the paravertebral musculature of rabbits for 1 week and observed for signs of hemorrhage, inflammation, necrosis, discoloration, and encapsulation, or infection.

3. RESULTS:

Within 72 h after injection, no abnormal toxicity of mice and erythema and edema of rabbit skin in the test and control were found. Meanwhile, there was no obvious bleeding, inflammation, necrosis, discoloration or infection were found at the test implant site and control implant site, and the thickness of fibrotic sac formation on both sides was similar.

4. CONCLUSION:

The test article met the requirements of USP <88>, Official as of 01-Aug-2013 - BIOLOGICAL REACTIVITY TESTS, IN VIVO for the Biological Test for Plastics, Class VI.

5. AUTHORIZED PERSONNEL:

Colin Lu
Report Drafter

杭州爱普医疗器械技术服务有限公司 检验检测专用章

Patryk Chen
Study Director

* The brief report cannot be used for any purpose except test certificate. A complete test report that complies with the GLP specification is available upon request.

EPINTEK

TEST RESULT CERTIFICATION

Sponsor:	Hangzhou Cobetter Filtration Equipment Co., Ltd.	Test start date:	2024-12-10
		Test completion date:	2024-12-19
		Report completion date:	2024-12-23
Address:	Cobetter Park, Heshang New Material Industry Park, Xiaoshan District, Hangzhou City, Zhejiang Province	Study Number:	SZB24110408C-011 SZB24110408C-027 SZB24110408C-017

Test Article:	Grid B	Ratio:	0.2 g/mL
Lot#:	/	Vehicles:	0.9% sodium chloride for injection (SC) Sesame Oil (SO) 1:20 Alcohol in SC (AL) Polyethylene glycol 400 (PEG-400)
Model/Size:	/		
Physical State:	Solid		
Color:	white		
Test Article Material:	PP		
Study:	Biological Test for Plastics, Class VI	Temp/Time:	70℃ 24h 40 rpm

1. REFERENCE:

USP <88>, Official as of 01-Aug-2013 - BIOLOGICAL REACTIVITY TESTS, IN VIVO

2. GENERAL PROCEDURE:

The test article extraction and corresponding blank were injected systemically and intracutaneously in mice and rabbits, respectively. The injections were in the amounts and routes set forth by USP 88; including the further dilution of the extracts prepared with PEG-400. The animals were observed for signs of toxicity and skin reactivity for up to 72 hours post treatment. In addition, the test article components were implanted into the paravertebral musculature of rabbits for 1 week and observed for signs of hemorrhage, inflammation, necrosis, discoloration, and encapsulation, or infection.

3. RESULTS:

Within 72 h after injection, no abnormal toxicity of mice and erythema and edema of rabbit skin in the test and control were found. Meanwhile, there was no obvious bleeding, inflammation, necrosis, discoloration or infection were found at the test implant site and control implant site, and the thickness of fibrotic sac formation on both sides was similar.

4. CONCLUSION:

The test article met the requirements of USP <88> Official as of 01-Aug-2013 - BIOLOGICAL REACTIVITY TESTS, IN VIVO for the Biological Test for Plastics, Class VI.

5. AUTHORIZED PERSONNEL:

Colin Lu
Report Drafter

杭州爱普医疗器械有限公司 检验检测专用章

Patryk Chen
Study Director

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EPINTEK

TEST RESULT CERTIFICATION

Sponsor:	Hangzhou Cobetter Filtration Equipment Co., Ltd.	Test start date:	2024-12-10
		Test completion date:	2024-12-18
		Report completion date:	2024-12-23
Address:	Cobetter Park, Heshang New Material Industry Park, Xiaoshan District, Hangzhou City, Zhejiang Province	Study Number:	SZB24110408A-011 SZB24110408A-027 SZB24110408A-017

Test Article:	housing	Ratio:	0.2 g/mL
Lot#:	/	Vehicles:	0.9% sodium chloride for injection (SC) Sesame Oil (SO) 1:20 Alcohol in SC (AL) Polyethylene glycol 400 (PEG-400)
Model/Size:	/		
Physical State:	Solid		
Color:	white		
Study:	Biological Test for Plastics, Class VI	Temp/Time:	121°C 1h

1. REFERENCE:

USP <88>, Official as of 01-Aug-2013 - BIOLOGICAL REACTIVITY TESTS, IN VIVO

2. GENERAL PROCEDURE:

The test article extraction and corresponding blank were injected systemically and intracutaneously in mice and rabbits, respectively. The injections were in the amounts and routes set forth by USP 88; including the further dilution of the extracts prepared with PEG-400. The animals were observed for signs of toxicity and skin reactivity for up to 72 hours post treatment. In addition, the test article components were implanted into the paravertebral musculature of rabbits for 1 week and observed for signs of hemorrhage, inflammation, necrosis, discoloration, and encapsulation, or infection.

3. RESULTS:

Within 72 h after injection, no abnormal toxicity of mice and erythema and edema of rabbit skin in the test and control were found. Meanwhile, there was no obvious bleeding, inflammation, necrosis, discoloration or infection were found at the test implant site and control implant site, and the thickness of fibrotic sac formation on both sides was similar.

4. CONCLUSION:

The test article met the requirements of USP <88>, Official as of 01-Aug-2013 - BIOLOGICAL REACTIVITY TESTS, IN VIVO for the Biological Test for Plastics, Class VI.

5. AUTHORIZED PERSONNEL:

Colin Lu
Colin Lu
Report Drafter

杭州爱普质量技术服务有限公司 检验检测专用章

Patryk Chen
Patryk Chen
Study Director

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EPINTEK

TEST RESULT CERTIFICATION

Sponsor:	Hangzhou Cobetter Filtration Equipment Co., Ltd.	Test start date:	2024-12-10
		Test completion date:	2024-12-18
		Report completion date:	2024-12-23
Address:	Cobetter Park, Heshang New Material Industry Park, Xiaoshan District, Hangzhou City, Zhejiang Province	Study Number:	SZB24110407C-011 SZB24110407C-027 SZB24110407C-017

Test Article:	EPDM O-ring	Ratio:	0.2 g/mL
Lot#:	/	Vehicles:	0.9% sodium chloride for injection (SC) Sesame Oil (SO) 1:20 Alcohol in SC (AL) Polyethylene glycol 400 (PEG-400)
Model/Size:	/		
Physical State:	Solid		
Color:	Black		
Study:	Biological Test for Plastics, Class VI	Temp/Time:	121°C 1h

1. REFERENCE:

USP <88>, Official as of 01-Aug-2013 - BIOLOGICAL REACTIVITY TESTS, IN VIVO

2. GENERAL PROCEDURE:

The test article extraction and corresponding blank were injected systemically and intracutaneously in mice and rabbits, respectively. The injections were in the amounts and routes set forth by USP 88; including the further dilution of the extracts prepared with PEG-400. The animals were observed for signs of toxicity and skin reactivity for up to 72 hours post treatment. In addition, the test article components were implanted into the paravertebral musculature of rabbits for 1 week and observed for signs of hemorrhage, inflammation, necrosis, discoloration, and encapsulation, or infection.

3. RESULTS:

Within 72 h after injection, no abnormal toxicity of mice and erythema and edema of rabbit skin in the test and control were found. Meanwhile, there was no obvious bleeding, inflammation, necrosis, discoloration or infection were found at the test implant site and control implant site, and the thickness of fibrotic sac formation on both sides was similar.

4. CONCLUSION:

The test article met the requirements of USP <88>, Official as of 01-Aug-2013 - BIOLOGICAL REACTIVITY TESTS, IN VIVO for the Biological Test for Plastics, Class VI.

5. AUTHORIZED PERSONNEL:

Colin Lu
Report Drafter

杭州昌晖生物医药检测技术服务有限公司 检验检测专用章

Patryk Chen
Study Director

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