Summary of Extractables from Sartoflow®[1] Single-Use Tangential Flow Filtration (SUTFF) Flow Kits

Technical Note

Technical Summary for Sartoflow® 150, 1000, and 4500

[1] In order to integrate the acquired Allegro™ SUTFF systems into the existing TFF portfolio of Sartorius, the product names are beeing changed to Sartoflow®. The product names will be equivalents until the successfull harmonization of all collaterals towards Sartoflow®.

Summary

As SUTFF technologies continue to be adopted in downstream processing, it is important to provide extractables data to support these activities.

This document provides data to support the use of the Sartoflow® SUTFF systems in a range of processes in providing data for water and water | ethanol extraction.

Extractables studies were performed on the Sartoflow® SUTFF flow kits using water and 50% ethanol as extraction fluids. These data can be used to estimate the worst case, potential leachables contributed by the SUTFF flow kits while in contact with a drug product during processing. Extractables studies are intended to represent worst case or exaggerated processing conditions; actual leachables are typically expected to be much lower.

The test systems were designed to contain all the components that are part of the feed, permeate and retentate flow kit of the Sartoflow® SUTFF system (apart from the SUTFF distribution plates) and therefore represent the entire fluid pathway. Prior to extraction, the SUTFF flow kits were gamma irradiated at 50 +/- 5 kGy.

The test was performed with fluid circulated dynamically through the SUTFF flow kits. These extraction and recirculation conditions were chosen to reflect typical customer usage.

Test conditions and extraction fluids used are summarized in Table 1.

Table 1
Extraction Conditions

Extraction Fluid	Time of Extraction*	Total Extraction Time	Temperature of Extraction
Water	2 × 8 hours	16 hours	40 +/- 2.5 °C
50% Water | 50% Ethanol	2 × 8 hours	16 hours	40 +/- 2.5 °C

* "2 x 8 hours" indicates 2 successive extractions of 8 hours each. The solvent volume was replaced with an equal volume of fresh solvent for the second successive extraction.

The extraction fluids from the first and second exposure periods were subjected to detailed analyses, including Non-Volatile Residue (NVR), Fourier Transform Infrared Spectroscopy (FTIR), Direct Injection Gas Chromatography | Mass Spectrometry (GC | MS), Headspace GC | MS, and Inductively Coupled Plasma | Mass Spectrometry.

Table 2 describes the analytical methods used for the determination of different extractables from the SUTFF flow kits.

Table 2
Analytical Methods Used for the Assessment of Extractables

Analytical Method	Target Compounds | Property
Non-Volatile Residue (NVR)	Total mass of extractables after test solvent evaporation
Fourier Transform Infrared (FTIR) Spectroscopy	Oligomers of the materials of construction and functional group identification of the materials in the NVR
Gas Chromatography | Mass Spectrometry (GC | MS) - Headspace	Volatile organic compounds that may come from monomers and oligomers, residual solvents from various production steps, additives, residues from polymer treatment, and degradation products
Gas Chromatography | Mass Spectrometry (GC | MS) – Direct Injection	Semi-volatile compounds including lubricants, plasticizers, antioxidants, and residual solvents with higher boiling points
Liquid Chromatography | Ultraviolet | Mass Spectrometry (LC | UV | MS)	Non-volatile organic compounds (and some semi-volatile organic compounds), including hindered phenolic antioxidants and plastic additives such as plasticizers, anti-slip agents, fatty acids, and other plastic processing aids
Inductively Coupled Plasma | Mass Spectrometry (ICP | MS)	Metals typically related to catalysts used in the polymerization process and plastic additives

Non-volatile residue analysis (NVR) was performed by evaporating the extracted fluid to dryness until a constant weight, residue was achieved.

Table 3 lists the sum total NVR values of the first and second extraction obtained for the different extraction fluids.

Table 3
NVR Analysis

Extraction Fluid	Maximum NVR Value (mg)
Water	4.3
50% Water | 50% Ethanol	13.1

In addition to the total weight of extractables obtained, direct analysis of the extraction fluids by headspace GC | MS, direct injection GC | MS and LC | UV | MS indicated the presence of trimethylsilanol, ethoxytrimethylsiloxane, and cyclic siloxanes such as octamethyl cyclotetrasiloxane, decamethyl cyclopentasiloxane, and dodecamethyl cyclohexasiloxane. Elementals detected using ICP-MS included ppb levels of Boron, Sodium, Magnesium, Aluminum, Potassium, Calcium, Iron, Nickel, Copper, Zinc, Barium, and Lead.

Detailed study reports for the two test solutions with quantitative results of the screening analyses are available on request. Additionally, a detailed description of the system tested is available.[1-3]

The extractables data summarized within this document provides a good indication of potential leachables. Based on the worst-case nature of these test conditions, it is anticipated that the extractables will be of a sufficiently low amount as to not present a safety concern to the final product. A significant part of the extractables will be eliminated during the pre-use flush of the TFF cassette connected on the SUTFF flow kits. In addition, the extractables contribution of the test system from the permeate channel has been included as a worst case in this report. Typically, all extractables from the SUTFF components in the permeate section would be discarded and not contribute to actual leachables in the drug product.

Table 4
Sartoflow® Single-Use TFF Flow Kit Component List and Material of Construction (MOC)

Components	Materials
Tubing	Silicone
Sensor	Polysulfone
Connectors	Polypropylene, Polycarbonate
Sensor	Polyvinylidene fluoride (PVDF), Polysulphone
Gaskets	Silicone
Diaphragm Valves	Polypropylene | Thermo Plastic Elastomer (TPE)
Quattroflow Pumphead	Polypropylene, Santoprene*, Ethylene Propylene Diene Monomer (EPDM)

*Santoprene is a trademark of Exxon Mobil

Sartorius continuously improves products to implement new customer requirements and to increase their quality. In this context, standardized systems Sartoflow® 150, Sartoflow® 1000, and Sartoflow® 4500 are available with a predefined and harmonized selection of components that are optimal for the intended use. This includes use of tubing such as AdvantaPure APSH tube or connectors such as Colder MPX. All components were carefully selected to highest quality standards; and for example materials meet USP Class VI requirements. No new materials are introduced compared to the system tested (Table 4). Extractables data of the components is available and should be requested directly by the end-user from the component's supplier if considered necessary.

Sartorius' Service Confidence Validation Services can provide further support with customer-specific leachables studies or for assessment of special ETO single-use flow kits.

References

1. Sartoflow-SUTFF-Ethanol-Water-Technical-Note-en-B-2724610-Sartorius

2. Sartoflow-SUTFF-Water-Technical-Note-en-B-2724613-Sartorius

3. Sartoflow-SUTFF-Test-Systems-Technical-Note-en-B-2724705-Sartorius

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