Extractables Study for Single Use Components: Sensors and Sensor Bodies

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Purpose:

Single use systems (SUS) are becoming routinely incorporated in bioprocess manufacturing offering several advantages over traditional glass and stainless steel vessels, including ease of setup, quick process change-over, and assurance of sterilization. However, extractable and/or leachable data are required to ensure that the concentration of leachables (if any) are below a level that would pose a safety risk in the final drug product.

Figure 1. Selected Components Evaluated in the **Controlled Extraction Study**



A controlled extraction study (CES) is currently in progress aligned with the Bioprocess Systems Alliance (BPSA) and BioPhorum Operation Group (BPOG) recommendations for single use components. Emerging industry expectations are that the device manufacturers (e.g. PendoTECH) should provide extractable data for the end-users' evaluation of the device for their intended use. This poster is focused on the design of a comprehensive CES.

TABLE 1. COMPONENTS AND BASE POLYMERS

Component	Base Polymer Fluid Contact Material		
Pressure Sensor	Polysulfone		
Pressure Sensor	Polycarbonate		
UV Sensor	Polysulfone		
Conductivity Sensor	Polysulfone		
Sensor body	Polycarbonate		
Sensor body	Polysulfone		
Sensor body	Polysulfone		
Sensor body	Polyolefin		

TABLE 2. INSTRUMENTAL ANALYSIS OF SAMPLE EXTRACTS

Discussion

Several best practices have been taken into consideration during the design of this program, including:

• Using gamma irradiated components

- Exposing only fluid contact surfaces to the extraction solvents
- Following BPOG recommended solvents appropriate for the devices
- Maintaining a 6:1 SA/V ratio under dynamic conditions
- Using a pre-defined instrumental screening threshold of $\leq 0.1 \, \mu g/mL$
- Screening method controls during the evaluation of trace intensity peaks
- Including reference standards such as antioxidants & Bisphenol A (BPA)
- Assaying extracts by multiple spectroscopic and chromatographic analytical techniques appropriate for the fluid contact material(s)
- Confirming tentatively identified extractables with authentic standards

Solvent	HPLC-DAD/MS (Extractable Antioxidants and Additives)	DI-GC/MS (Extractable Semi-Volatiles)	Headspace GC/MS (Extractable Volatiles)	ICP/MS (Extractable Metals)
1:1 EtOH:H ₂ O	Yes	Yes	No	No
pH 9 Water	Yes	Yes	Yes	No
0.1 M H ₃ PO ₄	Yes	Yes	Yes	Yes
0.5N NaOH	Yes	Yes	Yes	No

Discussion

PendoTECH requested Chemic Laboratories to assess eight single use sensors and sensor bodies (Table 1) representing a broad range of materials used in their single use products that come into conduct with various processing fluids. These selected sensors and bodies will in turn provide extractable data for over 20 primary part numbers and numerous derivative parts; including potential future part numbers as the PendoTECH single use sensor product line evolves.

The extraction study has been designed to expose the components at a 6 cm2 to 1 mL surface area to volume ratio using solvents, incubation temperatures and residence times more aggressive than typical in-use conditions employed by end-users. Solvents of varying solvation strength and pH range were chosen to generate an extractable profile appropriate for these single use devices. Multiple components were needed to generate sufficient volume(s) for the analytical assays and PTFE closures engineered to contain the extraction solvents. The gamma irradiated components were incubated at 40 degrees C for a 24 hours with continuous orbital shaking. Method controls of each solvent were placed into inert containers and incubated with the devices.

(where possible)

Conclusions

PendoTECH has embraced industry expectations and made the decision to have their single use components assessed for extractables. The results of this investigation will be made available to PendoTECH's customers for their evaluation in their single use application.

Reference

Bio Process System Alliance, Recommendations for Extractables and Leachable Testing, By the Extractables and Leachables Subcommittee of the Bio-Process Systems Alliance

Part 1: BioProcess International 5(11): p36-49 (December 2007)

Part 2: BioProcess International 6(1): p44-53 (January 2008)

Standard Extractables Testing Protocol for Single-Use Systems in Biomanufacturing, (Pharmaceutical Engineering November/December 2014,

Solvent extracts from the CES are being assayed by HPLC-DAD/MS, DI-GC/MS, Headspace-GC/MS and ICP/MS, thereby providing a comprehensive extractable profile for non-volatile, semi-volatile, volatile organic and metallic extractables from the test materials as summarized in Table 2.





