Savillex
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Savillex Technical Note
Fluoropolymer Bottle Extractables Profile

Summary

When choosing a container for critical drug substances, cell therapies, and regenerative medicines, due consideration should be given to the effects that extractables can have on products.

Extractables refer to the organic and inorganic chemical compounds released from container systems under aggressive laboratory conditions (i.e., elevated temperatures and using aggressive solvents). Under standard storage and use conditions, these extractables could potentially migrate into drug products over time as leachables. Therefore, if extractable compounds exist, they need to be examined for potential characterization as leachables based on their concentration.

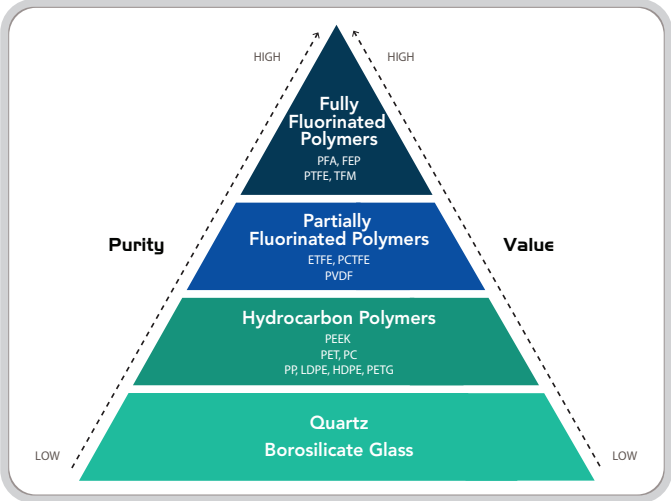

Figure 1: Fluoropolymers are innately higher in purity, and due to improved performance, higher in value than common hydrocarbon plastics like PE and PP

Fluoropolymers are the materials of choice for high purity applications. They may be the highest purity materials currently available for drug substance storage applications. Fluoropolymer vials made from PTFE and PFA store QC control samples during extractables screening protocols and are specifically called out in several industry-standard procedures.

A comparison of the properties of commonly used bioprocessing container materials is shown in Figure 1.

This technical note outlines a study performed by a major biopharmaceutical company establishing a comprehensive extractable profile of a fluoropolymer (PFA) bottle. The study used aggressive extraction conditions chosen to bracket the drug product applications.

The outcome of this study provided a foundation for a simulated leachable testing study which was performed to validate the fluoropolymer container for its intended use.

Test Procedure

Materials

- Savillex Purillex® 100 mL PFA bottles
- Extraction solutions
  - Water (pH 7.0) — Milli-Q water adjusted to pH 7.0-7.4 appropriately
  - Isopropanol — HPLC/Analytical Grade Isopropanol (IPA)
  - Nitric Acid (5 %, v/v%) — Trace Metal Grade Nitric acid (HNO_3, 67-70 % purity)

Savillex Purillex® 100 mL PFA bottle

Procedure

- The representative container closure system (CCS) was defined as one unit composed of two test articles, including a bottle and a closure
- Each extraction condition in the study was performed in triplicate. Duplicate blank control extractions were performed for all conditions.
- For the extraction processes intended for organic analyses, the representative bottles were extracted using water (pH 7.0) at 121°C for 1 hour. The CCS was also extracted using IPA at 50°C for 72 hours.
- For the extraction process intended for inorganic analysis (ICP-OES), the representative containers were extracted using 5% nitric acid for 24 hours at room temperature
- For HSGC-MS analysis, bottle and closure samples were cut and sealed in a headspace vial and equilibrated for 2 hours at 80°C for headspace air enrichment analysis
- If a portion of the container was needed for an extraction process, fragments of a bottle and closure were used in amounts proportional to their weight ratios
- Appropriate amounts of corresponding extraction media were stored in glass and PTFE vessels as QC controls during each extraction procedure. For empty samples' headspace air enrichment process, blank headspace sample vials were sealed as QC controls.
- Extraction solutions were prepared and analyzed by HSGC-MS, GC-MS, LC-MS, and ICP-OES according to internal test methods and procedural guidelines

CCS	Extraction Condition	Analysis			
		HSGC-MS	GC-MS	LC-MS	ICP-OES
Bottle Closure	Water (pH 7.0) 1 h/121°C	+	+	+	-
	IPA 72 h/50°C	-	+	+	-
	Headspace Air Enrichment (Neat CCS) 2 h/80°C	+	-	-	-
	Nitric Acid (5%, v/v %) 24 h/RT	-	-	-	+

+ Analysis performed
- Analysis not performed

Results

The results indicate that no organic extractables and inorganic extractables were detected at or above the analytical evaluation threshold based on seven days of product/container contact. The extractables testing study outcome served as a foundation for a subsequent leachable study, which provided a profile of probable leachables.

Conclusion

The results of this study indicate that Purillex PFA bottles release insignificant levels of organic and inorganic materials when exposed to solvents of different physicochemical properties under aggressive laboratory conditions. Fluoropolymers are well-accepted as the highest purity, lowest extractable materials available for drug substance storage applications.

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