

# Technical Bulletin

## Chemical Characteristics of Polyethylene and Ethyl Vinyl Acetate BIOEAZE™ Bioprocess Bags: Leachable and Extractable Chemical Data

BIOEAZE™ disposable process bags are flexible bioprocess containers and have many applications for biotechnology and biopharmaceutical industries. SAFC Biosciences provides bags manufactured with either polyethylene (PE) or ethyl vinyl acetate (EVA) films. To evaluate the suitability and safety of these films for use as bioprocess bags, SAFC Biosciences performed many physical, mechanical and biocompatibility tests on both PE and EVA bags. To further assess the films, chemical characterization studies were designed to identify and quantify manufacturing residuals and leachable/extractable compounds which may migrate from the bags when filled with different manufacturing solutions. The study was planned using guidance provided in the International Organization for Standardization (ISO) 10993-18 standard: Biological Evaluation of Medical Devices — Chemical Characterization of Materials.

The study quantitatively determined the concentrations of Volatile Organic Compounds (VOC's) and Semi-Volatile Organic Compounds (SVOC's). VOC's such as monomer residues, solvent residues and polymer breakdown products were analyzed by Purge-and-Trap Gas Chromatography/Mass Spectrometry (GC/MS). This technique allows for the identification of compounds based on chromatographic retention time and the mass spectrum of the compound. SVOC's are compounds such as lubricants, plasticizers, anti-oxidants, polymer degradation products and solvents with an elevated boiling point. The analytical method utilized for SVOC detection was GC/MS preceded by solvent extraction.

Five solutions were prepared in PE and EVA BIOEAZE™ bags: 20% ethanol (EtOH), Water for Injection (WFI), Dulbecco's Phosphate Buffered Saline (DPBS), 1N Hydrochloric Acid (HCl) and 1N Sodium Hydroxide (NaOH). Bags were filled at a volume-to-surface area ratio of 1 mL per 2 cm<sup>2</sup> and were

stored at 2 to 4 C, 15 to 30 C and 40 C for 30, 60 and 90 days. The 40 C temperature range was chosen and designed as an accelerated aging study, to help determine the effects of time and temperature on the chemical properties of the bag films (for more information please refer to ASTM F1980). At 40 C, the real-time equivalent ages of the 30, 60 and 90 day samples were 72 days, 145 days and 217 days respectively.

The summary tables illustrate the volatile and semi-volatile organic chemical groups found in each solution. The data represents the highest concentrations (in parts per million, or ppm) of compounds found in each solution, at all temperatures and all time periods. It was determined that certain compounds migrated from the films into solution over time, but also that compounds were present from the start, indicating the presence of manufacturing residuals. Overall, the majority of compounds were below 0.1 ppm; the highest concentration of any detected compound was 3.1 ppm.

The International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH), guidance for industry *Q3C Impurities: Residual Solvents (1997)* provides guidance and recommendations to the levels of residual solvents that are considered safe in pharmaceuticals. According to this document, no Class 1 solvents were identified in any solution, at any temperature. Two Class 2 solvents were identified, but both were well below their respective concentration limits. Five Class 3 solvents were also identified; these solvents are regarded to pose a lower level of risk and the detected concentrations were less than 1 ppm (the acceptable level is 5000 ppm).

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### Volatile and Semi-Volatile Organic Compounds found in PE BIOEAZE™ Bags

Solution	0 - 0.1 ppm	0.1 - 0.3 ppm	0.3 - 1 ppm	1 - 3 ppm
Water for Injection	alcohols aldehydes alkanes alkenes			ketones
20% EtOH	aromatics fatty acids quinones	alkanes amines ethers phenolics		alkenes ketones
1N NaOH	aldehydes alkenes	alcohols fatty acids		ketones phenolics
1N HCl	aldehydes alkanes alkenes	alcohols	fatty acids	ketones
DPBS, pH 7	alcohols aldehydes alkanes alkenes	fatty acids		ketones

### Volatile and Semi-Volatile Organic Compounds found in EVA BIOEAZE™ Bags

Solution	0 - 0.1 ppm	0.1 - 0.3 ppm	0.3 - 1 ppm	1 - 3 ppm	3 - 4 ppm
Water for Injection	alcohols aldehydes alkanes alkenes				ketones
20% EtOH		alkanes		ketones	
1N NaOH	aldehydes alkanes alkenes amines ethers	phenolics	alcohols	ketones	
1N HCl	acetate aldehydes alkanes fatty acids sulfides	alcohols		ketones	
DPBS, pH 7	alcohols aldehydes alkanes alkenes fatty acids			ketones	

The purpose of this study was to provide a comprehensive assessment of the semi-volatile and volatile organic compounds that can potentially leach from, or be extracted from the fluid contact surfaces of PE and EVA films. The intended use of this data is to provide quantitative chemical information to supplement a safety and toxicological risk assessment of BIOEAZE™ bags. SAFC Biosciences is committed to providing the appropriate tools and information to identify, evaluate and determine the overall safety of BIOEAZE™ bioprocess bags.

For more information about this subject or other SAFC Biosciences' products and services, please call our Technical Services department or e-mail us at [technicalservices@sial.com](mailto:technicalservices@sial.com).

#### References

1. International Organization for Standardization (ISO) 10993-18 standard: Biological Evaluation of Medical Devices — Chemical Characterization of Materials (ISO 10993-18:2005)
2. ASTM International F 1980-02, Standard Guide for Accelerated Aging of Sterile Medical Device Packages
3. International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH), ICH Harmonized Tripartite Guideline, Q3C *Impurities: Residual Solvents* (1997)

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