



Standard Guide for Determining the Impact of Extractables from Non-Metallic Materials on the Safety of Biotechnology Products¹

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1. Scope

1.1 This guide covers procedures and test methods for process component qualification by the end user. The goal is to assess the safety impact of extractables from non-metallic process components used in contact with bioprocessing solutions. This encompasses the impact of extractables on the safety of the final product as it passes through the various stages of the manufacturing process. This guide is not designed for evaluation of metallic materials, final product container/closures or those components intentionally added to the product or production streams during the manufacturing process. Testing of solids and extracts is specified in other ASTM standards. Materials must be qualified by specific use.

1.2 The values stated in SI units are to be regarded as the standard.

1.3 There is no companion guide available.

1.4 *Safety/Fire hazards:* Extractions with organic solvents will be infrequent under this Guide, but, when used must be treated as potential fire/explosion hazards.

1.5 *This guide does not purport to address all of the safety concerns, if any, associated with its use. It is the responsibility of the user of this standard to establish appropriate safety and health practices and determine the applicability of regulatory limitations prior to use.*

2. Referenced Documents

2.1 ASTM Standards:

D 1203 Volatile Loss from Plastics Using Activated Carbon Methods²

D 4754 Two-Sided Liquid Extraction of Plastic Materials Using FDA Migration Cell³

D 4874 Leaching Solid Material in a Column Apparatus⁴

D 4951 Determination of Additive Elements in Lubricating Oils by Inductively Coupled Plasma Atomic Emission Spectrometry⁵

¹ This guide is under the jurisdiction of ASTM Committee E48 on Biotechnology and is the direct responsibility of Subcommittee E48.03 on Unit Processes and Their Control.

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² *Annual Book of ASTM Standards*, Vol 08.01.

³ *Annual Book of ASTM Standards*, Vol 08.03.

⁴ *Annual Book of ASTM Standards*, Vol 11.04.

⁵ *Annual Book of ASTM Standards*, Vol 15.03.

F 619 Standard Practice for Extraction of Medical Plastics⁶

F 749 Evaluating Material Extracts by Intracutaneous Injection in the Rabbit⁶

F 750 Evaluating Material Extracts by Systemic Injection in the Mouse⁶

F 813 Direct Contact Cell Culture Evaluation of Materials for Medical Devices⁶

F 895 Agar Diffusion Cell Culture Screening for Cytotoxicity⁶

3. Terminology

3.1 See the Compilation of ASTM Standard Definitions. Review with the Terminology Committee, E48. See A7.2.1 for details of set up and Part E, Terminology in ASTM Standards.

3.2 Definitions:

3.2.1 *biopharmaceutical*—any drug product produced from living organisms.

3.2.2 *biotechnology solution*—a solution containing or producing products from living microbial, animal or plant cells or by the enzymes from those cells.

3.2.3 *biotechnology product*—a discrete chemical entity produced by growing single cell organisms with unique genetic information.

3.2.4 *elution cytotoxicity*—see USP.

3.2.5 *emission spectrographic analysis (ESA)*—an analytical technique for determining metals in a sample vaporized in a plasma arc.

3.2.6 *extractables*—residues from solid process components not intentionally part of the product process stream.

3.2.7 *fermentation*—the biochemical reaction process where microorganisms in a nutrient medium convert a feedstock to a product.

3.2.8 *inductively coupled plasma (ICP)*—an analytical technique designed to quantitate chemical elements.

3.2.9 *materials of construction*—high molecular weight or solid materials, used in biopharmaceutical process equipment which contact process solutions and can potentially release extractable residues.

3.2.10 *non-volatile residue (NVR)*—non-volatile material remaining after evaporating a solvent into which the residue has been extracted (See USP).

3.2.11 *oxidizable substances (OS)*—chemical compounds

⁶ *Annual Book of ASTM Standards*, Vol 13.01.