Mérieux NutriSciences

Extractables & leachables studies
in pharmaceutical packaging and medical devices

Pharmaceutical packaging can release chemicals into the drug product that can not only impair its effectiveness, but also be harmful to the patient. Similarly, **medical devices can undergo leaching processes** during their use that could negatively affect their clinical outcome, and compromise their biocompatibility.

This is why **international authorities** such as WHO, FDA, and EMA all agree upon chemical characterization being a fundamental step in **ensuring patients' safety**.

Chemical characterization is the process of **"obtaining chemical information about a medical device or a pharmaceutical packaging, relevant to their biological evaluation and any toxicological risk assessment"**. When it comes to generating information, chemical characterization can be performed by extractables and leachables testing: guidelines change whether we are testing a pharmaceutical packaging or a medical device, but nonetheless are very similar to one another.

EXTRACTABLES & LEACHABLES GUIDELINES

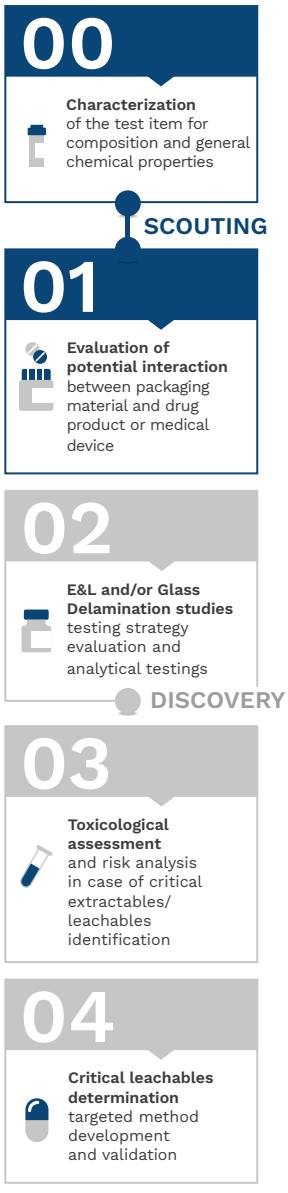
PHARMACEUTICAL PACKAGING	MEDICAL DEVICES
▪ Product Quality Research Institute (PQRI) Parenteral and Ophthalmic Drug Products Leachables and Extractables Working Group (2009) ▪ USP General Chapter <661> - Plastic Packaging Systems and their materials ▪ USP General Information Chapter <1663> - Assessment of Extractables Associated with Pharmaceutical Packaging / Delivery Systems ▪ USP General Information Chapter <1664> - Assessment of Drug Product Leachables Associated with Pharmaceutical Packaging / Delivery Systems ▪ USP General Information Chapter <1664.1> - Orally Inhaled and Nasal Drug Products ▪ EMEA Guideline on plastic - Immediate Packaging Material (2005) ▪ FDA Guidance for industry: container-closure system for packaging human drugs and biologics (1999)	▪ ISO 10993 – Biological evaluation of medical devices. Part 1: Evaluation and testing within a risk management process (2018) ▪ ISO 10993 – Biological evaluation of medical devices. Part 17: Toxicological risk assessment of medical device constituents (2002, now under development) ▪ ISO 10993 – Biological evaluation of medical devices. Part 18: Chemical characterization of materials (2018)

Mérieux NutriSciences performs Extractables and Leachables studies providing a full integrated testing strategy together with toxicological assessment and risk analysis, taking advantage from more than 20 years' experience developed in food contact materials, medical devices and containers for pharmaceutical products.

Our capabilities

Extractables and Leachables studies provide a full-integrated testing strategy together with toxicological assessment and risk analysis, in six main steps:

1. Profiling of extractables: generation of the extract.
2. Characterization of **extractables**:
   a. **Screening research** of VOC, SVOC and NVOC using different techniques (e.g. TOC, HS-GC/MS, GC-MS, GC-HRMS, HPLC UV/DAD, LC-MS/MS, LC-HRMS)
   b. **Targeted analysis of elemental impurities** and **anions** using different techniques (e.g. AAS, ICP-MS, IC)
   c. **Targeted analysis** for specific compounds of toxicological concern, using dedicated methods that focus on monomers, additives and extractables typical of the material considered (more than 150 targeted methods available)
   d. **Extractable nanoparticles and microplastics identification**
3. Primary and secondary **leachables profile**.
4. **Unknown** extractables/leachables tentative identification by HRMS techniques (if needed).
5. Toxicological evaluation and risk assessment.
6. **Development and validation of targeted methods** suitable for the quantification of critical leachables.



GLASS DELAMINATION

Testing strategy according to USP <660> "Containers – Glass" and USP <1660> "Evaluation of the inner surface durability of glass containers":

1. Determination of visible and subvisible glass particles
2. Determination of extracted elements
3. Characterization of glass inner surface by SEM/EDS or TEM/EDS

Analytical techniques

- HPLC-ELSD, HPLC-MS/MS, HPLC UV/DAD, IC
- LC-MS/MS, LC-HRMS Q/Orbitrap
- HS-GC, HS-GC/MS, GC/FID, GC-MS, GC-HRMS Q/Orbitrap
- ICP-OES, ICP-MS, AAS
- MALDI-TOF
- TOC
- SEM/EDS, TEM/EDS

OUR ACCREDITATIONS

Our experience on validation studies for drug products, and our high laboratory standards - in compliance with GMP, GLP, and ISO 17025 - allow us to perform extractables and leachables studies that have recognized value by international regulatory authorities such as the FDA:

- Mérieux NutriSciences E&L laboratories employ methods compliant with **ISO 17025:2005 standard**, and **certified by Accredia**, the Italian accreditation body;
- accreditation and validation of **migration test methods on specific FCM compounds** (depending on compound).

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