Mérieux NutriSciences

Extractables & leachables studies
in pharmaceutical packaging and medical devices

Pharmaceutical packaging and manufacturing components 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
▪ USP General chapters <661> <661.1> <661.2> - Material and packaging assessment ▪ USP General chapters <1663> <1664> <1664.1> - Packaging and product assessment and qualification ▪ USP General chapters <665> <1665> - Manufacturing materials and process components assessment ▪ PQRI Safety Thresholds and Best Practices for Extractables and Leachables in Orally Inhaled and Nasal Drug Products. (2006) ▪ PQRI Safety Thresholds and Best Demonstrated Practices for Extractables and Leachables in Parenteral Drug Products (Intravenous, Subcutaneous, and Intramuscular). (2021)	▪ ISO 10993 – Biological evaluation of medical devices. Part 1: Evaluation and testing within a risk management process (2018, now under development) ▪ ISO 10993 – Biological evaluation of medical devices. Part 17: Toxicological risk assessment of medical device constituents (2023) ▪ ISO 10993 - Biological evaluation of medical devices. Part 18: Chemical characterization of medical device materials within a risk management process (2020)

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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. HS-GC/MS, GC-MS, GC-HRMS)
   b. **Targeted analysis of elemental impurities** and **anions** using different techniques (e.g. 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)
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.

MxNS E&L DATABASE

Identification of compounds can achieve various levels of confidence: Mérieux NutriSciences has developed a dynamic internal database to assist in the identification of extractables and leachables. Reference materials were characterized with the same methods used in the screening investigations, recording relevant information such as retention time, mass spectrum, molecular ion fragmentation (for UHPLC/HR-MS), relative response factor (RRF), etc... This information allows the laboratory to confirm with certainty the identification of many compounds, attribute a more accurate concentration, and limit the number of unknown compounds. The database is continuously updated and expanded.

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).

Analytical techniques

- HS-GC/MS, GC/MS, UHPLC/HR-MS Q-Orbitrap
- GC/HR-MS Q-Orbitrap
- ICP/MS, IC
- UHPLC/MS/MS, HPLC/UV-Vis

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