eurofins | BioPharma Product Testing

# Extractables and Leachables Testing

During the drug development process, it is important to evaluate the potential for **various chemicals to migrate from container closure systems, manufacturing components or delivery devices into pharmaceuticals and biologics**. Regulatory agencies require extractables and leachables (E&L) testing to identify any risks of product adulteration.

Whether you are evaluating pharmaceutical manufacturing equipment (such as single-use systems), container closure systems, delivery devices, or other medical devices, Eurofins offers a broad range of services to support extractables and leachables testing. **With over 20 years of experience and more than 100 scientists** dedicated to E&L testing, we conduct hundreds of controlled extraction studies each year, along with the associated leachables stability studies.

We offer a **variety of controlled extraction techniques to generate an extractable profile** that will best match the intended use of the components being evaluated. In addition, we conduct simulated and real-time leachables studies to evaluate the presence of leachable compounds in the drug product. Our toxicologists can then evaluate the E&L data to determine the impact to patient safety. If needed, we can use our extensive experience to successfully develop and validate fully GMP- and GLP-compliant methods to monitor leachables in your drug product or intermediates.

## Why Choose Eurofins BioPharma Product Testing?

We work with our clients to design a study that provides them with meaningful extractables data and we assist them in performing a risk assessment of their product configuration or manufacturing chain. With over 20 years of experience designing and conducting E&L studies, we have the expertise to recommend testing options that are up to current industry standards and will meet regulatory expectations.

We have the ability to write GMP-compliant protocols to direct extractables and leachables testing or to define conditions for stability studies.

Our extractables studies include a customizable report detailing the results of the study, including instrument parameters, system suitability results, sample chromatograms, and result tables.

Our proprietary spectral database, the Eurofins Extractables Index (EEI), contains reference spectra for over 1,500 non-volatile compounds (including common plasticizers, anti-oxidants, stabilizers, elastomers, lubricants and accelerants) that we use to identify extractable compounds detected by LC/MS.

If a compound cannot be identified with the Eurofins Extractables Index, we are able to perform additional investigative testing to identify the unknown compound. Our experienced analysts and top-of-the-line instrumentation, such as LC/MS QTOFs and Orbitraps, allow us to identify nearly all unknown compounds.

We offer toxicological evaluations on extractables and leachables data.

Our E&L methods have been qualified in order to ensure accurate results and meet regulatory expectations.

## Our Approach

Our extractables studies can be designed per guidances such as USP <665>, <1663> and <1664>, as well as ISO 10993, PQRI, BPSA and BPOG documents. We design studies to meet the expectations of FDA's CDER/CBER/CDRH, EMEA, and other regulatory bodies.


## Extraction Techniques

- Reflux
- Soxhlet
- Sonication
- Microwave
- Incubation at controlled temperature conditions (with agitation or recirculation if needed)

## Extraction Techniques

We have established the following semi-quantitative screening methodology to analyze extraction solutions by LC/MS, GC/MS, LC/UV, ICP/MS and ICP-OES.

If needed, quantitative methods can be developed for specific compounds.

- Semi-quantitative screening for both volatile and semi-volatile organic compounds
  - Use of GC/MS instrumentation with direct injection sample introduction and electron impact ionization.
  - Use of GC/MS instrumentation with headspace sample introduction and electron impact ionization.
  - For extractables compounds detected by GC/MS analysis, we utilize the up-to-date Wiley/NIST databases to assist in identification.
- Semi-quantitative screening for non-volatile organic compounds
  - Analysis using LC/MS TOF (in positive and negative mode using electrospray and atmospheric pressure chemical ionization), Orbitrap and LC/UV.
  - For extractables compounds detected by LC/MS analysis, we utilize the Eurofins Extractables Index (containing over 1,500 compounds) to assist in identification.
- Semi-quantitative analysis for metals
  - Evaluation of samples for 42 metals, including all those listed in USP <232> and ICH Q3D using ICP-OES or ICP/MS
  - Gravimetric determination of extractables
  - TOC
  - FTIR
  - pH

## Toxicological Evaluation

Our team of toxicologists have the capability to evaluate compounds by referring to both toxicological databases and QSAR methods. We are experienced in performing toxicological analyses on medical devices, including dental and gas pathway devices, as well as pharmaceutical container/closure systems according to standards such as ISO 10993-17 and ISO 18562 and guidance documents from the FDA and PQRI.

## Instrumentation

- Agilent LC/MS TOF and QTOF
- Agilent/Waters HPLC/UHPLC – including UV/Vis,
- RI, Fluorescence, ELSD, CAD, and Conductivity detectors
- Agilent GC/MS – with headspace, direct injection, and thermal desorption sample introduction
- Agilent GC/FID/TCD – both headspace and direct injection sample introduction
- Agilent ICP/MS
- Thermo Scientific iCAP ICP-OES
- Thermo Scientific ICP-MS
- Thermo scientific GC-MS with headspace and direct injection
- Thermo Scientific LC/MS/MS
- Thermo Scientific LC/MS Orbitrap
- Perkin Elmer ICP-OES

**Comprehensive GMP Testing Services**

Method Development & Validation • Release Testing • Raw Materials Testing
Cell Banking Services • Virology Services • Facility & Process Validation
Chemistry • Biochemistry • Molecular & Cell Biology • Microbiology
Stability Testing & Storage • Primary & Secondary Package Testing

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