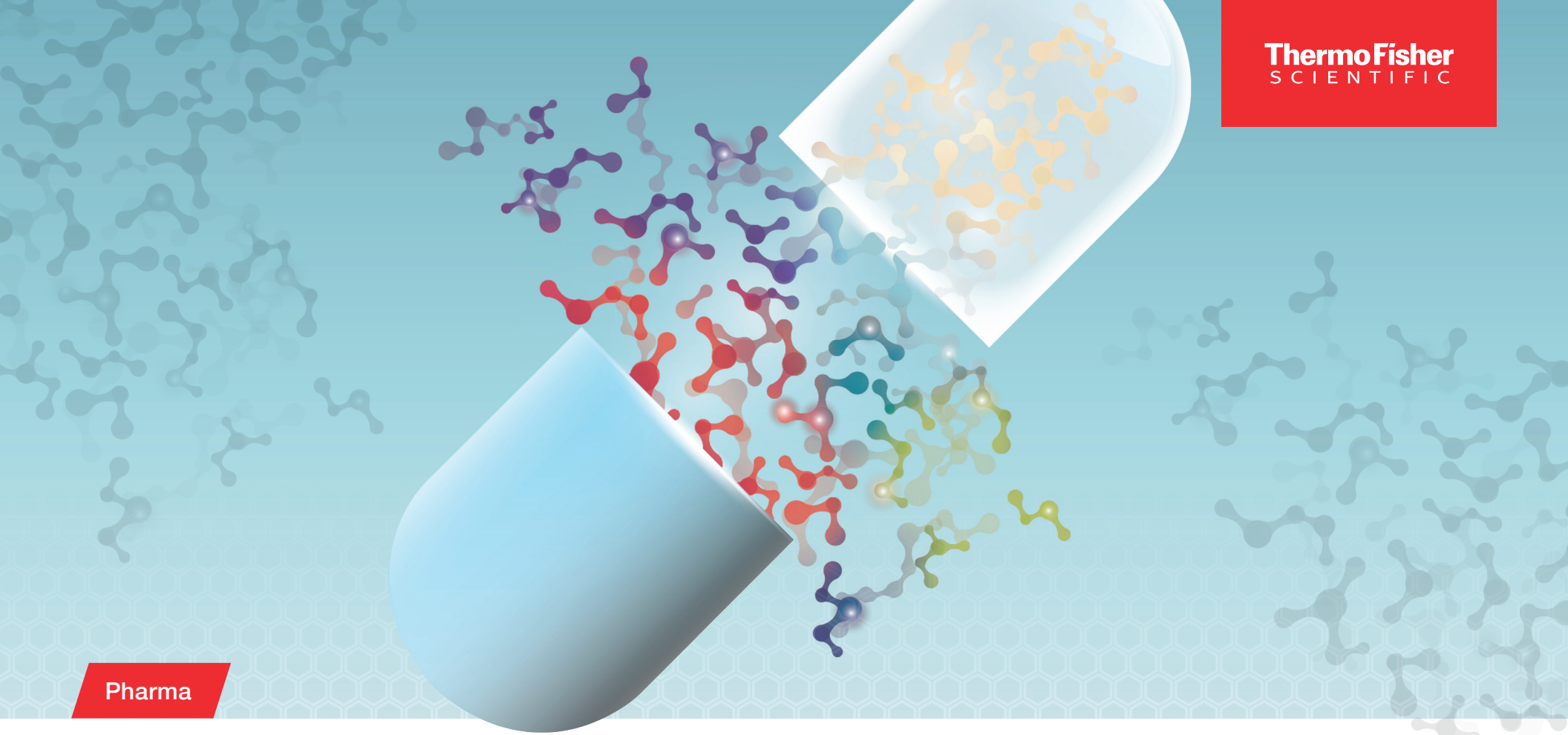


Pharma

Solutions for pharmaceutical, medical device and food contact material extractables and leachables analysis

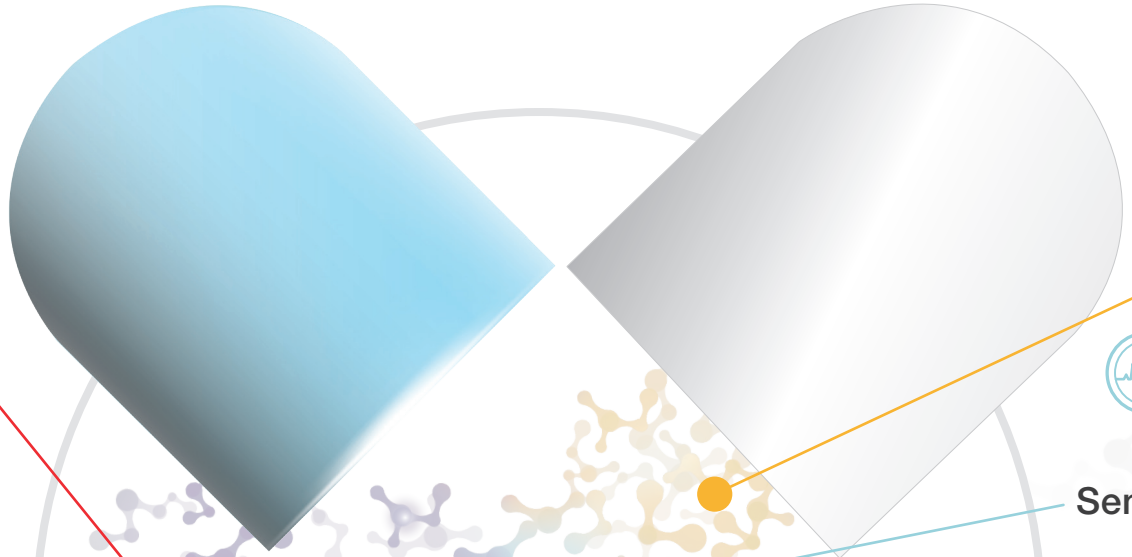
Enhance your capabilities

Unknown impurity identification and quantification workflows for:

- Pharmaceutical, packaging and contact-closure materials
- Medical devices
- Food contact materials

thermo scientific

Contents



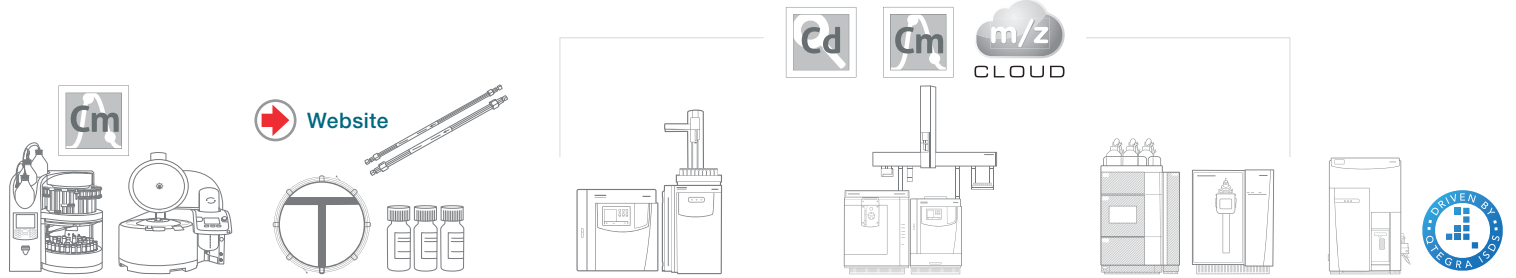
Extractables and leachables background

Extractables and leachables (E&L) studies enable identification, quantification and risk assessment of potentially toxic leachable impurities migrating into a drug from container closure systems, processing equipment drug delivery components or packaging.

The US Food and Drug Administration (FDA) and the European Medicines Agency (EMA) are progressively focusing on the interactions between different manufacturing components including; single use systems (SUS), drug delivery devices and container-closure systems, and the finished drug product.

We offer differentiated solutions to test extractables in single use systems, container materials, medical devices, and other consumables used in pharmaceutical production, such as stoppers, o-rings, bags, tubings, filters that are commonly used in manufacturing process and may introduce leachables into the final drug product.

Thermo Scientific extractables and leachables workflows



Preparation | Consumables | Volatiles | Semi-volatiles | Non-volatiles | Elemental

Extraction | Analysis and Reporting

Accelerated Solvent Extraction and automated, fast evaporation to achieve up to 200x concentration effect.

SureSTART vials, UHPLC and GC columns and ultrapure solvents.

TriPlus 500 GC for headspace sampling and complaint GC/MS.

Untargeted screening with the Orbitrap Exploris GC MS.

Orbitrap HRAM MS technology with charged aerosol detection.

Robust and sensitive iCAP RQ ICP-MS.

Run eWorkflows in seconds

Extractables and leachables website

Everything you need to know about extractables and leachables

Website | Extractables and leachables learning center

Industry recognized experts for designing and conducting E&L studies

PPD® Part of Thermo Fisher Scientific

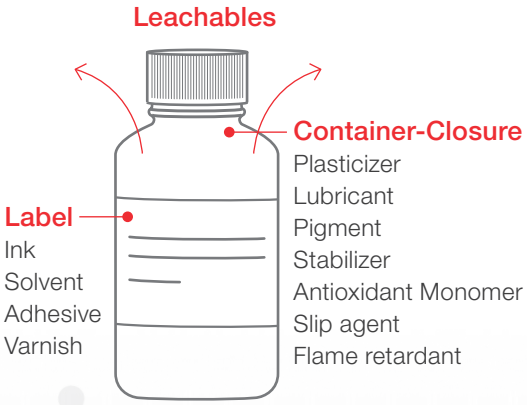
- Extractables and leachables studies
- Complete testing solutions
- All of your extractables and leachables needs met

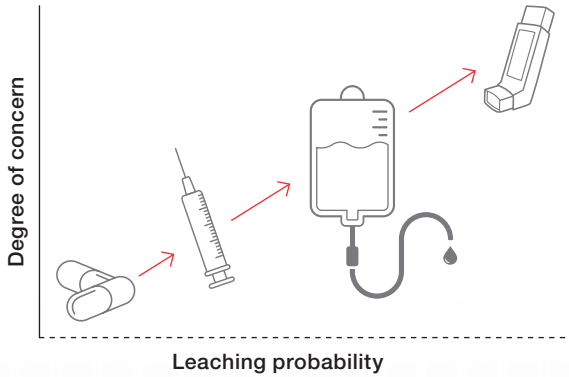
Pharmaceutical contact-closure materials

Extractables and leachables compounds and elements can migrate from polymeric materials used in container closure, production, delivery and packaging systems for pharmaceuticals and biopharmaceuticals.

Extractables migrate from container materials when exposed under laboratory conditions to solvents under exaggerated temperature and time environments.

Leachables are chemical species that migrate into the product under normal storage or use conditions.





Quantification

These challenges require an arsenal of analytical techniques and workflows to meet the ever demanding challenges of compliance with global regulations.

Regulations and methods

USP <381>	USP <1663>	PQRI Guidelines
USP <660>	USP <1664>	ASTM F 1980-07
USP <661>	USP <1665>	BPOG Guidelines
USP <665>	ISO 10993	ICH Q3

Medical devices

A medical device, according to the US Food and Drug Administration (FDA), is an instrument, apparatus, implement, machine, contrivance, implant, in vitro reagent, or other similar or related article, including a component part, or accessory which is:

- Recognized in the official National Formulary or USP
- Intended to be used in the diagnosis of disease, medical conditions, treatment of disease
- Intended to affect the structure or any function of the body of man or other animals, and which does not achieve any of its primary intended purposes through chemical action within or on the body

Confident identification

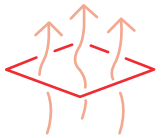
The analysis of medical devices involve a diverse range of chemicals; from volatiles to high molecular weight non-volatile molecules and even metals.

Regulations

Extractables Study (ISO 10993-18)
Leachables/Simulation Study
Cytotoxicity test of Leachables (ISO 10993-5)
Sensitization test of Leachables (ISO 10993-10)
Article IX of the EU Council Directive 93/42/EEC

Factors affecting migration

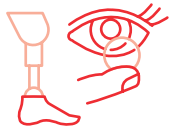
Matrix type
i.e. blood, saliva, saline solutions, drug product solutions etc.



Heat
Higher temperatures increase leaching.

Time
Long exposure time increases risk for leaching.

Medical device type
Certain devices can leach more compounds such as implants, prostheses compared to others.



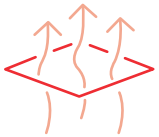
Size
Smaller devices leach more due to higher surface area to volume ratio.

Food contact materials

A food contact material (FCM) is any material approved for food use, which comes in contact with food or drink products during manufacturing, packaging, preparation and storage.

- A FCM must not transfer chemicals to, or cause changes to, foods that may impact consumer health.
- Testing is driven by regulation and demands migration studies that assess all 'unknown' non-intentionally added substances.

Factors affecting migration

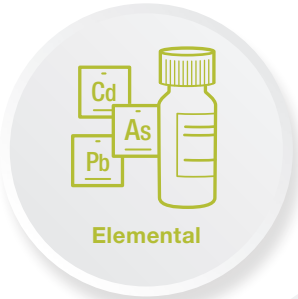


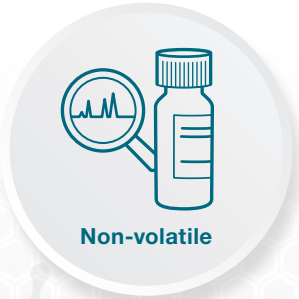
Heat
Higher temperatures increase leaching.

Time
Long storage time increases leaching.

Food type
Fatty/acidic foods and liquids have influence on migration.

Packaging size
Smaller packaging leaches more per volume of food.





Confident identification

The analysis of packaging impurities involve a diverse range of chemicals; from volatiles to high molecular weight non-volatile molecules and even metals.

Regulations

US FDA 21 CFR 174 to 1CFR 190
EU Regulation 10/2011

Extract smarter

Traditional Soxhlet or reflux techniques recommended by PQRI, and BPOG are labor intensive (>24 hours) and consume a large quantities of solvent (>150 mL/sample).

Accelerated solvent extraction delivered by the Thermo Scientific™ Dionex™ ASE™ 350 system is an automated alternative with several advantages, including efficient extraction, reduced extraction time (<0.5 h/sample) and reduced solvent use (<30 mL/sample).

Conditions can be carefully controlled to ensure that the material is not deformed or damaged during the extraction process.

The ASE technique delivers comparable or more efficient extractions than the traditional Soxhlet methods; whilst saving time and solvent and delivering confidence through control by compliance-ready Chromeleon software.

Rocket evaporator

Website

Extractables and leachables

Thermo Scientific™ Dionex™ ASE™ 350 Accelerated Solvent Extractor Systems

Use less bench space, extract up to 10 times faster, and use less solvent with ASE extraction.

Website Brochure

Volatiles

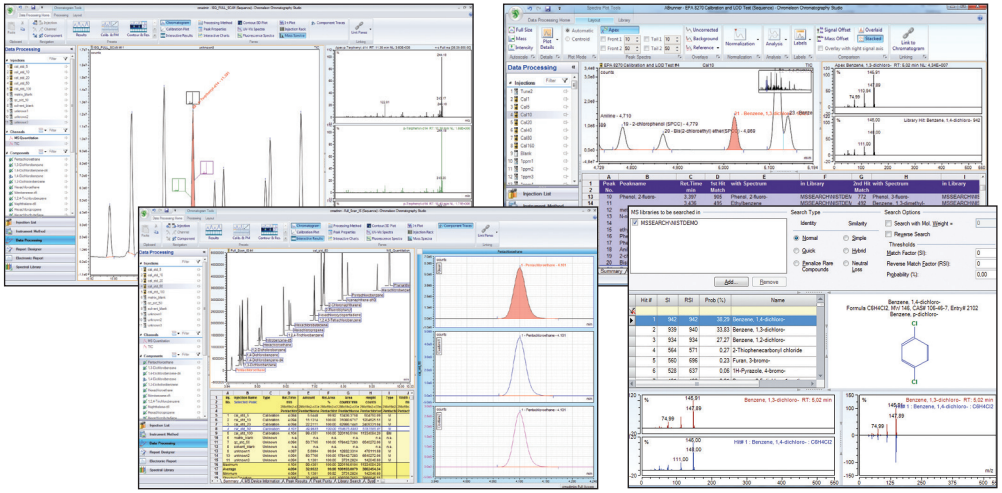
Low molecular weight, polar and non-polar organic compounds are typically volatile and have the highest probability to migrate from or through polymeric contact closure systems.

Thermo Scientific™ TRACE™ 1600 series Gas Chromatograph

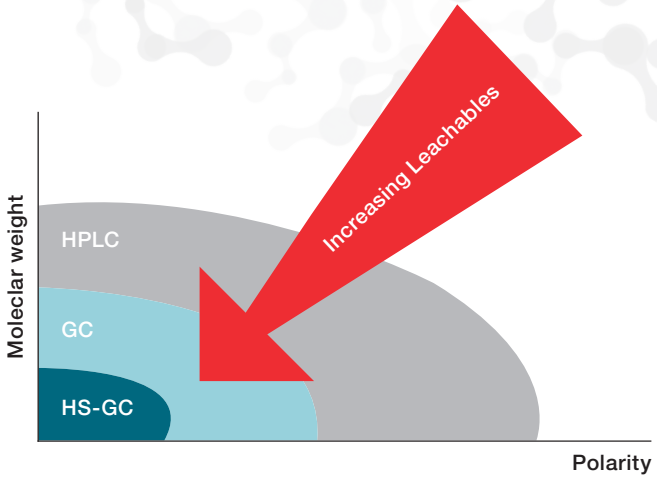
Thermo Scientific™ TriPlus™ 500 Headspace Autosampler.

No more volatile unknowns

In many extractables and leachables laboratories, sample preparation often accounts for more than twice the time spent on actual chromatography. Improved sample handling can reduce turnaround times and significantly lower the cost per analysis. Automate and accelerate organic volatiles determinations, to increase sample turnaround and lower the cost per analysis, with the powerful Thermo Scientific™ Triplus™ 500 headspace autosampler.



Qualitative and quantitative GC-MS with full 21 CFR 11 compliance.



Low molecular weight, polar and non-polar organic compounds are typically volatile and have the highest probability to migrate from or through polymeric contact closure systems.

Testing of the contact closure material is typically conducted by headspace sampling followed by gas chromatography and mass spectrometry.

Volatile organic impurities and residual solvents

Volatile organic impurities and residual solvents website

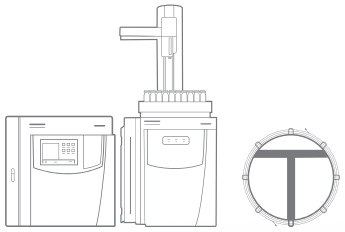
Everything you need to know about volatile organic impurities in one place.

Website

Autosampler vials

Ultraclean SureSTART headspace vials ensure low background and leak free seals.

Website



Thermo Scientific™ TRACE™ 1600 Gas Chromatograph

Reliable and robust GC quantification.

Website Brochure

Thermo Scientific™ TriPlus™ 500 Headspace Autosampler

Automated headspace sampling for pharmaceutical residual solvent analysis.

Website Brochure

Thermo Scientific™ Chromeleon™ Chromatography Data System (CDS)

Compliant and intuitive CDS for GC and GC-MS.

Website

Brochure

Thermo Scientific™ Compound Discoverer™ Software

Advanced software for identification of unknowns.

Website

Brochure

Semi-volatiles

Semi-volatile compounds are among the most frequently detected migration impurities. Testing is performed through liquid injection of an extract of the material or product. Often extracts are derivatized to increase analyte volatility. Testing demands absolute confidence in unknown identification and quantification.

Thermo Scientific™ Orbitrap™ Exploris™ GC 240 coupled with Thermo Scientific™ TRACE™ 1310 Gas Chromatograph.

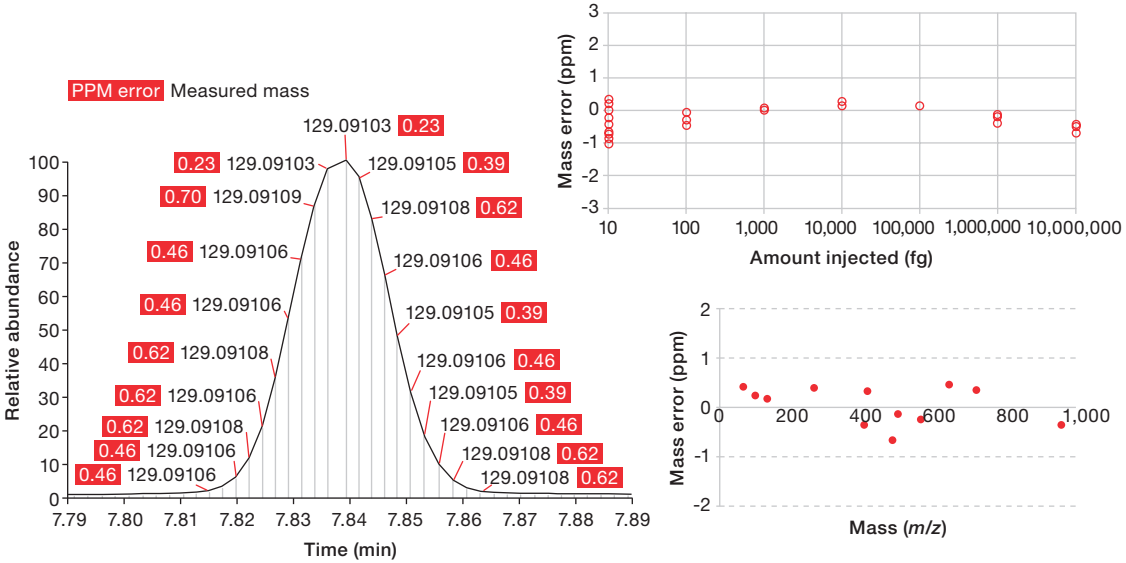
Confident identification

Demand the 'quanfirmation' power of orbitrap high-resolution, accurate-mass (HRAM) mass spectrometry. Resolve interferences for the cleanest spectra; achieve exceptional mass accuracy for confident identification of unknowns; deliver accurate quantification at the lowest levels.

Orbitrap comes to GC-MS

The Thermo Scientific™ Exploris™ GC Orbitrap™ Mass Spectrometer system provides comprehensive characterization of samples in a single analysis for the highest confidence in compound discovery, identification, and quantitation. This system offers the quantitative power of a GC triple quadrupole MS combined with the high precision, full scan HR/AM capabilities only available in combination with Thermo Scientific™ Orbitrap technology.

Deconvolve, identity and quantify.



Exceptional <1ppm mass accuracy is achieve on every scan, on every mass, and at every concentration.

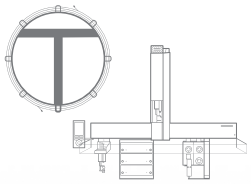
Semi-volatile organic impurities

Semi-volatile organic impurities website
Everything you need to know about semi-volatile organic impurities.

Website

Ultra clean Thermo Scientific™ MS Certified vials
Ensure the lowest backgrounds to reduce false positives.

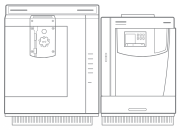
Website



Sample preparation and consumables
Thermo Scientific™ TraceGOLD™ GC columns and Thermo Scientific™ TriPlus™ RSH Autosampler.

GC columns website

TriPlus website



Thermo Scientific™ Orbitrap™ Exploris™ GC or LC Mass Spectrometer
Fast, unambiguous identification and quantification of semi-volatile organic impurities using GC or LC HRAM-MS.

GC HRAM website

LC HRAM website

Thermo Scientific™ Chromeleon™ Chromatography Data System (CDS)
Compliant and intuitive software solution for HRAM GC-MS.

Website

Brochure

Thermo Scientific™ Compound Discoverer™ Software
Advanced software for identification of unknowns.

Website

Brochure

Non-volatiles

Non-volatile impurities are among the most difficult to identify. Ever-changing polymer additives and monomers represent an ongoing analytical challenge. Confident identification using a range of targeted libraries or advanced high resolution accurate mass (HRAM) cloud based spectral libraries simplify the workflow.

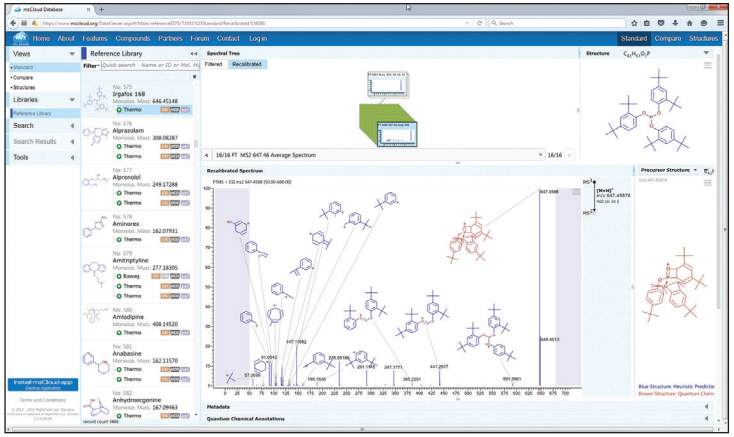
Thermo Scientific™ Vanquish™ Core HPLC system coupled with Thermo Scientific™ Orbitrap Exploris™ 120 mass spectrometer.

Proven performance for extractables

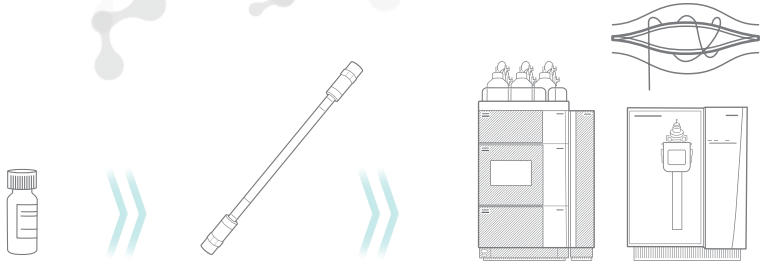
Identify and confirm more compounds rapidly and with confidence using the Thermo Scientific™ Exploris™ hybrid Quadrupole-Orbitrap mass spectrometer and Thermo Scientific™ Vanquish™ UHPLC system.

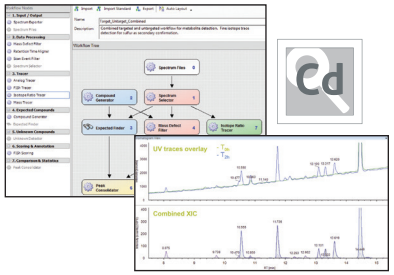
Proven performance for extractables

This benchtop LC-MS/MS system combines industry leading chromatography with quadruple precursor ion selection and high-resolution, accurate-mass Orbitrap detection to deliver exceptional performance and versatility.



Search spectra on-line with mzCloud,™ a free to search online HRAM mass spectral library. mzCloud also contains full spectral annotation with MSn data, spectral trees and substructure search capabilities.

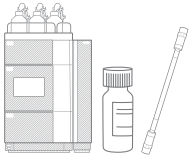




Non-volatile organic impurities

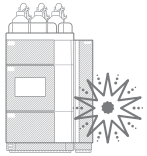
Non-volatile organic impurities website
Everything you need to know about non-volatile organic impurities.

Website



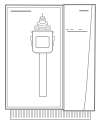
Thermo Scientific™ Vanquish™ UHPLC systems, columns and vials
Ensure the best LC separation.

HPLC/UHPLC product tour
LC columns
SureSTART vials/caps



Vanquish Charged Aerosol Detectors
See everything with near-universal CAD detectors.

Product tour
Website



Thermo Scientific™ Orbitrap Exploris™ Mass Spectrometers
Qualitative and quantiative confidence with HRAM LC-MS.

Website

Thermo Scientific™ Compound Discoverer™ Software
Advanced software for identification of unknowns.

Website

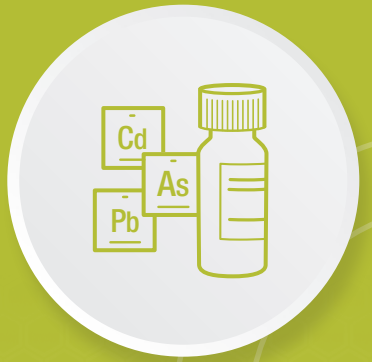
mzCloud™ mass spectral library
A free to search online high resolution mass spectral library.

Website

Thermo Scientific™ Compound Discoverer™ software ensures confident compound identification and structural elucidation with advanced algorithms that quickly process and identify changes between different sample groups and identify compounds based on multiple search approaches; including matching against HRAM libraries like mzCloud™, and compound databases. Searches are conducted in parallel and a single unified report is delivered.

Combining information from multiple detectors increases the confidence that all components in a study are found. Here data from DAD and HRAM mass spectrometry are combined.

Elemental impurities



Elemental impurities are common in printed materials, pigments, foil based packaging and delivery systems. Elemental impurities are analyzed following ICH Q3D or USP 232 and 233 guidelines. Another key application for ICP-OES for extractables and leachables is for silicone oil (polydimethylsiloxane) quantitation.

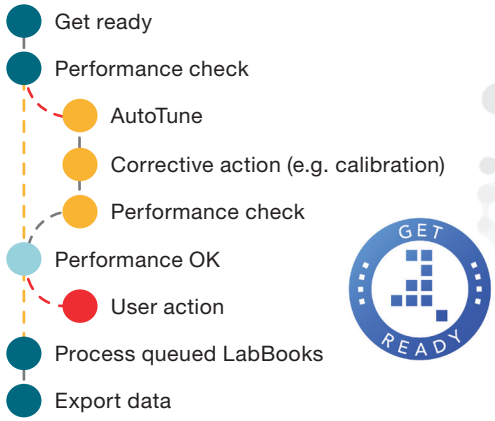
Robust, compliant analysis at the lowest levels is provided by ICP-MS or ICP-OES.

Simplicity, productivity, robustness

Gain complete confidence with accurate results. Enjoy minimal maintenance thanks to our intelligently engineered design. The Thermo Scientific™ iCAP™ RQ ICP-MS has the analytical performance to comfortably meet the most challenging pharmaceutical regulatory requirements for elemental impurities, including limits from the international council on harmonization (ICH) guideline Q3D and the U.S. Pharmacopeial convention (USP) chapters 232, 233 and 2232.

Automate more

Your time is precious. Spend less time at the instrument by using automated, unattended system set-up routines like the advanced single-click ‘Get Ready’ function in Thermo Scientific™ Qtegra™ Intelligent Scientific Data Solution™ (ISDS) software.



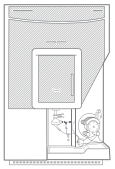
Elemental impurities

Elemental impurities website
Everything you need to know about elemental impurities in one place.

Website

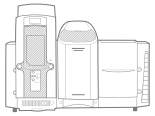
Inductively Coupled Plasma Mass Spectrometry (ICP-MS)
Expand your analytical capabilities with this complete trace elemental analysis solution for your high-throughput compliant lab with ICP-MS.

Website



Inductively Coupled Plasma-Optical Emission Spectrometry (ICP-OES)
Robust, fit-for-purpose, compliant ICP-OES.

Website



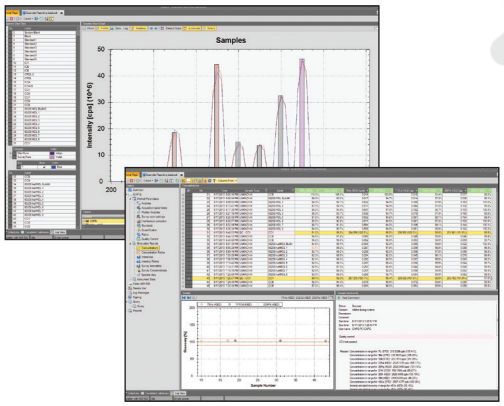
Atomic Absorption (AA) Spectroscopy
Cost-effective, simple, compliant AA.

Website

DRIVEN BY QTEGRA ISDS

Designed to comply with the most rigorous data audit and security measures, Qtegra ISDS software is FDA 21 CFR Part 11 ready and comes with full IQ/OQ procedures for simple implementation in GMP/GLP regulated environments.

Website



With a clean, logical workflow, Qtegra ISDS software displays QC results in a LabBook. Full isotopic mass spectra are retained in the LabBook for further interrogation post analysis.

PPD® Laboratory Services, GMP Lab

Extractables and leachables services

Extractables and leachables testing solutions

PPD is a leading global contract research organization focused on delivering life-changing therapies

Nitrosamines testing solution

GMP Lab Capabilities | PPD

GMP Laboratory Services | PPD

Contact PPD Laboratories | PPD

Extractables and leachables laboratory testing solutions PPD® Laboratory Services

Leveraging 20+ years of experience

- PPD® Laboratory services (PPD) – industry leader in providing comprehensive extractables and leachables testing services.
- Extractables and leachables program consulting, risk-assessment, design and testing services expertise since 2002.
- Wide-ranging breadth and depth of experience from container and delivery components to medical devices and device-drug combination products.
- Large collaborative team (75+ scientists) with locations in Middleton, Wisconsin U.S. and Athlone, Ireland.
- Thought leadership participation applied to quality focused study design for regulatory approval.
  - Active participation in conference presentations, publications, and industry educational events.*
- Supporting extractables and leachables for numerous successful product approvals year over year.

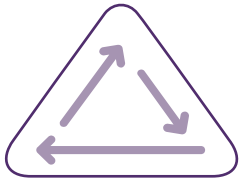
PPD Tech Talks extractables and leachables

Extractables and leachables

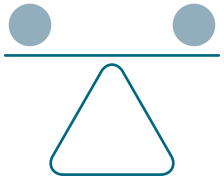
Study design
Designing and conducting extractables and leachables studies – industry/regulatory approach recommendation.

Extraction studies
Performing controlled extraction studies for material profiling.

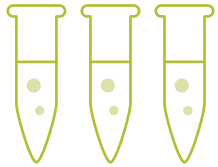
Toxicology
Toxicology assessments for extractables and leachables.



Methods
Development and validation of extractables and leachables methods.



Stability
Stability programs for leachable monitoring.



Batch testing
Batch extractable testing/support specification setting.

Special case compounds (e.g. N-nitrosamines*, polycyclic aromatic hydrocarbons (PAH), MBT)

PDF *PPD Nitrosamines Analysis

Extractables and leachables instrumentation

- Gas chromatography-mass spectrometry (GC-MS)
  - Agilent GC and mass spec detectors
  - Headspace and direct injection auto-sampler and pyrolysis
  - New Capability Q3 2022: High resolution accurate mass GC/MS
- Liquid chromatography (LC-MS)
  - Nominal mass LC/MS
  - Accurate mass LC/MS
  - New Capability Q2 2022: High resolution accurate mass LC/MS
- High and ultra-high performance liquid chromatography (HPLC, UPLC)
  - UV, PDA and CAD
- Inductively coupled plasma (ICP-MS/OES)
  - ICP-MS
    - Agilent 7700x
    - Thermo Scientific™ iCAP™ Q and XSERIES 2
  - ICP-OES
    - Thermo Scientific iCAP 6500 Duo and 7600 Duo
- Extraction apparatus
  - Soxhlet, reflux, microwave, sonication, autoclave and ASE

TS GMP Lab Capabilities

Extractables and leachables laboratory

Custom-designed space

- Isolated weighing room for trace-level analysis
- Separated extractable and leachable laboratories
- Purpose-built gas generator and supply room dedicated to extractables and leachables for increased sensitivity and improved control
- Built-in turbo evaporators
- Innovative instrument racking system to increase capacity and throughput

Virtual lab

Quality consumables you can rely on for dependable results

Liquid chromatography

With over 40 years as a leader in LC column technology, the Thermo Scientific™ HPLC and UHPLC family of products offers a variety of particle sizes and column designs to meet all separation needs, including improved resolution, enhanced sensitivity, faster analysis and consistent performance.

- Reversed-phase columns
- Normal phase columns
- HILIC columns
- Mixed-mode columns
- Ion-exchange columns
- Size-exclusion columns
- Application specific columns

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Gas chromatography

Our columns represent a leap forward in performance, delivering low bleed and superior inertness. Select from our comprehensive portfolio of Thermo Scientific GC columns that meet all of your analytical needs and achieve reliable, reproducible results.

- Application specific columns
- Non-polar GC columns
- Low-polar GC columns
- Mid-polar GC columns
- Polar GC columns
- PLOT GC columns
- Ultrafast GC columns

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Vials and closures

Autosampler vials and compatible inserts, septa, and closures designed for chromatography applications. Products come in various dimensions, material compositions, volume capacities, closure types, and colors. Products are available as individual components or kits.

- Screw top vials and kits
- Crimp top vials and kits
- Head space vials and kits
- Certified vial kits
- Micro vials and inserts
- 96 and 384 well plates
- Electronic crimpers and decrimpers
- Manual crimpers and decrimpers

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