

Identify all suspects

Unknown impurity identification and quantification workflows for:

- Pharmaceutical, packaging and contact-closure materials
- Food contact materials
- Non-intentionally added substances

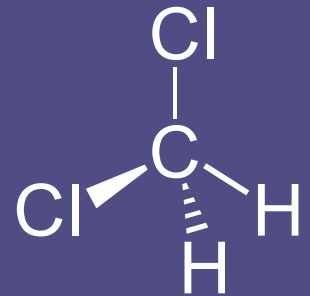
Food contact materials

OVERVIEW

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.

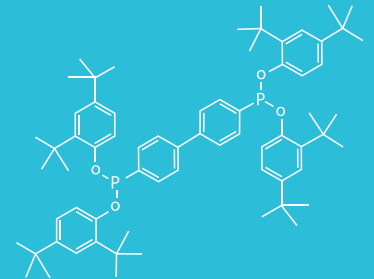
- A FCM must not transfer chemicals to, or cause changes to, foods that may impact consumer health.
- Testing is driven by regulation and demands migration studies that assess all 'unknown' non-intentionally added substances.

VOLATILES



Volatile

SEMI-VOLATILES



Non-volatile

NON-VOLATILES

Factors Affecting Migration



HEAT

Higher temperatures increase leaching.



TIME

Long storage time increases leaching.



FOOD TYPE

Fatty/acidic foods & liquids have influence on migration.



PACKAGING SIZE

Smaller packaging leaches more per volume of food.

ELEMENTAL IMPURITIES

Regulations

US FDA 21 CFR 174 to 21CFR 190

EU Regulation 10/2011



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.



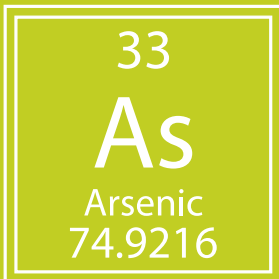
Pharmaceutical contact-closure materials

Extractable and Leachable compounds 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.



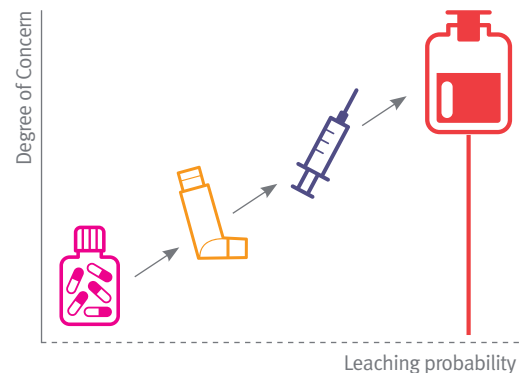
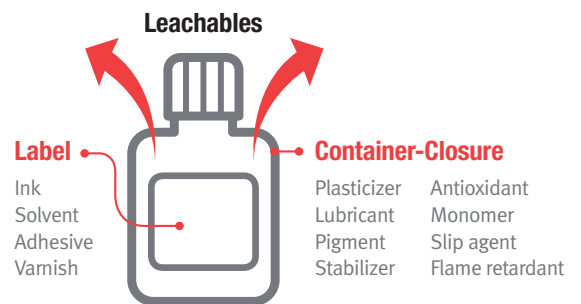
Semi-volatile



Elemental

AND QUANTIFICATION

THESE CHALLENGES REQUIRE AN ARSENAL OF ANALYTICAL TECHNIQUES AND WORKFLOWS TO MEET THE EVER DEMANDING CHALLENGES OF COMPLIANCE WITH GLOBAL REGULATIONS.



Methods

USP
1633 & 1634

PQRI
Guidelines

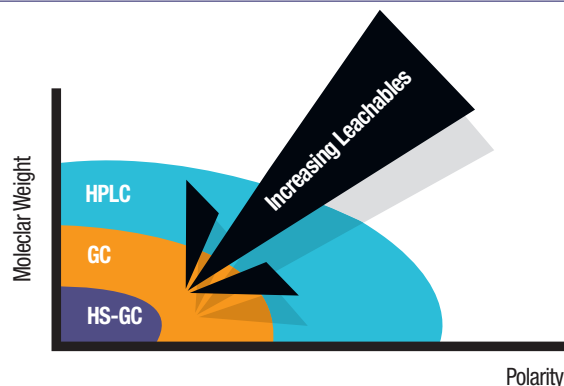
BPOG
Guidelines



Volatiles

OVERVIEW

Low molecular weight, 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.



VOLATILES

NO MORE VOLATILE UNKNOWNNS

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™ 300 HEADSPACE AUTOSAMPLER.**

SEMI-VOLATILES



NON-VOLATILES

Volatiles are released from materials using headspace sampling. USP methods suggest the use of valve-and-loop headspace sampling systems. Ultraclean **Thermo Scientific™ Chromacol™** headspace vials ensure low background and leak free seals.

Modular GC allows your choice of injectors, together with helium saver options and the widest range of advanced column technologies, including **Thermo Scientific™ TraceGOLD™** GC column phases for volatiles.

Sensitive mass spectrometry delivers both quantitation and qualification of volatiles. **Thermo Scientific™ ISQ™ Series Quadrupole GC-MS** features a new source design ideal for continuous high-throughput operation.

ELEMENTAL IMPURITIES





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

Simple to operate and fully compliant **Thermo Scientific™ Dionex™ Chromeleon™ Chromatography Data System (CDS)** software provides mass spectrometry data acquisition and processing for GxP environments.

Retention Time (min)	Peak Label	Library Match
4.712	Peak 1	1,3-dichlorobenzene
4.893	Peak 2	1,4-dichlorobenzene
5.000	Peak 3	1,2-dichlorobenzene



Semi-volatiles

OVERVIEW

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.



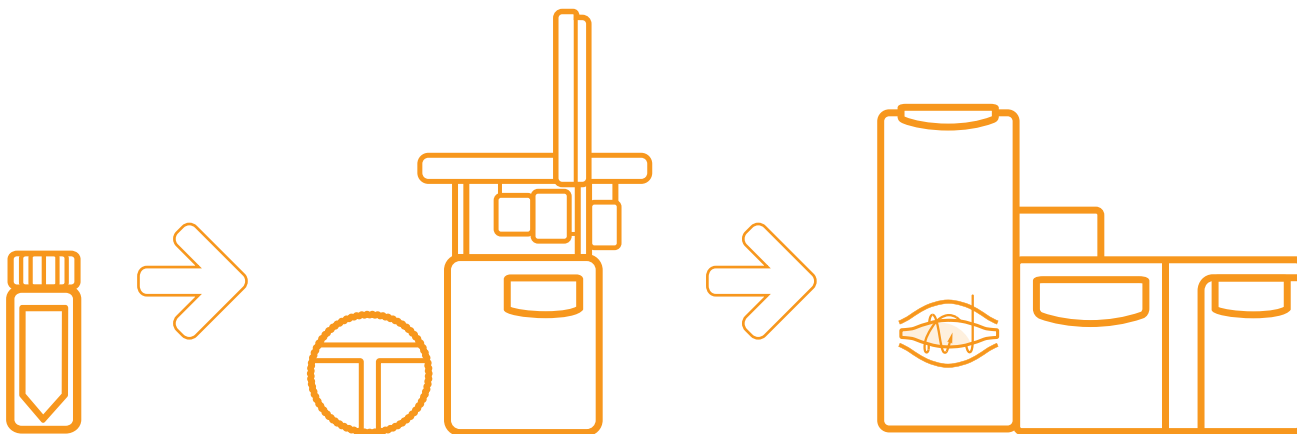
VOLATILES

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 UNKNOWN; DELIVER ACCURATE QUANTIFICATION AT THE LOWEST LEVELS.

SEMI-VOLATILES

NON-VOLATILES



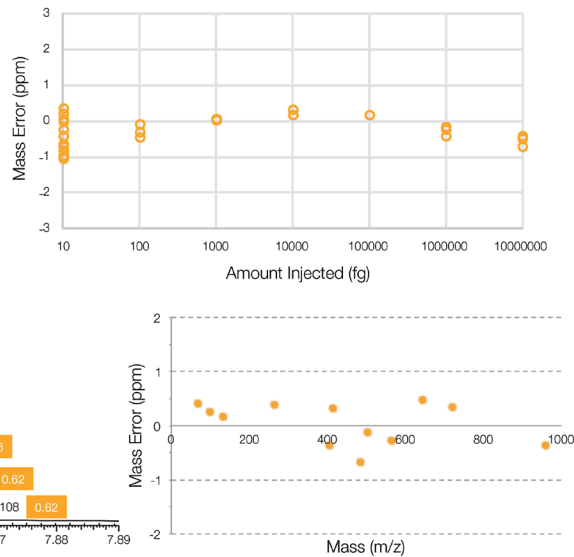
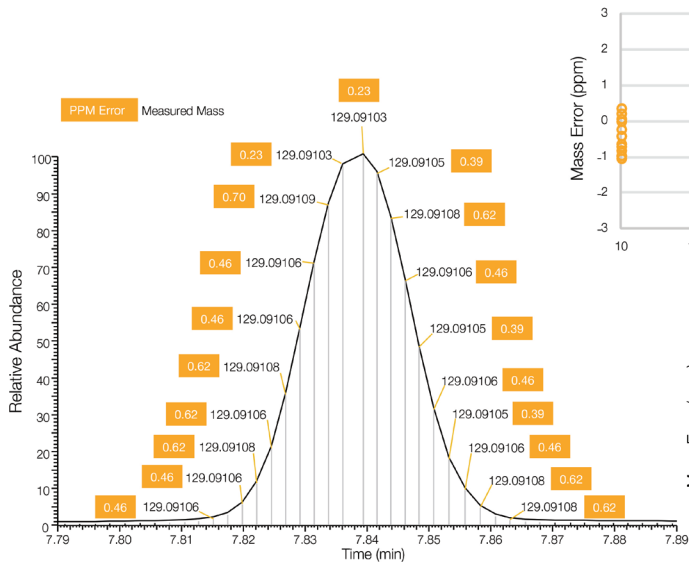
Ultra clean **Thermo Scientific™ MS Certified vials** ensure the lowest backgrounds to reduce false positives.

Simplify preparation with accurate, automated sample handling. Prepare standards, spike samples and automate derivatization with the **Thermo Scientific™ TriPlus™ RSH Autosampler**. With built-in robotics that deliver exceptional precision, flexibility, and reliable operation.

Absolute confidence in your analyte identification is required. Demand HRAM GC-MS with <1ppm mass accuracy, femtogram sensitivity and 6 orders linear dynamic range.

ELEMENTAL IMPURITIES

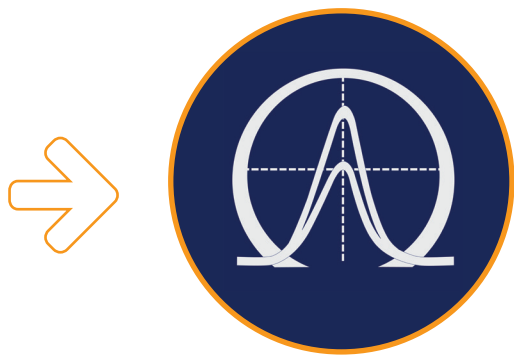




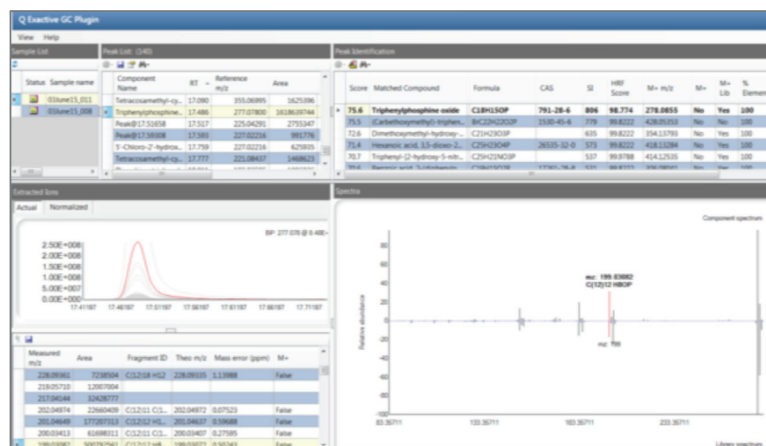
Exceptional <1ppm mass accuracy is achieved on every scan, on every mass, and at every concentration.

ORBITRAP COMES TO GC-MS

The **Thermo Scientific™ Q Exactive™ GC Orbitrap™ GC-MS/MS** 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.



Perform targeted screening, routine quantitation, and qualitative review of data with **Thermo Scientific™ TraceFinder™ software**. Use advanced high resolution filtering (HRF) algorithms to provide a new dynamic in confident identification of unknowns.



Deconvolve, identify and quantify.



Non-volatiles

OVERVIEW

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 advance high resolution accurate mass (HRAM) cloud based spectral libraries simplify the workflow.

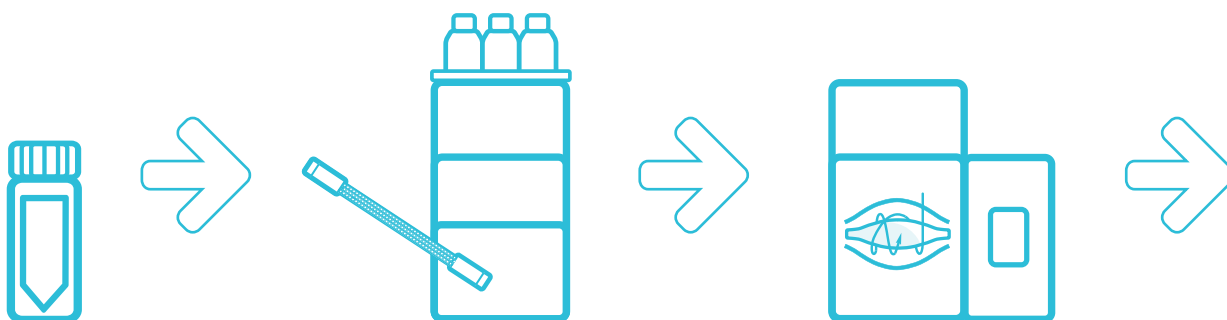


VOLATILES

PROVEN PERFORMANCE FOR EXTRACTABLES

IDENTIFY AND CONFIRM MORE COMPOUNDS RAPIDLY AND WITH CONFIDENCE USING THE **THERMO SCIENTIFIC™ Q EXACTIVE™** HYBRID QUADRUPOLE-ORBITRAP MASS SPECTROMETER AND **THERMO SCIENTIFIC™ VANQUISH™** UHPLC.

SEMI-VOLATILES



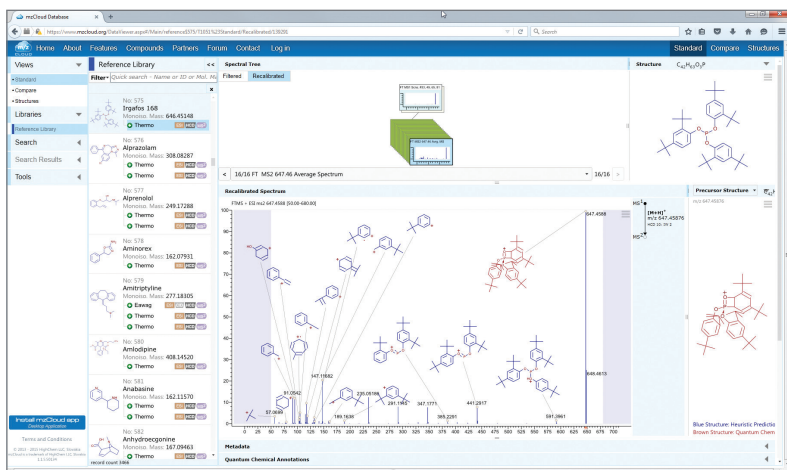
NON-VOLATILES

Robust chromatographic separations are delivered by **Thermo Scientific™ Vanquish™ UHPLC** system with orthogonal detection techniques such as Charged Aerosol Detection providing universal coverage for unknowns, complementing MS identification.

Quick exchange ionization modes including APCI & ESI are complemented by fast polarity MS switching. Record both +/- scans within a single acquisition for complete ionization coverage. MSⁿ capabilities and exceptional mass accuracy, make the **Thermo Scientific™ Q Exactive™ Series** of mass spectrometers the perfect tool for structural elucidation of unknowns.

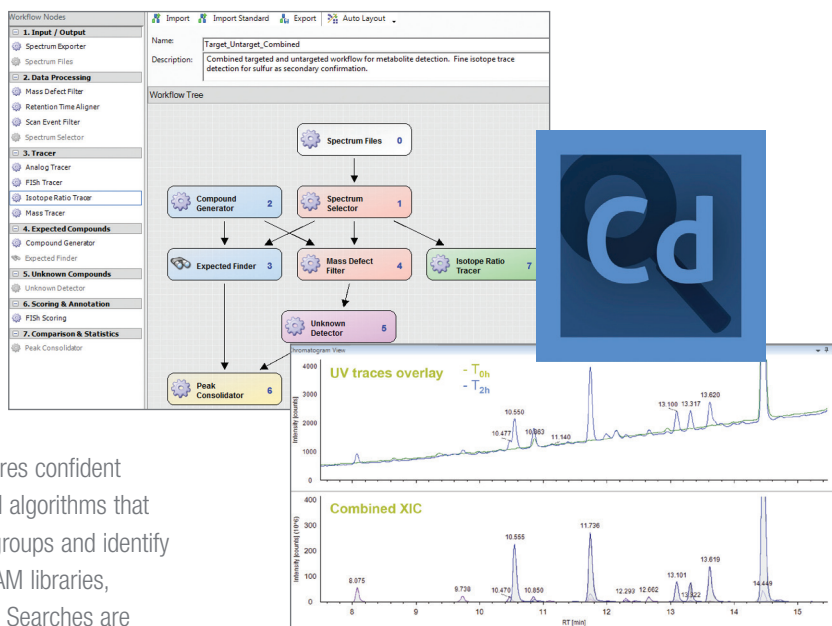
ELEMENTAL IMPURITIES





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

THIS BENCHTOP LC-MS/MS SYSTEM COMBINES INDUSTRY LEADING CHROMATOGRAPHY WITH QUADRUPEL PRECURSOR ION SELECTION AND HIGH-RESOLUTION, ACCURATE-MASS (HRAM) ORBITRAP DETECTION TO DELIVER EXCEPTIONAL PERFORMANCE AND VERSATILITY.



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 HRAM libraries, cloud based libraries like mzCloud™, and compound databases. Searches are conducted in parallel and a single unified report is delivered.

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



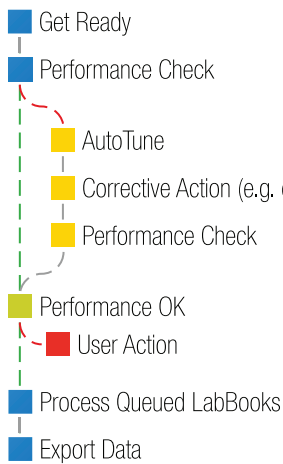
Elemental impurities

OVERVIEW

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.

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

VOLATILES



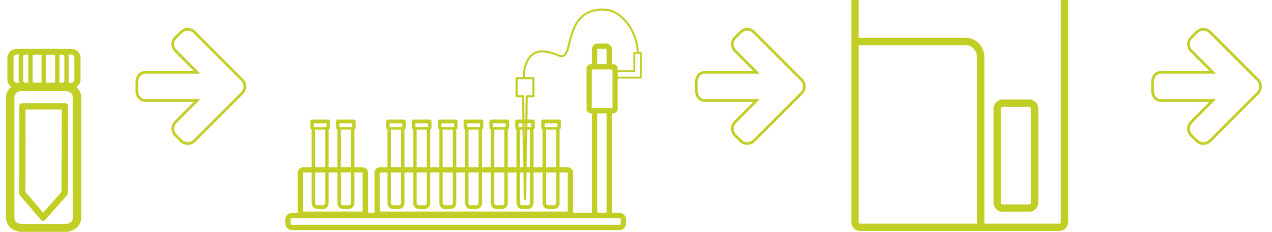
SEMI-VOLATILES



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.**

NON-VOLATILES



Automation of the lab workflow has taken a step forward with integration of intelligent auto-dilution, eliminating manual intervention, increasing productivity.

The **Thermo Scientific™ iCAP™ RQ ICP-MS** delivers simplicity, productivity and robustness, combined with the flexibility for unattended 24/7 operation in routine, compliant environments.

ELEMENTAL IMPURITIES



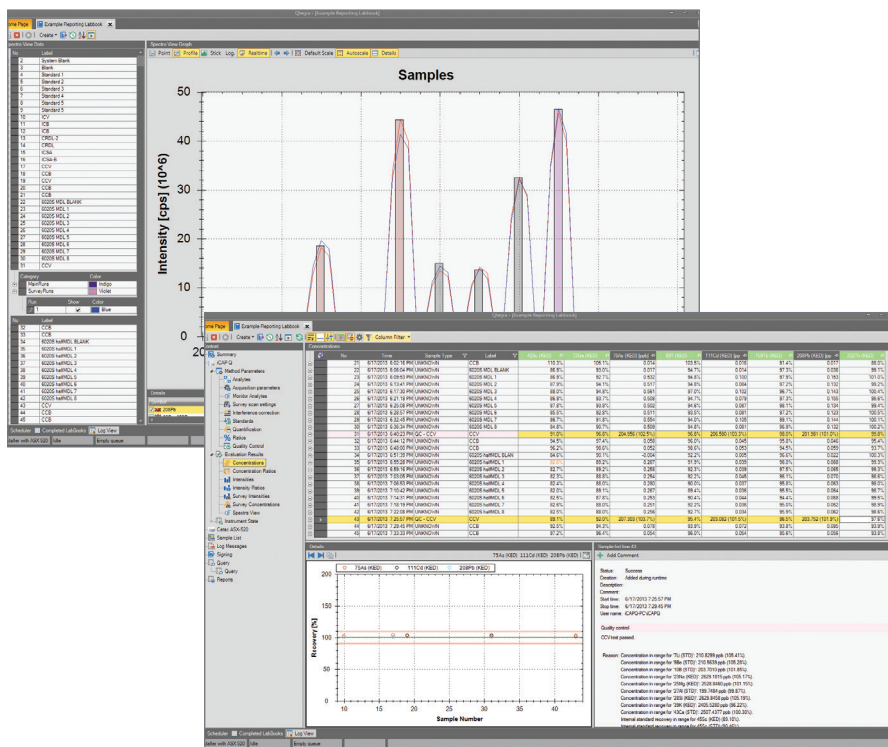
SIMPLICITY. PRODUCTIVITY. ROBUSTNESS

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 & 232A.



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.



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.



Extract smarter

Traditional Soxhlet or reflux techniques recommended by PQRI, & 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) & reduced solvent use (<30 mL/sample).



0.5 hour



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 compliant Chromeleon software.

Find out more about our extractables and leachables workflows

www.thermoscientific.com/Leachables

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Stay Ahead! Scan the QR code or follow the URL to watch the latest webinars on protein characterization.



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