

Ensuring Product Safety and Regulatory Compliance

Analytical Solutions for Extractables, Leachables, and Migration Testing



Waters

THE SCIENCE OF WHAT'S POSSIBLE.®



Reducing the Risks of Contact Materials

Product packaging – whether plastic, rubber, cardboard, metal, or glass – acts as a barrier against all sorts of contamination. But these materials can themselves provide a source of contamination. It is not a question of whether packaging components will leach into a product – it's a question of how much.

Aside from the direct migration of chemicals from containers, packaging can also be exposed to problematic materials during production, storage, and transport. These chemicals can later leach into the product stored in the containers.

The need for extractables and leachables testing is likely to grow. In pharmaceutical manufacturing, single-use systems (SUS) with plastic components are seeing increased use – and nearly three-quarters of biopharmaceutical manufacturers surveyed recently expressed concern about extractables and leachables from SUS. Meanwhile, the food industry continues to experience an increased focus on everything from food-safe inks to adhesives.

New regulations for ensuring the safety of packaging material and products in industries such as food, cosmetics, and pharmaceuticals are requiring analytical testing to be more rigorous – which can add time and cost to the process.

In this demanding environment, Waters provides analytical solutions to reliably and cost-effectively identify and quantify compounds, streamline workflow, and support compliance reporting.

A Challenging Mandate

The health risks posed when chemicals used in contact materials leach into products have raised concerns within government regulatory bodies. While packaging manufacturers can take preventive steps to minimize the use of materials containing these chemicals, the introduction of new materials and the widespread use of recycled fibers and plastics in packaging makes it impossible to avoid them entirely.

For packaging producers and product manufacturers, the challenge goes beyond meeting regulatory requirements. Inefficient testing of extractables and leachables can create bottlenecks, slow down the product development cycle and delay commercialization of new products. And ineffective testing can lead to costly product recalls that cause long-term damage to brand reputation and profitability.

To address these challenges, Waters provides analytical solutions and techniques that effectively address the chemical diversity found in samples so that you can:

- Maximize separation for complex samples reliably and routinely.
- Obtain the highest level of structural information that reveals even trace amount of compounds.
- Visualize, process, and report data more effectively to support compliance documentation.
- Make critical decisions in less time with greater confidence using tools and techniques to improve workflow and increase testing throughput.



Research

The goal in a controlled extraction study is to establish a systematic, risk-based approach packaging and device component analysis. This enables a clear understanding of structural information to determine whether the material or packaging is toxicologically acceptable for the intended purpose.

IDENTIFICATION AND ELUCIDATION OF UNKNOWN COMPOUNDS

The challenge with the compounds observed in a controlled extraction study is their identification. The original ingredients can degrade or undergo chemical changes during the manufacturing process.

This is a common bottleneck at the controlled extraction study level and requires extensive experience to be performed successfully. Waters addresses this need with an approach based on fast and simple differential analysis combining liquid chromatography (LC) or atmospheric pressure gas chromatography (APGC) with advanced time-of-flight (ToF) mass spectrometry (MS).



Xevo G2-XS QToF.



KEY WATERS SOLUTIONS

ACQUITY® UPLC® I-CLASS SYSTEM:

- The most powerful binary UPLC system, engineered for the lowest dispersion.
- Maximizes peak capacity, providing rapid, high-resolution separations to help resolve components of interest from complex matrix interference peaks.
- Lowest carryover enables analysts to reach the levels required by the legislation.

ATMOSPHERIC PRESSURE GC (APGC):

- API source interface adds GC capabilities to Waters' MS technologies.
- Atmospheric pressure GC provides soft ionization, which means less fragmentation compared to techniques such as EI, resulting in higher sensitivity and specificity.
- Maximize uptime and asset utilization – changeover from UPLC to GC is quick and simple, without the need to break the MS vacuum.

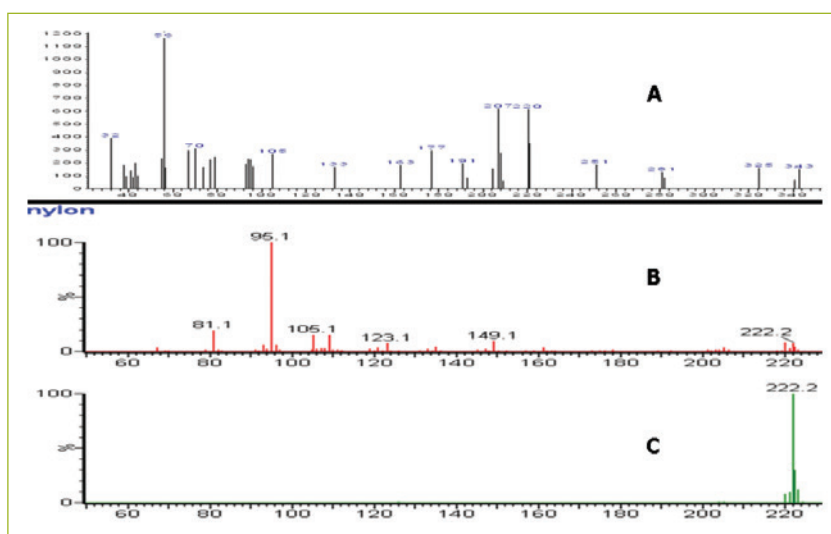
XEVO® G2-XS QTOF:

- A benchtop QToF mass spectrometer that provides comprehensive qualitative information together with quantitative performance.
- Identify, quantify, and confirm the broadest range of compounds in the most complex and challenging samples.
- Comprehensive collection of precursor and fragment ion data using data independent acquisition mode, or MS^E provides the highest levels of structural information for targeted and non-targeted analysis of unknowns or suspects.

EXTRACTABLES AND LEACHABLES SCREENING STANDARD:

- Comprised a mix of 18 common polymer additives enabling users to evaluate and benchmark high resolution LC-MS systems.
- Supports stable retention times for statistical analysis when analyzing unknown samples.
- Provides required information and compliance with regulatory requirement for instrument performance monitoring.

Detection and identification of extractable compounds from polymers in a nylon sample using APGC-QToF MS with MS^E. A = EI spectrum, B = high energy/fragmentation APGC spectrum, C = low energy/molecular ion APGC spectrum.



Extractables Screening Analysis

These studies involve solvent extraction techniques that encompass a range of polarity, solvent compatibility studies, and multiple analytical techniques. This can make it challenging and time-consuming to match the solvent extracts with the appropriate analytical technique. Waters provides analysts with a well-established workflow for extractable screening analysis to streamline the analytical process, ensure smooth interoperation with outside partners, and ease the workload associated with compliance documentation and auditing.

KEY WATERS SOLUTIONS

MV-10 ASFE® SYSTEM:

- Multi-vessel supercritical fluid extraction (SFE) system with tunable solvent for rapid method development and selective extraction.
- Provides a faster, greener, more selective alternative for analyte extractions from a wide variety of sample matrices.
- Enables both enrichment of target analytes for analytical purposes and removal of unwanted material from a product.

ACQUITY UPC²® ULTRAPERFORMANCE CONVERGENCE CHROMATOGRAPHY®:

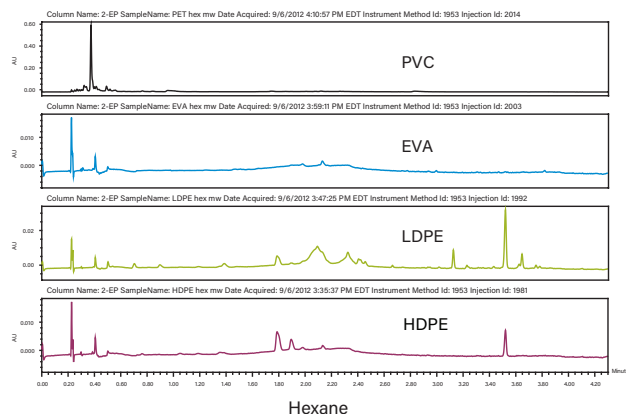
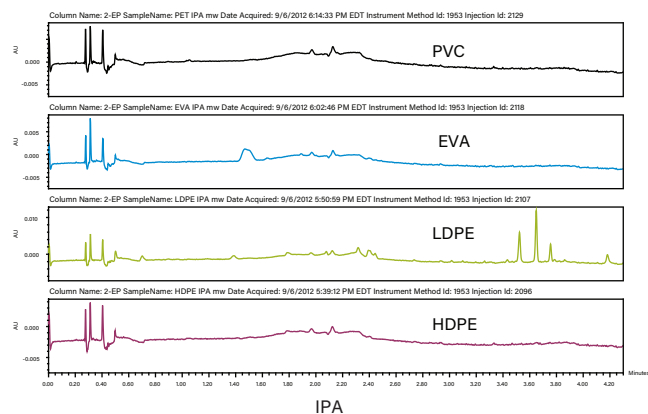
- Delivers faster separations and superior resolution for chiral and achiral applications.
- Utilizes supercritical carbon dioxide (CO₂) as the primary mobile phase to provide a more cost-effective and greener technology by reducing the use of organic solvents.
- Streamlines sample preparation workflow by eliminating evaporation and reconstitution steps.

SFC COLUMN CHEMISTRIES:

- **Trefoil® Columns**, for chiral SFC chromatography, are uniquely designed for the ACQUITY UPC² System for selectivity and speed in separations as well as reduced method development time.
- **Torus™ Columns** minimize unwanted surface interactions to achieve fast, robust achiral separations.
- **Viridis® SFC Columns** with proprietary OBD™ Technology provide optimum retention, peak shape, and selectivity for analytical and preparative chromatography.

VION® IMS-QTOF MASS SPECTROMETER:

- Combines the benefits of high-resolution tandem mass spectrometry and ion mobility separation in a single benchtop instrument.
- Collision cross section (CCS) provides an additional confirmation parameter for targeted screening in complex matrices.
- Quickly refine spectra and discount chromatographically co-eluting compounds and background interferences.

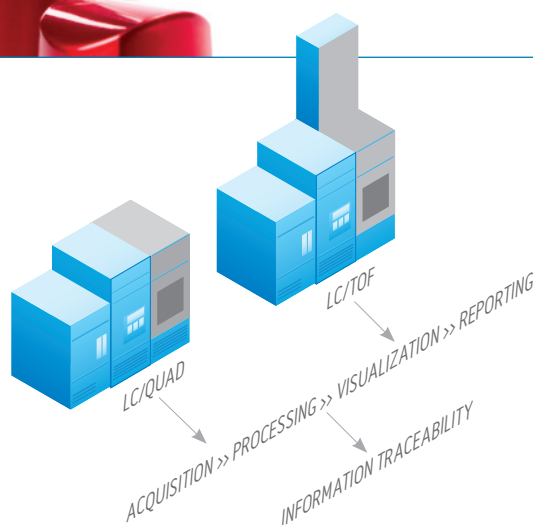


ACQUITY UPC² chromatograms for IPA and hexane sample extracts of four different types of packaging material, including a high density polypropylene pill bottle (HDPE), a low density polypropylene bottle (LDPE), an ethylene vinyl-acetate plasma bag (EVA), and a polyvinyl chloride blister pack (PVC). The extracts were screened for 14 common polymer additives.

KEY WATERS SOLUTIONS

UNIFI® SCIENTIFIC INFORMATION SYSTEM:

- Seamlessly combines LC, MS, and data management into a single software platform that encompasses data acquisition, processing, visualization, reporting, and configurable compliance tools within a workstation or networked laboratory environment.
- Provides a simple workflow that includes scientific library creation, multivariate statistical analysis, elucidation, and reporting.
- Transforms complex full scan data into components that can subsequently be used for targeted and non-targeted analysis.



The UNIFI binary comparison feature allows analysts to directly compare the chromatographic and spectral results of an analyte with those of a reference sample. Here, UNIFI's Binary Compare results window shows an IPA reference sample extract and a lipstick packaging sample. The red trace shows the BPI chromatogram of the reference sample (IPA blank extract); the blue trace shows the BPI chromatogram of a lipstick packaging extract; and the green trace shows the difference between the samples.

Routine Quality Control/Release Testing

The goal in routine quality control and release testing is to analyze products for targeted leachables to verify that they are below pre-defined limits. Laboratories that are able to expedite this process can make a significant impact on their business performance. However, there are many challenges that stand in your way, including analytical throughput, regulatory limits, and the number and complexity of product samples.

One effective way to overcome these challenges is to utilize mass detection in concert with a compliance-ready chromatography data system. This combination presents mass spectral data in a format familiar to chromatographers and supports full data traceability, enabling QC laboratories to keep up with changing regulations and remain prepared for audits.

KEY WATERS SOLUTIONS

ACQUITY ARC™ SYSTEM:

- Dual-flow path liquid chromatography system capable of emulating HPLC or UHPLC separations.
- Allows the efficient transfer, adjustment, or improvement of existing methods from any HPLC or UHPLC platform.
- Reduces run time and solvent consumption, while maintaining analytical resolution.

CHROMATOGRAPHY COLUMNS:

- **XBridge® HPLC Columns'** wide pH range and extreme mechanical stability have established these products as the number one starting point for any routine LC method development.
- **CORTECS® Columns** provide maximum efficiency for UPLC separations with 1.6 µm particles, and 2.7 µm particle columns for improved speed of analysis and flexibility for HPLC.

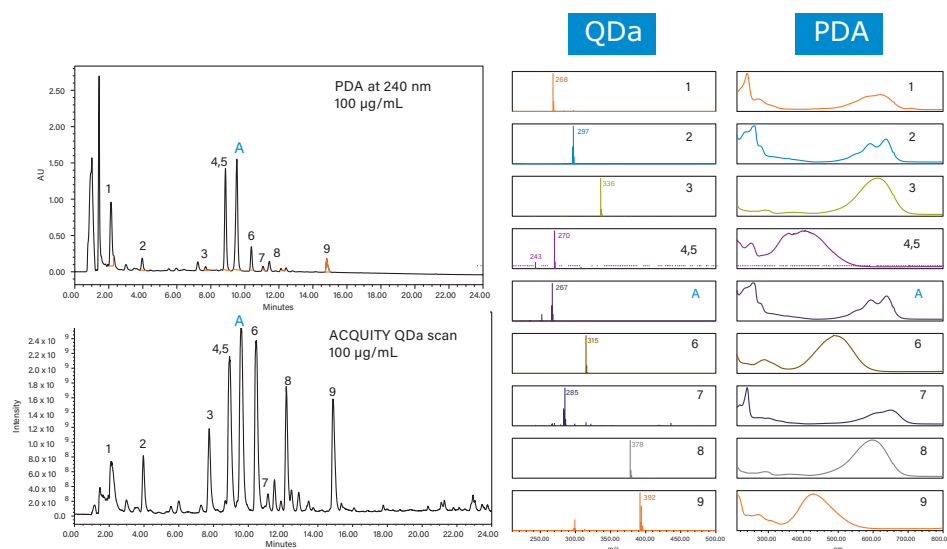


EMPOWER® CHROMATOGRAPHY DATA SOFTWARE (CDS):

- Acquires, processes, reports, and stores data from multiple analytical systems securely.
- Full data traceability to quickly recall requested data during an audit.
- Proven track record in regulated environments.

ACQUITY QDa® MASS DETECTOR:

- Minimizes the risk of unexpected coelutions or components and confirm trace components with the analytical confidence of mass detection.
- Quantifies compounds with no UV response at levels not accessible to optical detection.
- Chromatographers can generate high-quality mass spectral data routinely and consistently with no special training or expertise.



ACQUITY Arc chromatograms from the separation of nine disperse dye standards at 240 nm (top) (100 µg/mL, 5 µL injection) and QDa MS scan (100–600 m/z) (bottom) using the DIN 54231 standard method and an XBridge C₁₈, 2.1 x 150 mm, 5.0 µm Column. The MS and UV spectra are also shown. A prominent peak (peak A) was detected in the PDA data at a retention time (t_R) of 9.5 minutes. An MS full scan experiment was performed simultaneously with the PDA detector making it possible to determine the mass spectra as well as the UV spectra for all components in the mixture.

Waters Professional Services and Training

REDUCE THE TIME AND COST OF YOUR SOFTWARE DEPLOYMENT

Waters offers a comprehensive suite of professional services to reduce the time and cost of your Waters' software deployment. Whether you are upgrading to Empower 3 or installing Waters' Informatics Software for the first time, Waters' highly trained consultants have the skills and expertise to make your software implementation a success.

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Technologies and requirements can change quickly and training keeps your knowledge current. Waters Educational Services is the leading training organization empowering scientists to maximize their skills in UPLC, HPLC, LC-MS, and data management, offering classroom, virtual web-based, and on-demand e-learning courses to keep you up-to-date on the latest technologies and products. Waters provides an extensive course catalog designed to help you build your laboratory skills and further your knowledge in chromatography, Informatics, and mass spectrometry.

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Waters Service and Support offerings are tailored to optimize your laboratory productivity while addressing your budget realities. Our offerings help maintain system peak performance, minimize down time, address scientific application challenges, and support stringent compliance requirements. As your services and support provider, we are committed to the success of your laboratory and business. Waters quality support and consultative services ensure your success wherever your laboratory is located in the world.



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