thermo scientific

SGS CASE STUDY

SGS – Delivering Excellence in Compliant Extractables and Leachables Testing

A case study in unknown impurity identification & quantification

SGS is a world leading inspection, verification, testing and certification company. SGS has been a world leader in pharmaceutical outsourcing for decades, partnering with companies of all sizes, including the top 20 pharmaceutical companies in the world.

Extractables and leachables (E&L) studies enable drug sponsors to quantify and identify the risk of potentially toxic leachable impurities migrating into a drug solution from container closure systems, processing equipment or packaging. This makes the successful examination of extractable and leachable substances extremely important for both patient safety and adherence to regulatory requirements.

ThermoFisher SCIENTIFIC

SGS is an authority in E&L studies with several decades of experience in testing for extractables, leachables and packaging migration impurities; working with clients from a range of segments, including pharmaceutical, biopharmaceutical, bioprocess equipment manufacturers, and medical device manufacturers. SGS has three global centers of excellence for Extractables and Leachables testing, Figure 2.

Figure 1. SGS Fairfield, New Jersey.

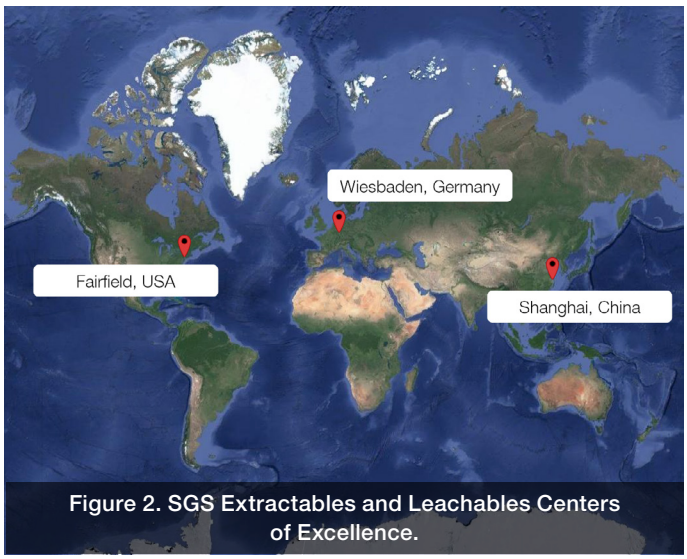


Figure 2. SGS Extractables and Leachables Centers of Excellence.

SGS' experts are specialized in analytical chemistry for the identification and quantification of unknowns, which is reinforced by their extensive knowledge of the packaging materials used by the pharmaceutical industry. Extractable and leachable analytes are typically small molecules (<1200 Da) and can come from numerous sources including plasticizers, adhesives, stabilizers, pigments, anti-oxidants, slip agents, label ink components and residual monomers and oligomers of the plastic polymer.

The testing capabilities at SGS include a wide range of analytical techniques designed to identify and test all possible additives and impurities, whilst adhering to regulatory guidance such as USP draft chapters <1663> and <1664>.

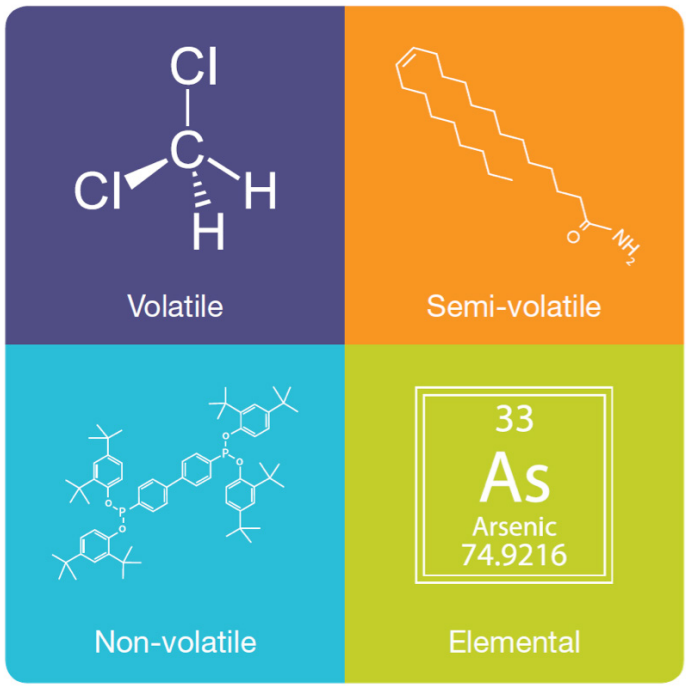
SGS determine volatile, non-volatile and elemental contaminants through the application of a range of instrumentation including:

- Non-volatiles – liquid chromatography-mass spectrometry (LC-MS/MS)
- Volatiles & Semi- volatiles – gas chromatography-mass spectrometry (GC-MS)
- Elemental – inductively coupled plasma spectroscopy (ICP, ICP-MS)

"What makes SGS different from other extractables & leachables testing providers is the quality of work that we provide our clients, together with the amount of expertise that we have in house"

—Danny Hower, Extractables & Leachables Supervisor, SGS

The use of selective, sensitive and robust analytical techniques are essential to ensure confidence in the identification of unknowns. The accuracy of unknown identification is based largely on spectral and compound database searches; the ability to confirm elemental composition and fragment substructures, expertise and an understanding of how different methods can be used to confirm one another. High resolution accurate mass (HRAM) mass spectrometry increases confidence in the identification of unknowns whilst simplifying interpretation steps.



Volatile impurity identification and quantification

SGS chose the Thermo Scientific™ ISQ™ LT Single Quadrupole GC-MS system as their routine workhorse for volatile and semi-volatile impurities. The ease of source removal and maintenance without venting the system were key factors for selecting the ISQ LT.

Key capabilities of the ISQ system for E&L:

- Full Scan/SIM simultaneous within one injection for qualitative and quantitative analysis
- Wide dynamic range detection system perfectly suited to the broad concentration range of extractable impurities
- Quick and easy maintenance with no-vent source removal and Thermo Scientific™ ExtractaBrite™ source for analytical robustness even when faced to heavy plastic matrix extracts
- Compliance-ready data acquisition and processing software for GMP applications

Dr. Megan Bergauff, Senior Scientist, Small Molecule Team Leader

"The ISQ is easy to use, we were able to install and validate the system in just a few days and start running client samples almost immediately. We chose the ISQ LT because of its fast source removal without venting and ease of maintenance."

—Dr. Megan Bergauff, Senior Scientist, Small Molecule Team Leader, SGS

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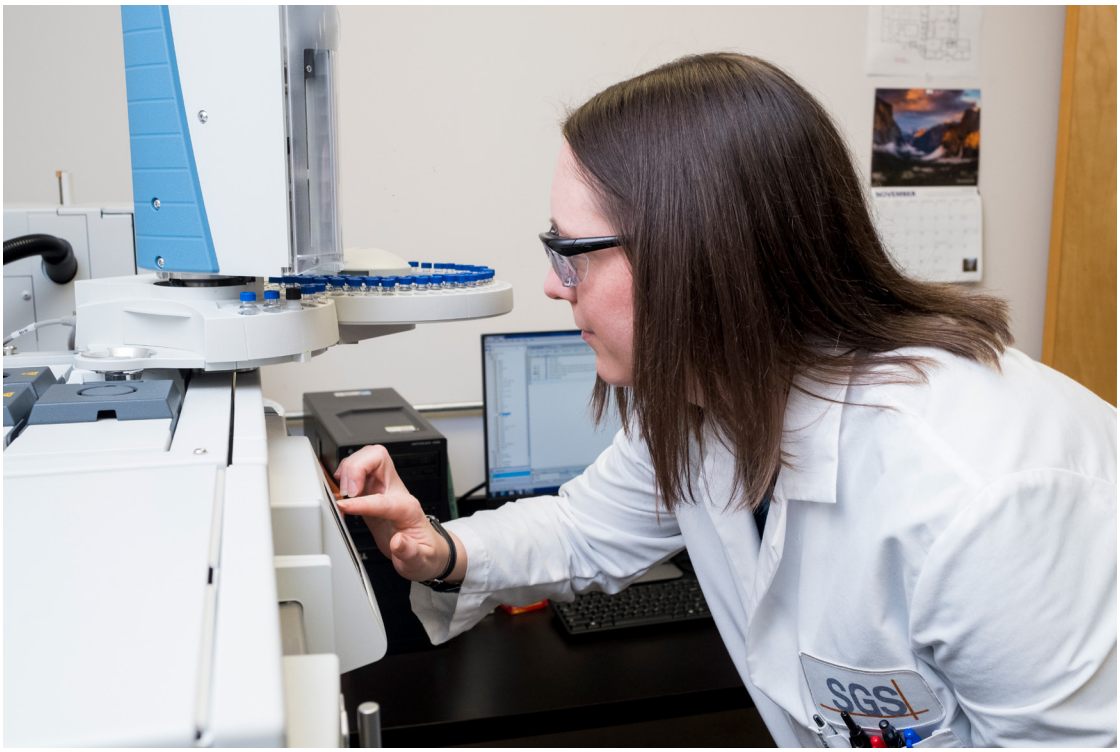


Figure 3. Analysis of volatile extracts at SGS West Chester PA.

Thermo Scientific Chromeleon software

The ISQ LT systems, like a multitude of analytical systems at SGS, are driven using Thermo Scientific™ Chromeleon™ 7.2 Chromatography Data System (CDS) software. It is the only CDS providing full control of chromatography instruments from Thermo Fisher Scientific. It also fully supports quantification workflows and compliant data acquisition for chromatography and mass spectrometry all using the same intuitive user interface.

Figure 4. Thermo Scientific ISQ LT Single Quadrupole GC-MS.

"Having one software that can drive both our high-resolution accurate mass systems, as well as our GC-MS, liquid and ion chromatography systems, is very advantageous. We are able to offer a full compliance-ready solution for multiple systems and workflows, reducing our training needs and audit challenges. We were able to easily pass all regulatory audits without concern."

—Dr. Bérangère Tissot, General Manager, West Chester, SGS

- **Full Control of LC, IC and GC Instruments** – Comprehensive, reliable control for over 450 different instrument modules, including over 300 chromatography instruments from other LC and GC vendors.
- **Integrated Control of Mass Spectrometry Instruments** – A single software to streamline your chromatography and MS quantitation workflows. Full integration of Thermo Scientific mass spectrometry instruments, including the Thermo Scientific™ Q Exactive™ series of HRAM Orbitrap-based mass spectrometers.
- **Advanced data integrity and compliance features** – Chromeleon CDS software simplifies meeting the latest demanding regulations. With sequence-level data organization and comprehensive audit trails tracking all actions in the software – including CDS-related external events – it enables you to easily achieve the highest standards of regulatory compliance and data integrity.
- **Flexible reporting** – Fully customizable spreadsheet-based Report Designer provides a familiar interface simplifying the creation of user-defined report templates and eliminating data export to external spreadsheets, reducing errors.
- **New methods at your fingertips with one-click** – The AppsLab Library of Analytical Applications is a fully searchable online, analytical method repository where you can find applications with detailed method information, chromatograms and related compound information. Download one-click eWorkflows, created and tested by Thermo Fisher Scientific application scientists, which can be directly executed in your chromatography data system.

Visit appslab.thermofisher.com to download your methods today.

"Chromeleon CDS can do many things – it has 'tailorability'. We have hundreds of clients, all with different reporting requirements and Chromeleon CDS allows the flexibility to easily interrogate and integrate the data whilst maintaining full security and regulatory compliance."

—Dr. Bérangère Tissot, General Manager, West Chester, SGS

Non-Volatile impurity identification and quantification

For the identification and quantification of non-volatile unknowns, SGS chose the Thermo Scientific™ Q Exactive™ Plus LC-MS high resolution system for it's consistent mass accuracy, sensitivity and ability to rapidly alternate from positive to negative ion mode within a run to ensure no unknowns get missed.

Key capabilities of the Q Exactive Plus system for E&L analysis:

- Ability to operate under Chromeleon CDS for GMP compliance.
- Rapid polarity switching means all sample data is captured, all of the time, enabling retrospective data analysis without need to re-run samples
- Resolving power up to 140,000 (FWHM) at *m/z* 200 significantly removes isobaric interferences, increasing confidence in results when analyzing samples in complex matrices
- Better than 1ppm mass accuracy in full- and all-ion fragmentation (AIF) scan modes ensures confident compound identification
- More than four orders of magnitude intrascan dynamic range, along with femtogram-level sensitivity, allow detection of trace-level and high-abundance compounds in the same scan

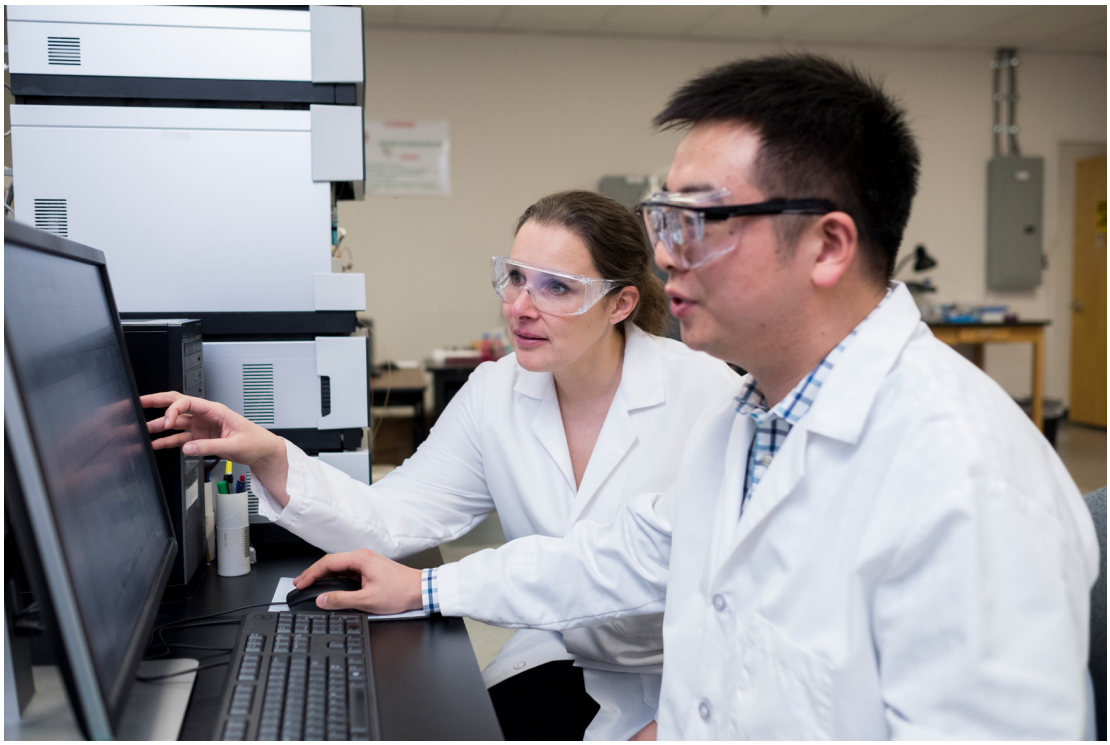
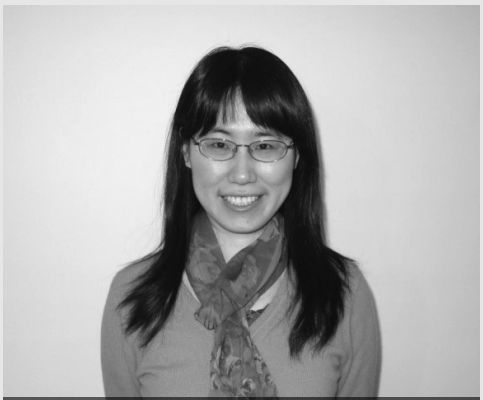


Figure 5. Dr. Bérangère Tissot, General Manager.



Dr. Dujuan Lu, Extractables & Leachables Technical Client Manager

"We have very good confidence when determining the chemical composition of unknowns, due to the accurate mass of the Thermo Scientific Q Exactive Plus. It routinely delivers below 1 PPM mass accuracy."

—Dr. Dujuan Lu, E&L Technical Client Manager, SGS

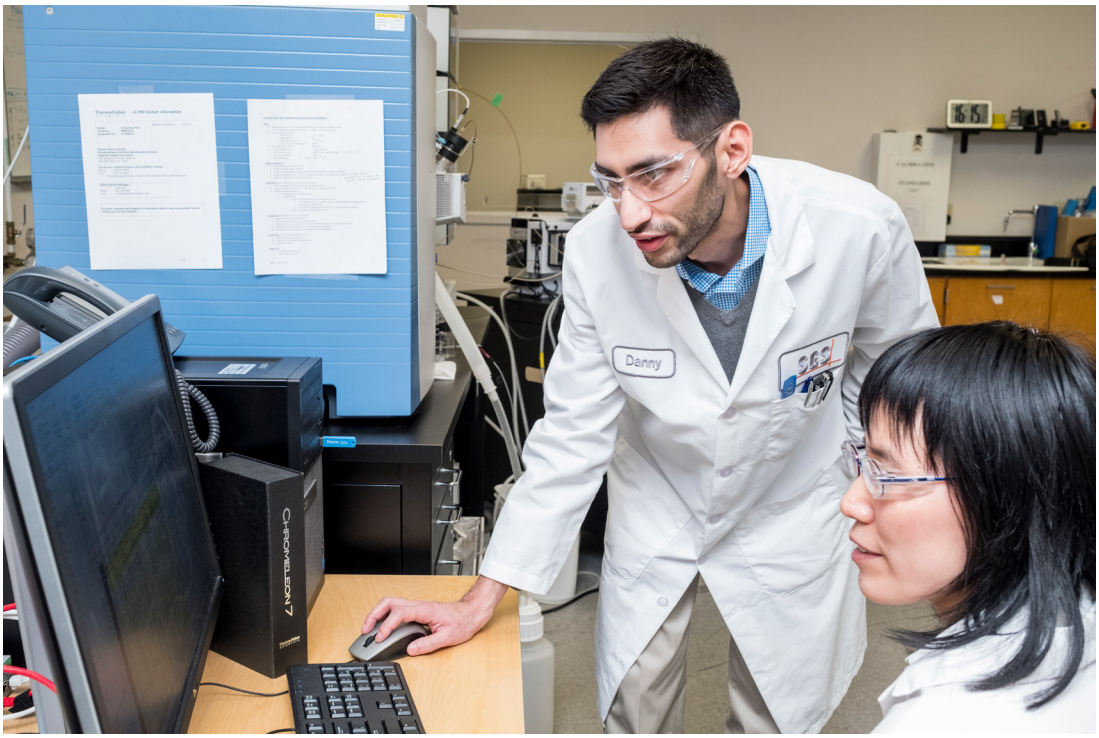


Figure 6. Identifying Extractable unknowns at SGS.

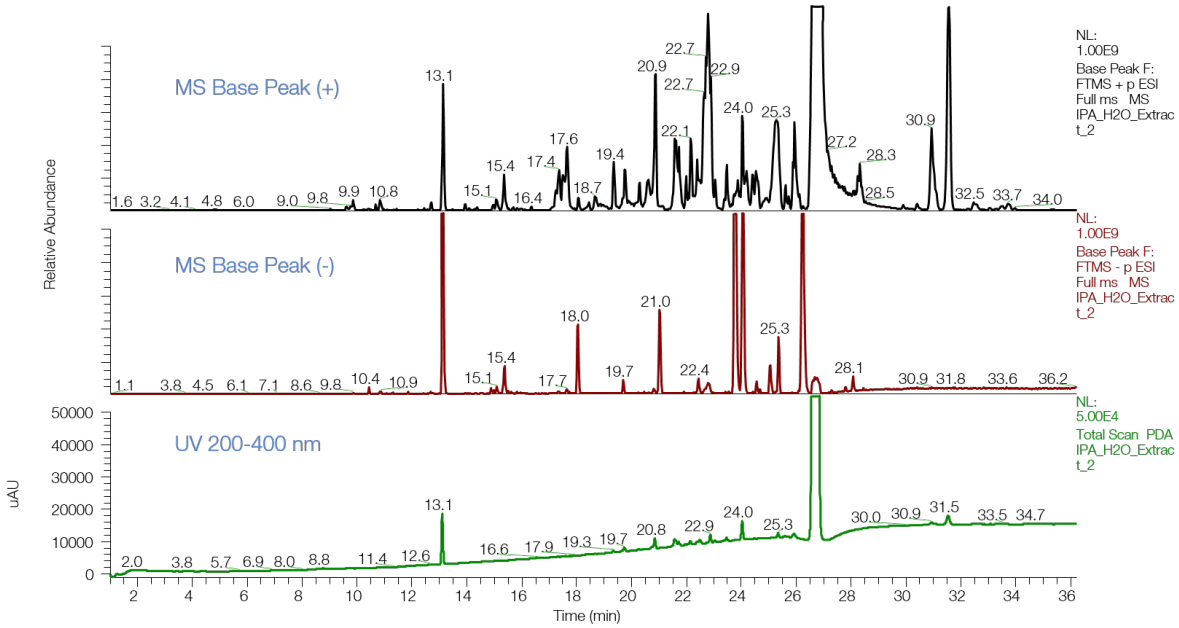


Figure 7. SGS Analysis of extractable unknowns from an intravenous drug drip bag using Q Exactive Plus and positive/negative ionization switching.

Thermo Scientific Compound Discoverer software

Identifying unknowns can be automated using Thermo Scientific™ Compound Discoverer™ small molecule identification software. Compound Discoverer empowers researchers to organize, store, and analyze high resolution accurate mass data for both targeted and untargeted workflows. The software simplifies data processing for complex data with its customizable workflows, integrated compound identification capabilities, and statistical analysis. Compound Discoverer offers a suite of tools to study impurities, degradants, extractables & leachables, and more.

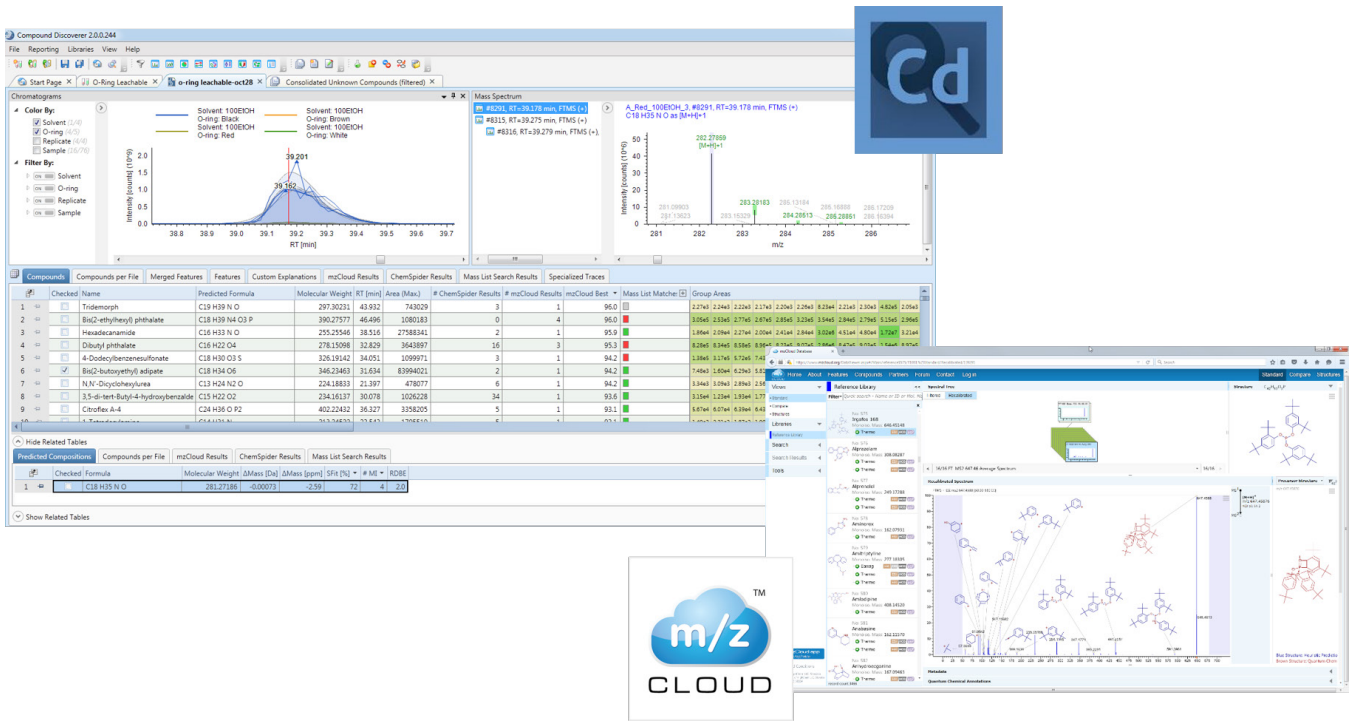


Figure 8. Compound discoverer searches multiple databases in parallel, including the free-to-search *mz*Cloud.org HRAM MS database with >40,000 Extractable and Leachable compound spectra.

"Working with Thermo Fisher Scientific as an instrument provider has been a very positive experience. Their instrumentation and service is top of the line."

—Danny Hower, Extractables & Leachables Supervisor, SGS

Danny Hower,
Extractables & Leachables Supervisor

"We feel like Thermo Fisher Scientific understand the agility requirements and pace of a CRO environment. They understand our challenges not just in buying equipment, but also in maintaining and supporting equipment."

—Dr. Bérangère Tissot, General Manager, West Chester, SGS

A partnership beyond extractables and leachables

SGS embrace the vital role played by technology suppliers like Thermo Fisher Scientific in helping their company deliver quality in everything they do. Working together, SGS and Thermo Fisher Scientific strive to lower cost, improve performance, and help drug manufacturers bring life sustaining treatments to market faster. These efforts allow us to meet the expectations of our customers and communities in making the world healthier, cleaner and safer.

For more information on SGS service for extractables and leachables please visit www.sgs.com/extractables

Find out more at **thermofisher.com/leachables**

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