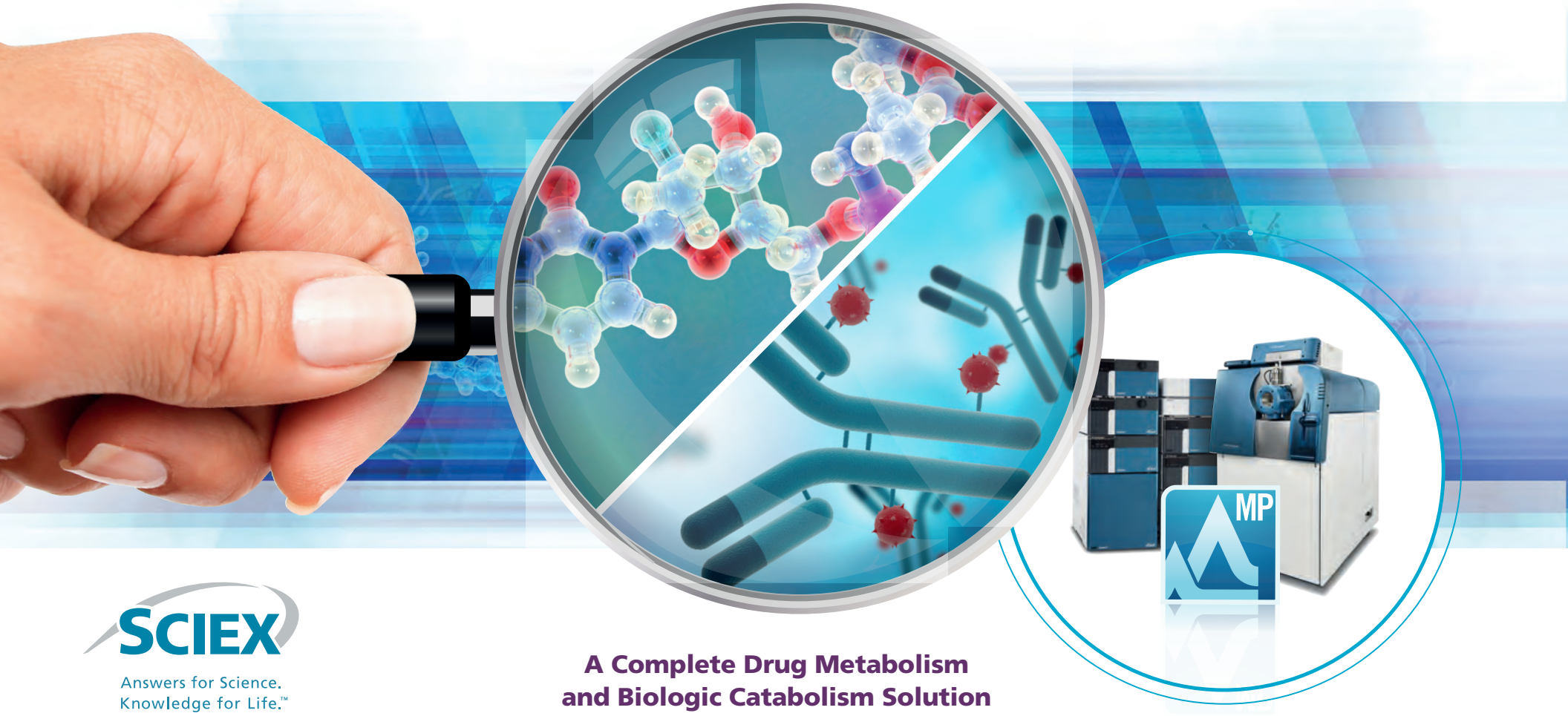
Comprehensive Detection Total Confidence

Advanced Biotransform Solution



SCIEX

Answers for Science.
Knowledge for Life.™

A Complete Drug Metabolism and Biologic Catabolism Solution

Advanced, Comprehensive Metabolism and Catabolism

When it's time for a comprehensive understanding of drug metabolites or biotherapeutic catabolites, you have to be 100% confident that you've identified everything in the sample. If something is missed, the risks can be substantial. You need a solution that is specifically designed for metabolite and catabolite detection, including those that are very low level or closely related to the parent.

The SCIEX TripleTOF® 6600 High Definition QTOF System offers the linear dynamic range and sensitivity to inspire your confidence. When used with unbiased SWATH® Acquisition, the TripleTOF 6600 will acquire MS/MS for every metabolite or catabolite it detects: nothing hides from this solution.

For drugs, peptides and ADCs, new MetabolitePilot™ Software 2.0 will automatically identify metabolites and catabolites within the confidence range that you define; you have control, even as the software does the heavy lifting of searching and assigning. Gain peace of mind in your metabolite and catabolite identification and the confidence to move your project forward.

Maximal Sensitivity and Dynamic Range for Low Level Metabolite ID

The **TripleTOF 6600** accurate mass system ensures the highest confidence for drug metabolism and catabolism studies with comprehensive and unbiased data collection using SWATH® Acquisition and >5 orders of linear dynamic range.

Robustness with Ultra-Low Downtime

The **ExionLC™ AD** delivers high accuracy, reliability and repeatability across thousands of injections, with maximum uptime.

Single Injection Comprehensive Coverage for Ultimate Confidence

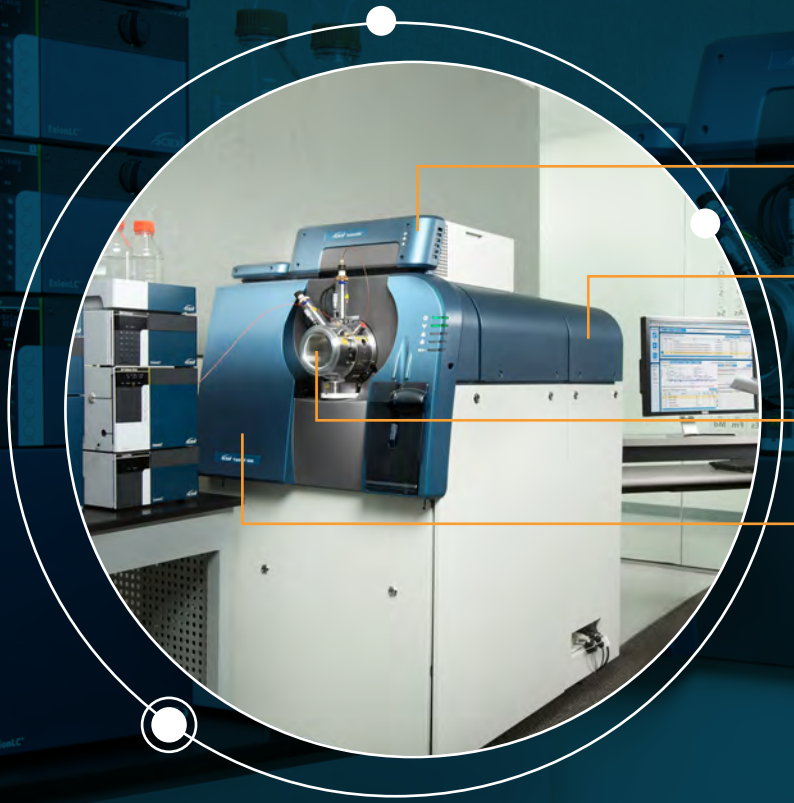
SCIEX proprietary **SWATH Acquisition** provides high-speed, high-resolution MS/MS data of all detectable analytes in your sample. Save time and energy with a true single injection workflow that offers a digital archive of your sample.

Small Molecule Metabolism and Biologics Catabolism Analysis in the Same Package

MetabolitePilot Software 2.0 offers small molecule drug metabolite profiling and structure determination as well as the industry leading solution for large molecule biologic catabolism analysis. All from the same platform and software you know and trust.

The Right Tools for the Task

You can't afford to miss low abundance metabolites in your sample. That's why the TripleTOF 6600 LC-MS System is the best choice for comprehensive metabolite and catabolite detection. The TripleTOF 6600 System not only gives you the extremely high sensitivity to see those low level metabolites, but its >5 orders of dynamic range means you can accurately follow the high level parent compound in the same experiment. Without both sensitivity and dynamic range, you risk missing metabolites...something you can't afford to do.

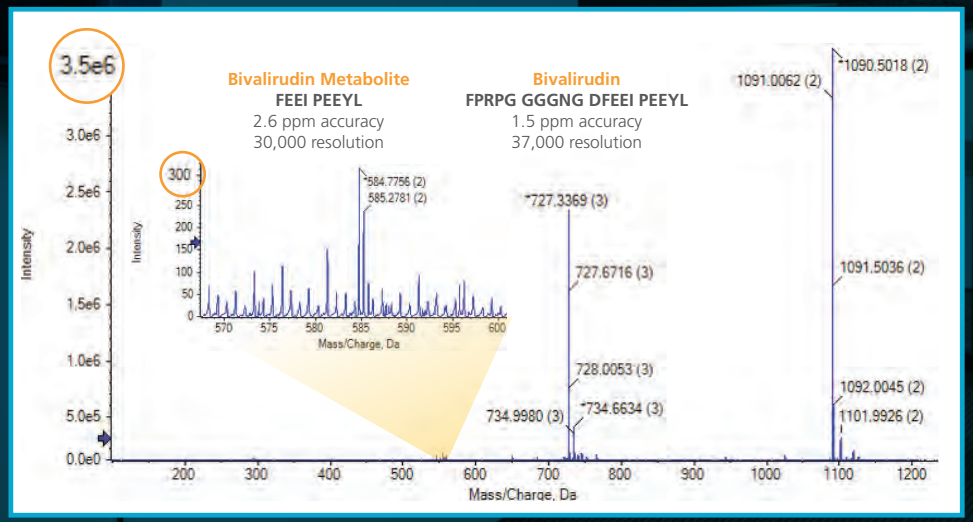


Utilize orthogonal separations, such as SelexION® Differential Mobility technology, to separate isobaric species and reduce matrix interferences

Fast acquisition rates are required to not miss co-eluting metabolites at UHPLC timescales. Get comprehensive MS/MS coverage in a single run using SWATH Acquisition and up to 200 MS/MS spectra per cycle

Ensure confident structure interpretation with high resolution MS (30-40K) at all scan speeds, and high mass accuracy that is stable over time

Detect low level metabolites and catabolites with the high sensitivity QTOF system with >5 orders of linear dynamic range (LDR)

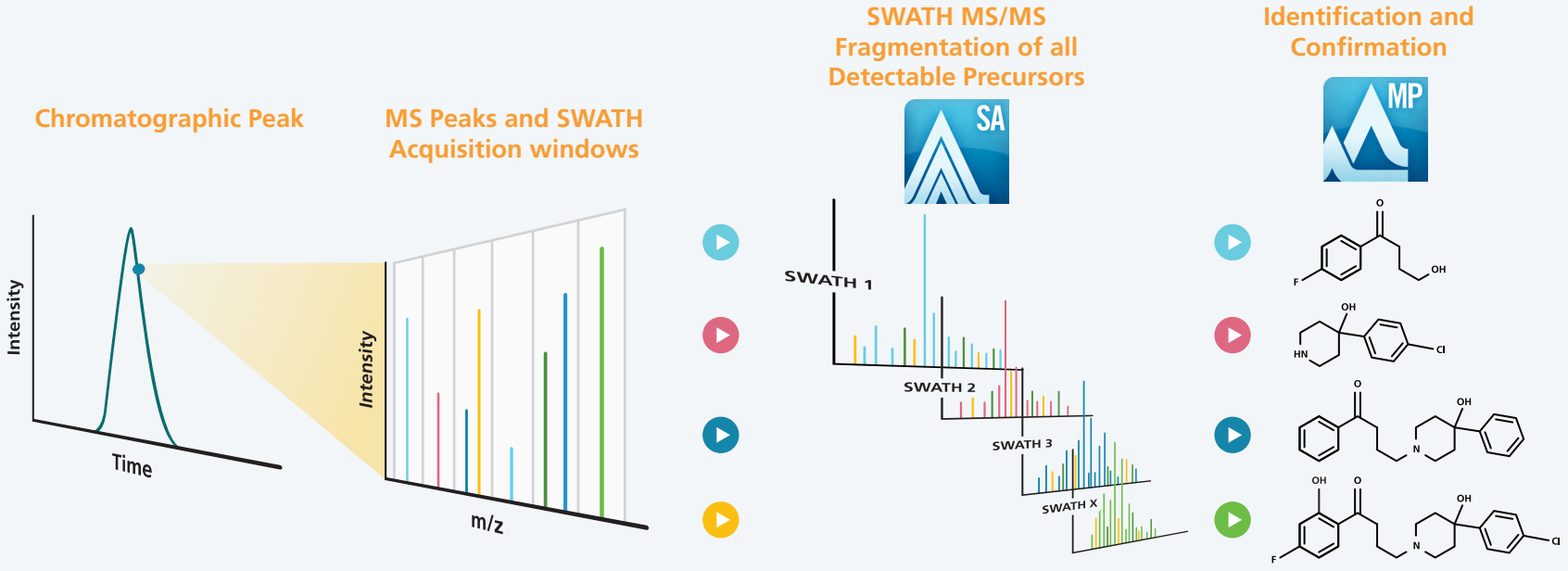


Detection of bivalirudin analyte and multiple metabolite structures in the same TOF-MS scan with >5 orders of intrascan dynamic range while maintaining high resolution and high mass accuracy

Flexible Acquisition Strategies to Maximize Productivity

For comprehensive metabolite and catabolite identification, one LC-MS data acquisition strategy may not suit everyone's needs. That's why the TripleTOF® 6600 allows you to choose standard, Information Dependent Acquisition (IDA), SCIEX Real-Time Multiple Mass Defect Filtering (RT-MMDF), or unbiased variable window SWATH® Acquisition.

- IDA is the LC-MS acquisition you're used to, where the top intensity MS peaks are further fragmented for MS/MS
- RT-MMDF adds built-in intelligence about the parent molecule, and picks the top most likely metabolite MS peaks for MS/MS acquisition
- Data-independent, variable window SWATH Acquisition captures MS/MS for every detectable peak, so you can identify potential metabolites or catabolites in your sample, even those that are present at very low levels.

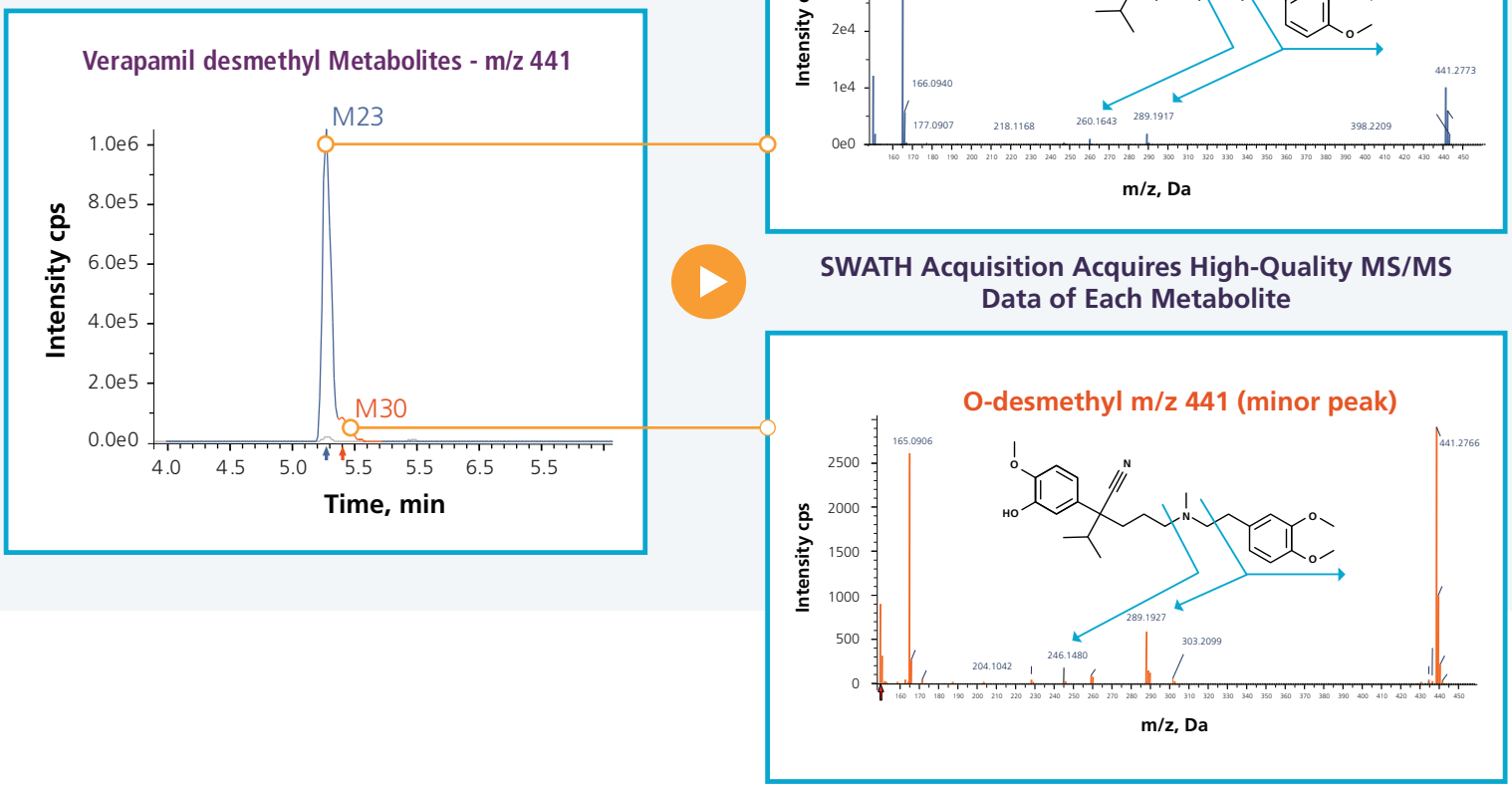


Complete Coverage by SWATH Acquisition for Small and Large Molecules

- SWATH Data Independent Acquisition (DIA) allows for single injection comprehensive qualitative and quantitative analysis, so you don't miss low level metabolites or catabolites
- Ensures consistent and reproducible MS/MS are collected for all detectable species, resulting in the most reliable detection and identification
- Provides a complete MS/MS isotopic pattern for more confident metabolite structure matching
- Re-interrogate your sample without the need to reacquire data, retrospective data analysis is possible with the SWATH digital sample record

Nothing Hides From SWATH

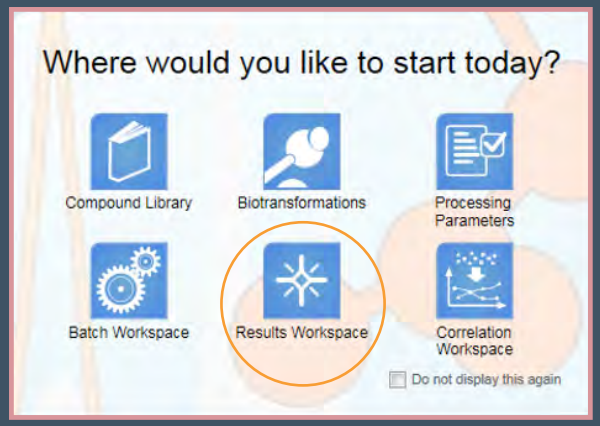
Variable window SWATH® Acquisition captures high-resolution MS/MS for all detectable peaks in a sample, so you can see low level metabolites which could be missed by an IDA method. Moreover the MS/MS data from SWATH Acquisition is very high quality, allowing you to make confident structural assignments of your metabolites and catabolites, even in the presence of high-intensity sample components at the same retention time.



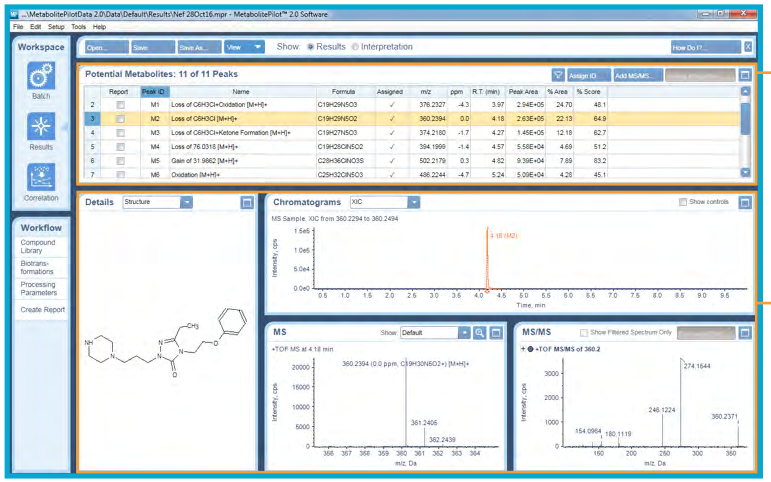
This minor metabolite may not be triggered for MS/MS acquisition by a traditional IDA method. SWATH Acquisition uncovers it even in the presence of its high-intensity parent.

Confident, Automated Identification

Once you've chosen your data acquisition strategy, you need to process, interpret, visualize, and report your findings. All-in-one **MetabolitePilot™ Software 2.0** makes metabolite identification fast and efficient, with batch data import and automated method generation for up to 200 samples at a time. MetabolitePilot Software interprets and correlates metabolite structures and profiles, so you always see your data in context.

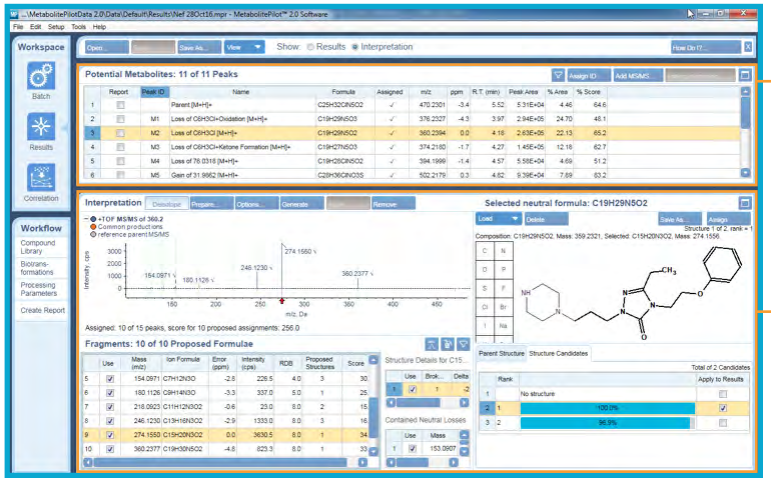


The user-friendly software interface puts processing, interpretation, visualization, and reporting all in one place



Results window gives a quick view of metabolites identified in the data

Advanced Visualization in a single screen: XIC, TOF-MS, MS/MS and predicted metabolite structure



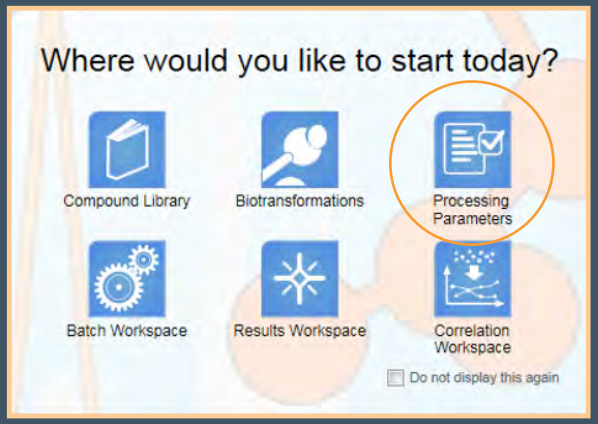
Dig deeper into metabolite data using the interpretation window

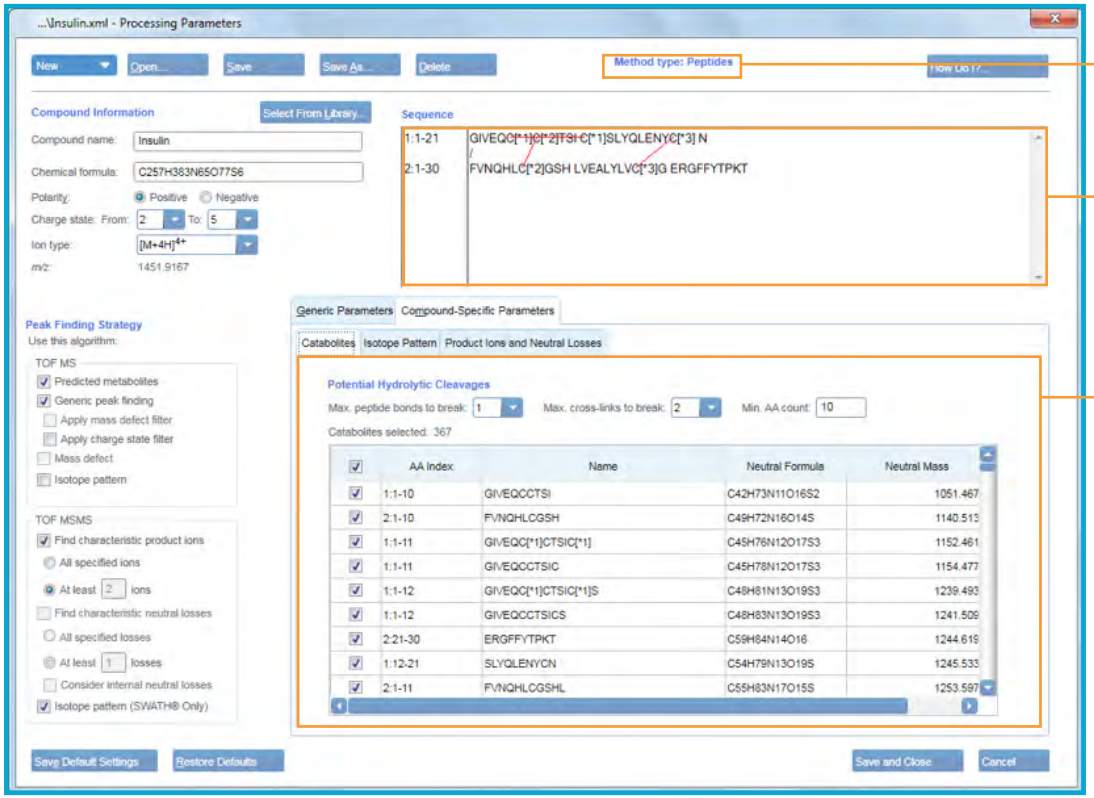
Confirmation of structure using high-resolution MS/MS spectra

Advanced Processing for Biotherapeutic Catabolism

The complexity of large molecule breakdown makes catabolite identification a very difficult manual task.

Now you can employ the same automated processing and assignment for large molecule catabolites as for drug metabolites. MetabolitePilot Software 2.0 enables automated catabolite identification using sophisticated processing algorithms. Fast, automated and comprehensive peptide catabolism and biotransformation identification allow you to find liabilities and soft spots in the molecule which may keep it from becoming a successful biologically active and safe drug.



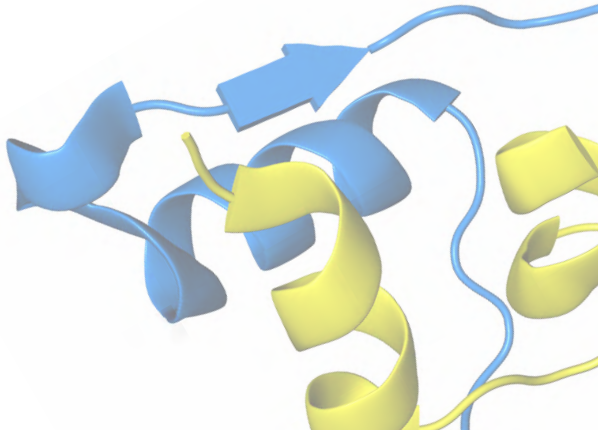


Example processing parameters for analysis of Insulin metabolism

Processing logic specific for large molecule catabolism

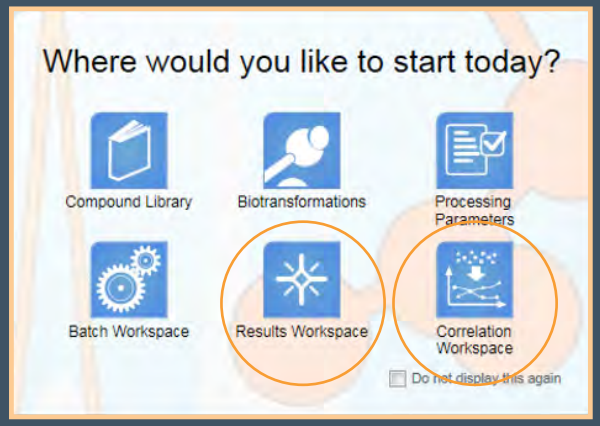
Supports linear, non-linear, cross-linked and cyclic peptides, as well as inclusion of engineered amino acids and modifications

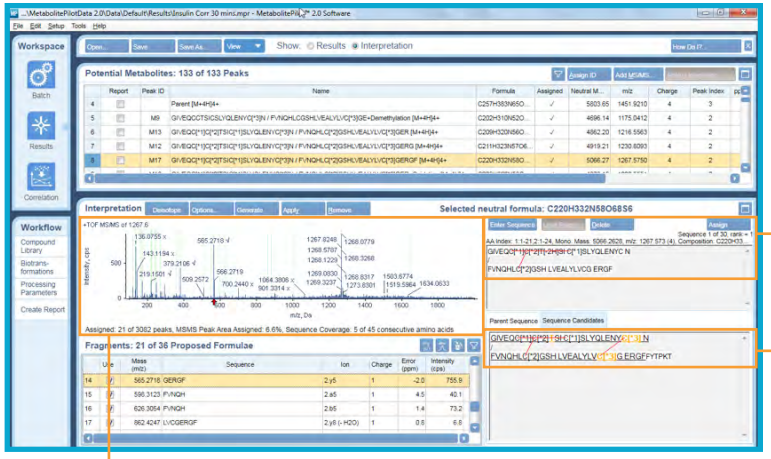
Prediction of catabolites and hydrolytic cleavages for use in targeted searching



Simplify Your Catabolism Workflows

With MetabolitePilot™ Software 2.0, you can use the same comprehensive SWATH® Acquisition workflow for both your small and large molecule metabolism studies. In a single Results interface, MetabolitePilot Software presents powerful analysis and visualization of biotherapeutic catabolism. The Correlation workspace offers three levels of review to maximize your confidence and minimize the time required for data analysis.



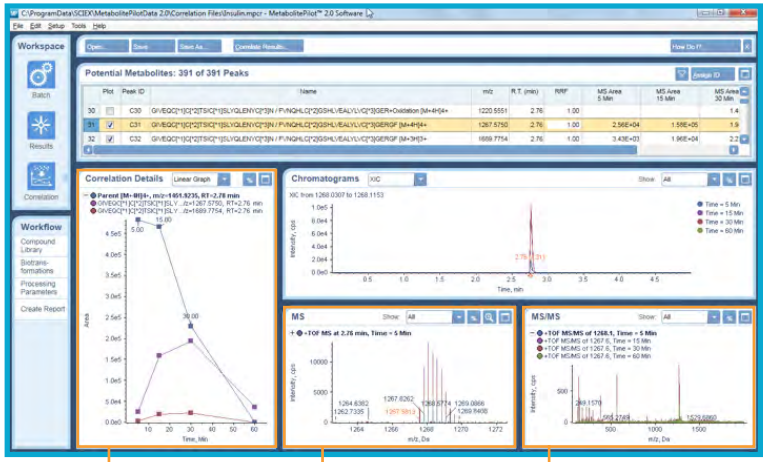


Results and correlation for analysis of Insulin metabolism

Review sequence of proposed metabolite

Simplified visual to show where side chain biotransformations are occurring on parent compound, and underlined sequence where catabolism has occurred

Increased confidence in identification with annotated high-resolution MS/MS spectrum



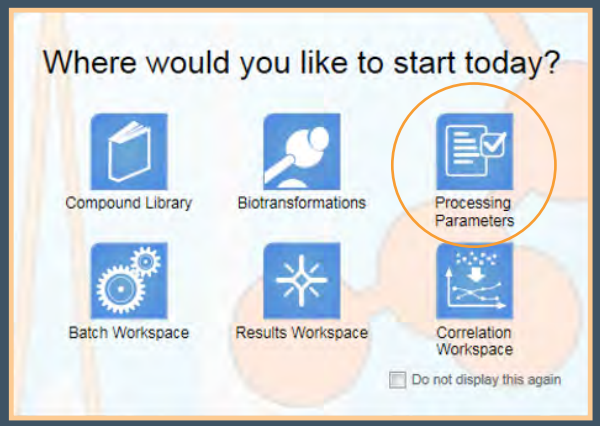
3 Sequence verification with high-resolution MS/MS spectrum

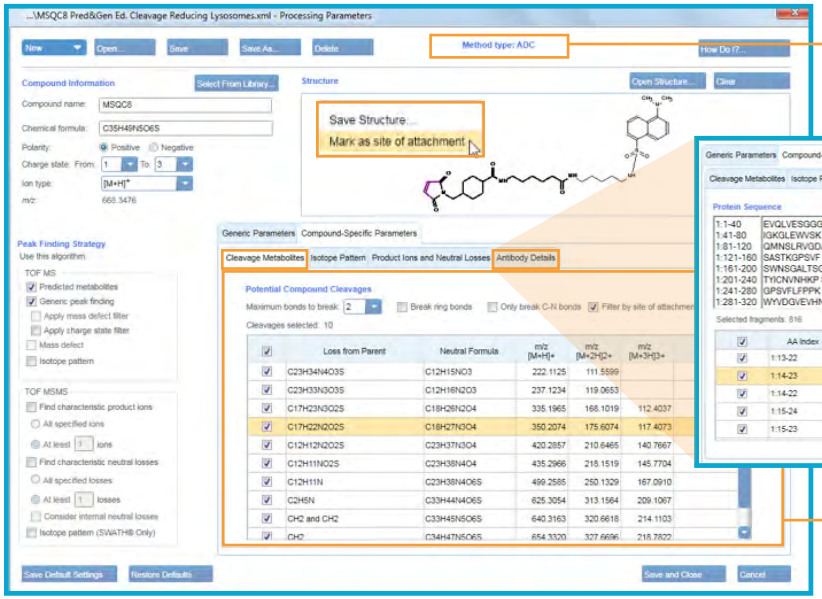
2 Confirmation using isotope pattern matching of overlaid XICs for additional confidence in assignment

1 Visual time profile of parent compound and selected metabolites

Set Up Your ADC Studies with Ease

Studying metabolism of antibody drug conjugates (ADCs) is especially complex, because you need to monitor the breakdown or release of the cytotoxic drug, as well as the ADC linker and antibody. Harness the built-in intelligence of MetabolitePilot Software 2.0 to set up your ADC metabolism analyses quickly, with dedicated templates in the Processing view.





Processing set-up for analysis of an antibody-drug-conjugate.

Dedicated biologic processing templates to simplify analysis of ADCs

Flexibility to define antibody, linker, conjugation chemistry and cytotoxic drugs with intuitive user interface

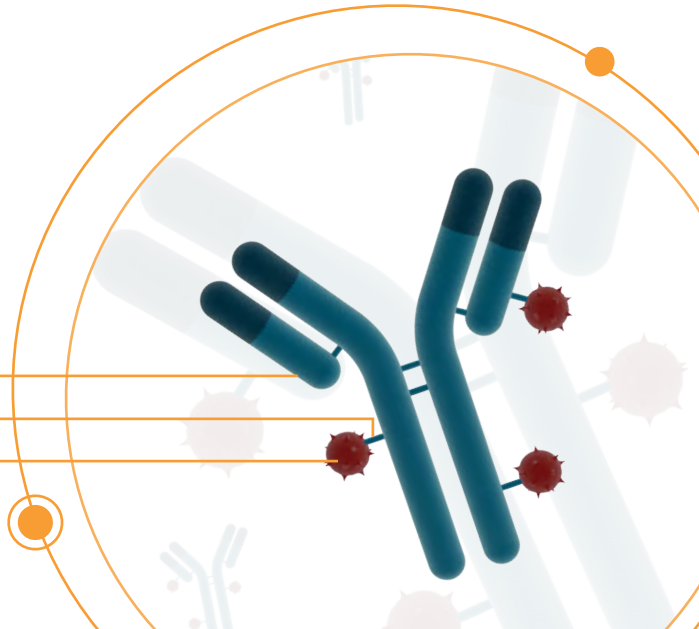
Prediction of cleavage metabolites for payload

ADC Structure

Delivery Antibody

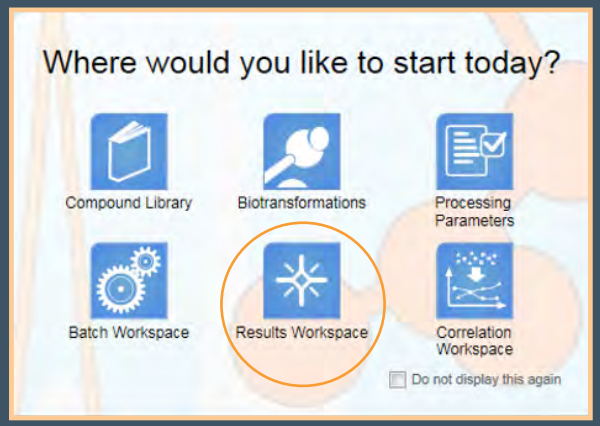
Drug-antibody linker

Cytotoxic Drug Payload

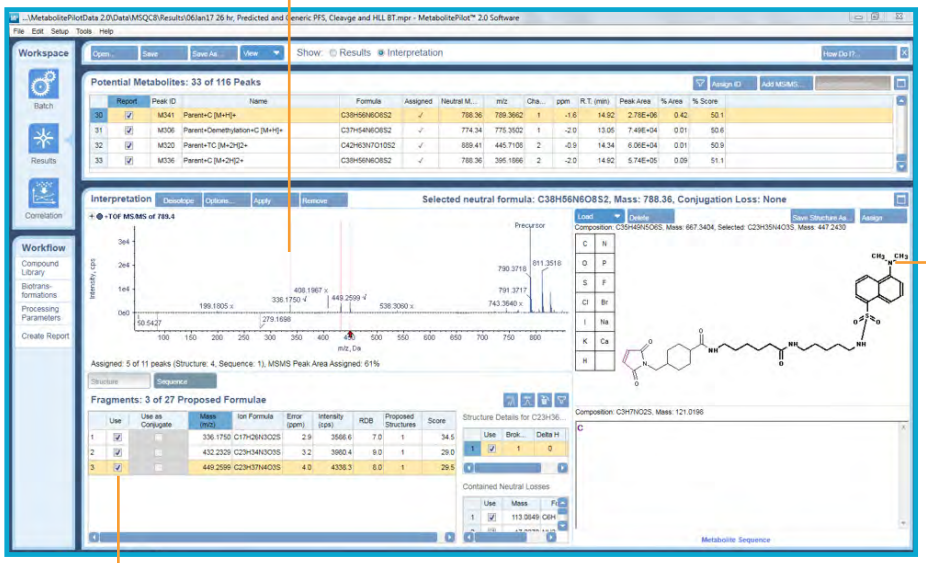


Increase your ADC Confidence

Although ADCs are inherently complex, MetabolitePilot™ Software 2.0 helps to make them easier to analyze. In the Results view, you'll be able to interactively confirm the association of ADC metabolite structures with their MS/MS spectra, so you can be confident in your results.



Confirm your metabolite assignment using the visual representation of the MS/MS, highlighted in the structure pane



Metabolite structure is automatically selected from corresponding MS/MS

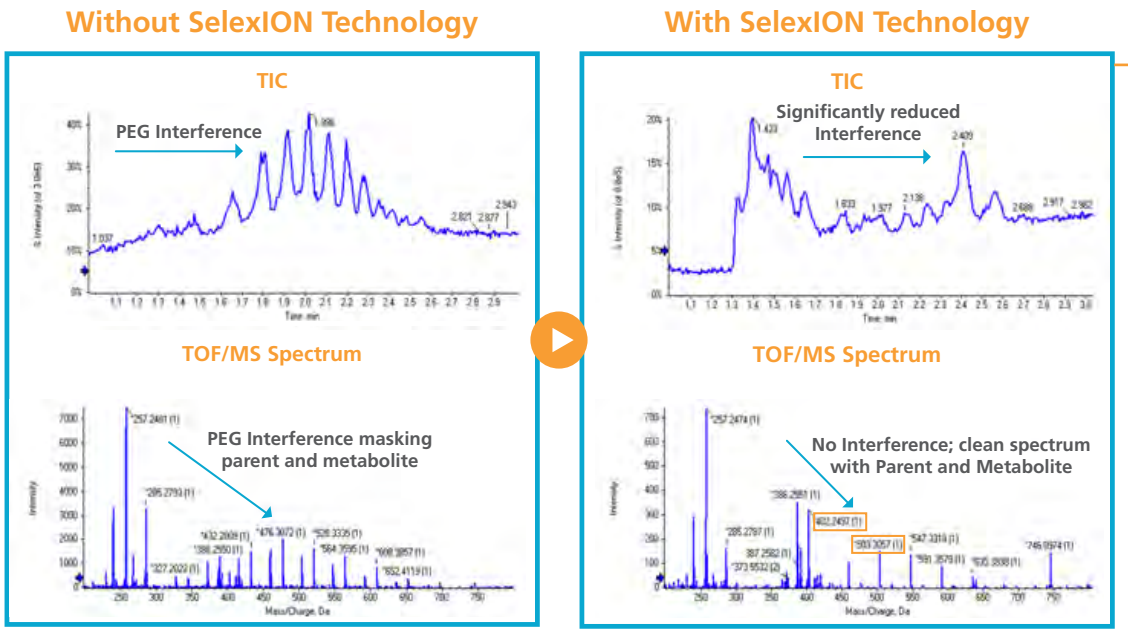
Select the metabolite to view the MS/MS spectrum as well as the structure

MetabolitePilot Software ADC Processing Logic Enables:

- Prediction of catabolite structure for cleavages and biotransformations on cytotoxic drug linkers
- Prediction of hydrolytic cleavages around ADC conjugation sites and specified amino acid modifications
- MS/MS annotations for antibodies and ADCs with combined assignment of small molecule fragments and peptide fragments
- Interactive interpretation tool for MS/MS annotation and assignment

Attain Higher Clarity with Differential Mobility Separation

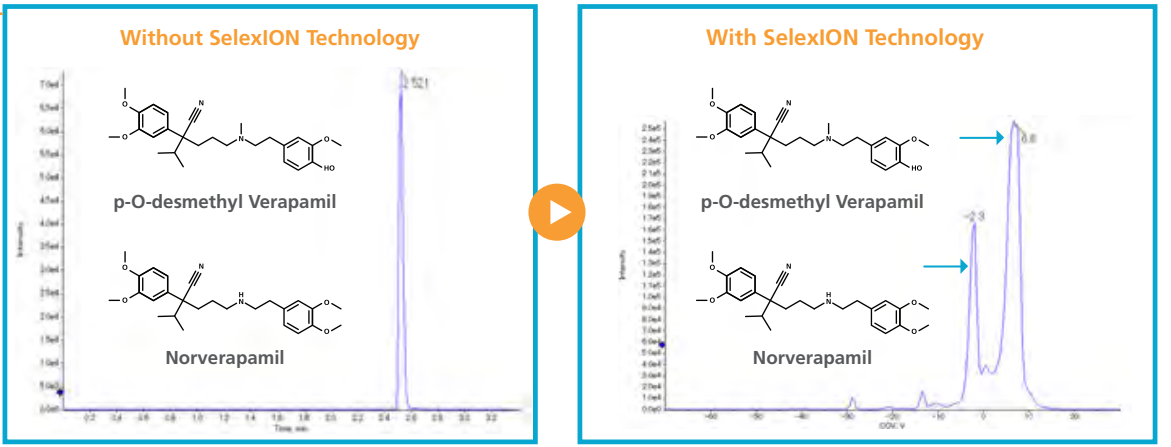
Avoid long runtimes and expensive or difficult LC separation with SelexION® DMS Technology. SelexION Technology can be added to your TripleTOF 6660 in minutes (without breaking vacuum), to help you remove background interferences or separate isobaric metabolite species that can make your metabolism results difficult to interpret.



Analysis of Buspirone metabolites in the presence of PEG excipient

Detect the presence of metabolites that may be masked by high intensity matrix interferences by using SelexION Technology to filter out interfering ions

Confidently identify and quantitate isobaric metabolites using SelexION Technology



Separation of isobaric metabolites, Norverapamil and o-desmethyl verapamil, using SelexION DMS Technology. Extracted ion chromatograms of XIC m/z 441

Your Success is Our Success

We take it personally

As a SCIEX customer you have access to a world-class customer support organization. Wherever you are, we're there with you as a trusted partner to answer questions, provide solutions, and maximize lab productivity.

Our customer support organization has access to the latest product updates, software revisions, methods and repair procedures to make sure that you stay on top of your game.

When you have questions, we have answers.

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For more information about SCIEX Metabolism Solutions, Visit **Sciex.com/biotransform**

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