Waters
THE SCIENCE OF WHAT'S POSSIBLE.™

QUANTITATIVE BIOANALYSIS SOLUTIONS

NO-COMPROMISE TECHNOLOGY THAT'S READY FOR YOUR OPPORTUNITIES

- Rapid and simple bioanalytical method development
- The sensitivity required for the most demanding assays
- Minimize and continuously monitor matrix effects
- Easier and faster identification of peaks
- One-step detection and confirmation of metabolites
- Maximize analytical productivity
- Powerful and reliable data analysis

NEW LEVELS OF SENSITIVITY THAT YOU ALWAYS WANTED FOR BIOANALYSIS. IN AN EASY-TO-USE SYSTEM.

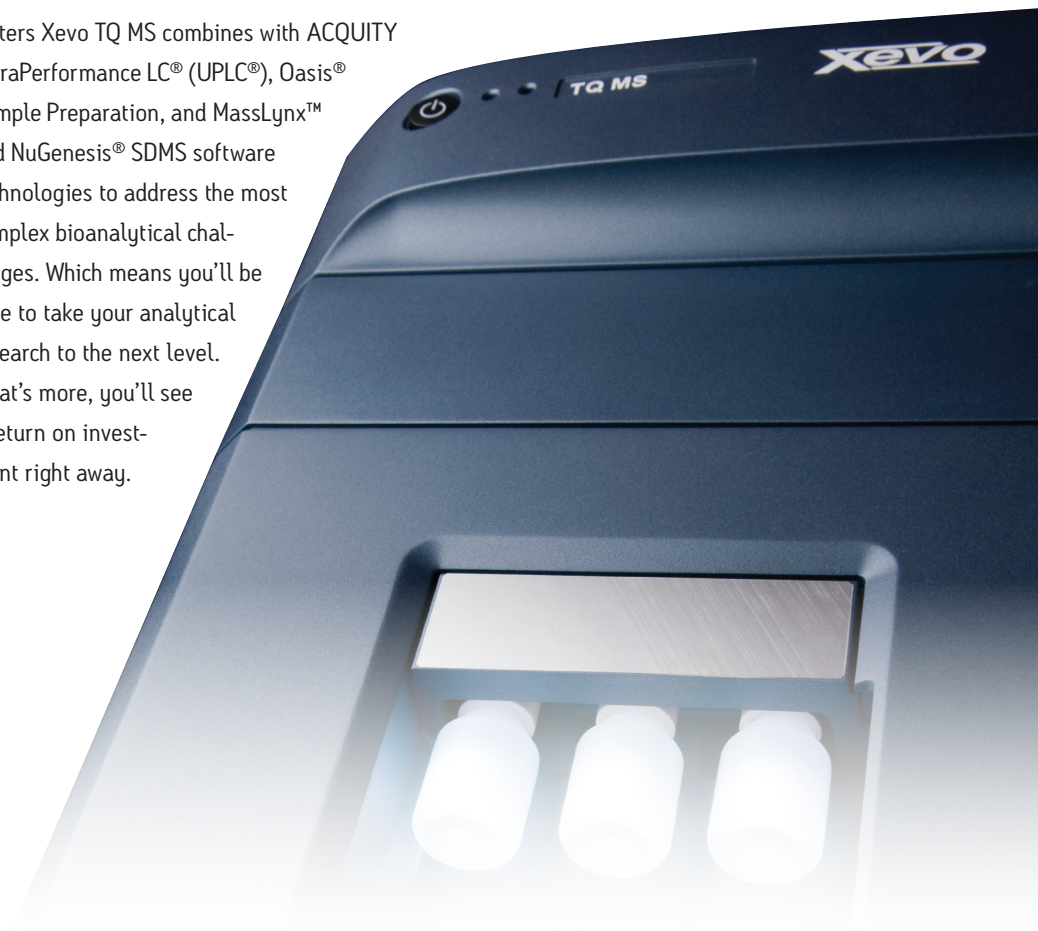
There's a new equation in bioanalysis. It combines the most sensitive tandem quadrupole mass spectrometer available with simplified instrument control, straightforward sample preparation, the power of Waters UPLC® chromatography, and streamlined reporting. Your bioanalytical laboratory will be ready to profit from both higher quality information and better productivity.

Developing a robust and compliant LC/MS/MS assay for regulated quantitative bioanalysis has traditionally been the domain of the experienced analysts. As the business drivers of pharmaceutical companies and the contract research organizations that support them evolve, your laboratories need streamlined bioanalytical solutions that improve results.

OPTIMIZE FOR SPEED, SUCCESS – AND YOUR LABORATORY'S FUTURE

With the introduction of the Xevo™ TQ MS System, Waters delivers the highest sensitivity MS with a unique, easy-to-use, and comprehensive approach to bioanalysis. Our solution synergistically combines each step in the bioanalytical method development process into an easier workflow that produces more robust results and that places your laboratory in a stronger position to address regulatory and data quality needs.

Waters Xevo TQ MS combines with ACQUITY UltraPerformance LC® (UPLC®), Oasis® Sample Preparation, and MassLynx™ and NuGenesis® SDMS software technologies to address the most complex bioanalytical challenges. Which means you'll be able to take your analytical research to the next level. What's more, you'll see a return on investment right away.



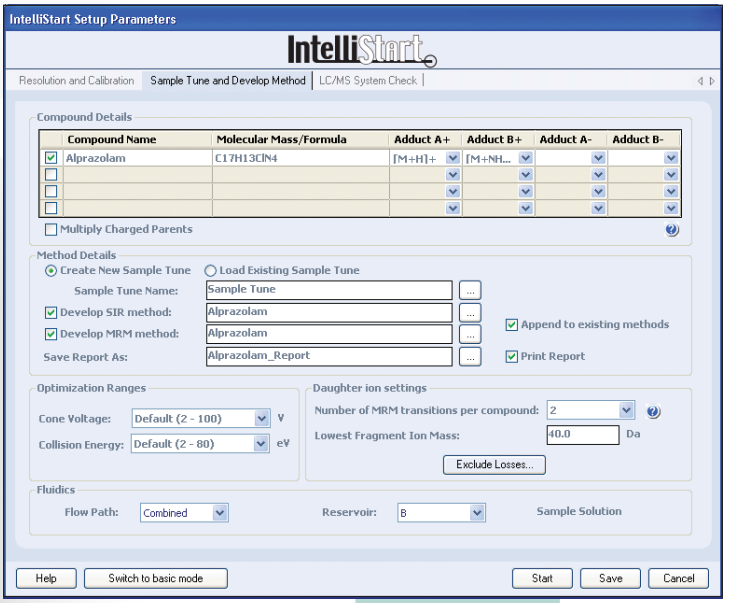
IMPROVE YOUR APPROACH TO BIOANALYSIS. EVERY STEP OF THE WAY.

Bioanalysis plays a critical role in discovery and development, providing drug concentration data to support compound selection, safety assessment, and clinical trials. Success in bioanalysis relies on a robust, sensitive assay with sufficient selectivity and specificity to give the right answers throughout the course of drug development. Rapid, reliable method development allows decisions to be made quickly in drug discovery and improves the efficiency of clinical development. Waters' innovative technologies holistically address all the interdependencies of bioanalysis.

- **ACQUITY UPLC:** Fast, high-resolution separations from the innovators of sub-2 micron chromatography that no one else can match
- **Xevo TQ MS:** Using traveling-wave[1] MS technology, performs simultaneous and multifunctional data acquisition within a timescale compatible with UPLC for the highest sensitivity MS/MS
- **Oasis SPE:** Achieve robust, selective, and sensitive sample preparation and clean-up for excellent recovery and cleanliness with no compromises
- **MassLynx MS Software:** Flexible and comprehensive software to match your data analysis and reporting goals, and improve the productivity of your laboratory

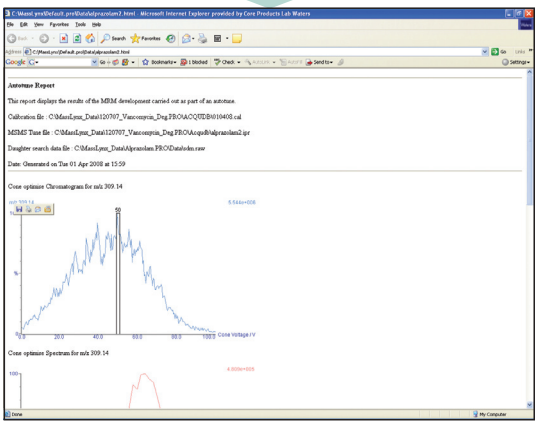
Don't get stuck waiting to develop your MS method.

The development of MS multiple reaction monitoring (MRM) conditions requires the optimization of several instrument parameters to achieve the best mass transitions, including temperature and cone, capillary, and lens voltages. This used to be a long, iterative process that required experienced skills in mass spectrometry. The Xevo TQ MS features IntelliStart™ Technology, which is specifically designed to streamline the MRM method development process. With just four clicks of the mouse, this simple software tool enables analysts with any level of MS expertise to easily develop an MRM method.



Just four clicks to create an MS method

IntelliStart Technology greatly simplifies MS method development. Just four clicks are required to step from creating an MRM method to generating a report.



THE SPEED AND FLEXIBILITY FOR BETTER LC METHOD SCREENING. ONLY WITH UPLC.

In bioanalysis, good chromatography is critical. You need a complete separation of analytes of interest from both endogenous interferences and drug metabolites to achieve a successful bioanalysis method. Good chromatography also gives you the opportunity to increase the selectivity and sensitivity of your LC/MS/MS method.

Since its introduction, ACQUITY UPLC has become the chromatographic system of choice, providing unprecedented throughput, increased sensitivity, and, most importantly, improved data quality and reliability due to its enhanced resolution of metabolites.

Bioanalytical LC method development used to be a challenging process due to its many interrelated variables. Until UPLC. The high resolution, speed, and high pH stability of ACQUITY UPLC BEH Columns with sub-2 µm particles allow the system to quickly evaluate multiple parameters, to optimize the assay to resolve metabolites and the matrix for the analytes of interest.

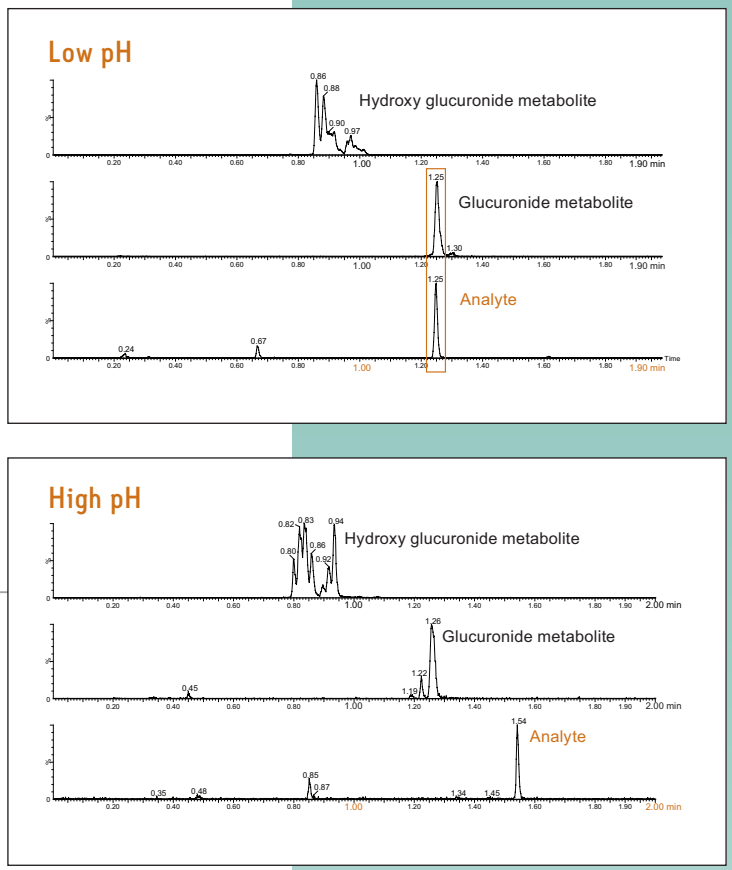
Better sample preparation. For more rugged assays.

The rigorous acceptance criteria placed on a bioanalytical method can be seriously compromised by the cleanliness of the sample when it is introduced to the assay. Sample preparation fulfills three major roles: removal of protein-related materials that may contaminate the chromatography column; elimination of endogenous compounds such as phospholipids that are the major cause of ion suppression or enhancement; and improvement of concentration to increase assay sensitivity. A highly selective sample preparation method is important to minimize matrix effects and sample variability to ensure compliance during method validation.

Using Oasis Solid Phase Extraction (SPE), the correct sorbent and elution protocol for removal of exogenous components can be selected using a very simple, structured, and effective methodology:

- Two Oasis wash protocols combine with four sorbents to provide the flexibility to simplify and streamline the extraction of acids, bases, and neutrals with high analyte recovery, minimized matrix effects, and the cleanest extracts. The result is an effective method yielding a very clean sample.
- The Oasis SPE product family is based around a hydrophilic-lipophilic balanced (HLB) co-polymer backbone to provide excellent water wettability (no drying out), no silanol interactions, stability across a wide pH range, and excellent recoveries for polar and non-polar analytes.
- The combination of Oasis SPE, appropriate mobile phase pH, and UPLC Technology provides significant advantages for reducing matrix effects that result from plasma components and in improving the ruggedness and sensitivity of bioanalytical methods.[3]

Develop a method with maximum resolution in less than 10 minutes



With ACQUITY UPLC and BEH column technology, we were quickly able to determine that high pH yielded the best resolution of two coeluting metabolites of our analyte.

"The excitement in our labs was tangible as the potential impact that [UPLC] could have on the business at HFL was discussed in terms of shorter run-times, greater instrument utilisation, enhanced chromatographic resolution, and perhaps even the elimination of LC-MS/MS matrix effects, scourge of the bioanalyst. For us, this constituted the biggest step change in main-stream chromatography in the last 25 years."[2]

Quotient Bioresearch, contract research organization

CAPABILITIES THAT NO OTHER LC/MS/MS SYSTEM CAN MATCH

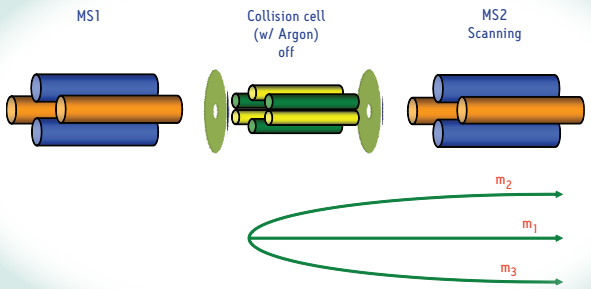
Matrix monitoring: Simultaneously collect full-scan and MRM MS data

Bioanalytical assay performance and reliability is challenged by the inherent variability of the matrix; this can be due to dosing media (in animal studies), species, diet, age, gender, or patient health, among a variety of factors. The impact of matrix effects on the assay can often be difficult to determine and, when using conventional mass spectrometers, requires a repeat analysis using full scan MS. The Xevo TQ MS entirely changes your approach to matrix monitoring.

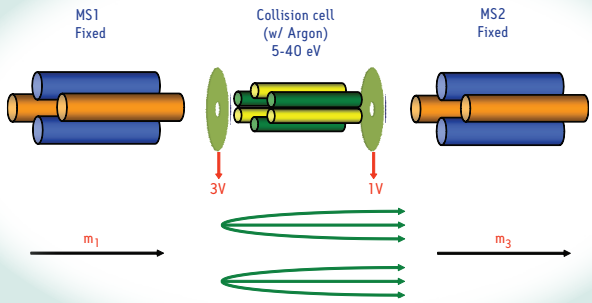
- The tandem quadrupole Xevo TQ MS is equipped with a novel collision cell design where the collision gas is always on. This allows simultaneous collection of full-scan MS and multiple reaction monitoring (MRM) data in a single analysis – without compromising speed, and with no loss in MRM sensitivity.
- The high scan-speed capability of the Xevo TQ MS combines with the Waters T-Wave™ collision cell to allow greater than 20 data points to be collected across both the MS and MRM peaks – in a UPLC peak's timeframe of one to two seconds for accurate and precise quantitation.

QUALITATIVE AND QUANTITATIVE

Full-scan MS



MRM MS



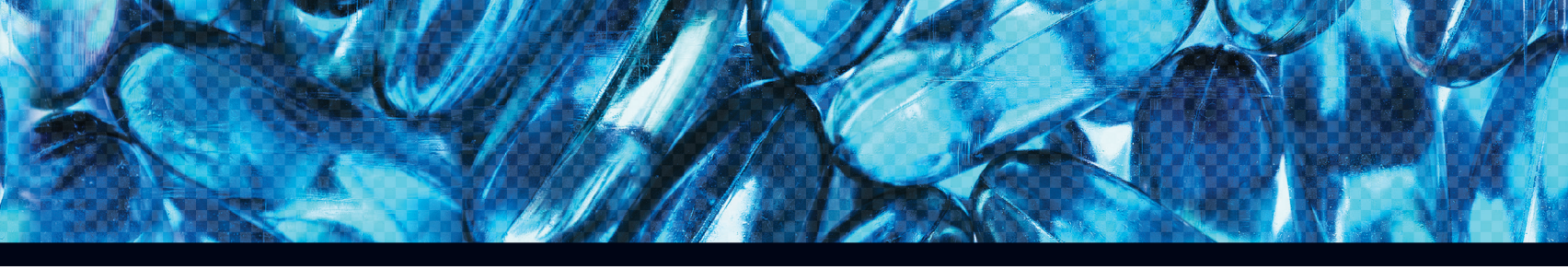
Xevo TQ MS and ACQUITY UPLC: A perfect workflow for bioanalysis

PREPARE

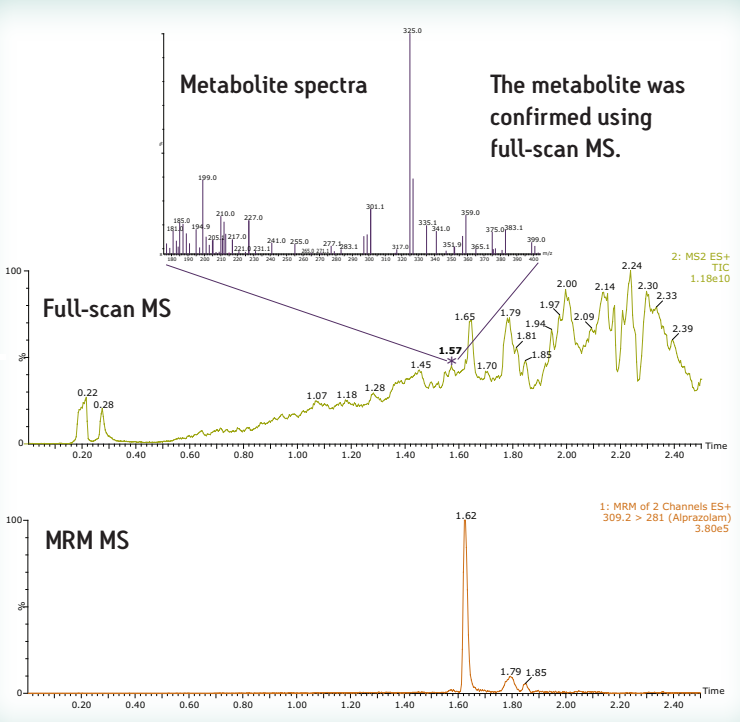
- With IntelliStart and QuanPedia,™ instrument workflow is simplified with automated tuning, method generation wizards, interactive LC/MS method database, and real-time data checking.
- Modern tool-free source simplifies the process of routine maintenance.
- Oasis SPE sample preparation allows you to start with a very clean sample for a more rugged assay.

ANALYZE

- Acquisition speeds of up to 10,000 Da/sec, a unique collision cell design, and ScanWave technology enabling high instrument duty cycles allows the maximum amount of data to be collected in one analytical run.
- High data-capture rate ensures that, even with the narrow peaks of one to two seconds produced by ACQUITY UPLC, sufficient points can be collected across the peak for accurate quantification.
- Fast positive/negative ion switching with ESCi® is ideal for multi-component assays.



DATA, ALL IN ONE RUN



The novel collision cell design of the Xevo TQ MS, where the collision gas is always on, allows for simultaneous collection of full-scan MS and MRM data in a single analysis, without compromising speed, and with no loss in MRM sensitivity. You collect both qualitative and quantitative data in one run.

Metabolite detection and confirmation: Now in a single analytical run

Drug-related metabolites and co-administered therapies can interfere with assay performance and result in inaccurate results if they are not chromatographically resolved from the analyte. Furthermore, recent regulatory guidelines recommend that all metabolites with an exposure of greater than 10% of the active compound are quantified and characterized. Using conventional tandem quadrupole MS instrumentation, multiple experiments are necessary to acquire such quantitative and qualitative data.

- The unique dual-scan MRM capabilities of the Xevo TQ MS allow bioanalytical laboratories to detect all drug-related peaks in an UPLC/MS chromatogram and confirm their identity in one single analytical run.
- The Xevo TQ MS's collision cell technology enables full-scan MS, MRM, and precursor ion scan MS/MS to be performed all in the same analytical run, allowing metabolites to be detected and identified without affecting productivity.

Incurred sample reanalysis: Easier to manage

Effective sample clean-up with Oasis SPE is key to the creation of rugged and robust methods, which should result in fewer incurred sample reanalysis (ISR) failures. When samples must be reanalyzed to meet ISR guidelines, the ACQUITY UPLC System dramatically improves laboratory throughput compared with any other LC system: run times decrease and more samples per MS can be processed, while data quality is maintained.

INTERPRET

- Rapid switching between MS and MS/MS allows the collection of full-scan qualitative data and quantitative MRM data in the same analytical run.
- Product ion confirmation (PIC) increases user confidence and reduces the need for reanalysis by collecting peak characterization data during a quantitative run.

DECIDE

- Rely on Waters' targeted software solutions that make our systems easy to use, easier to maintain, and easiest to synthesize, share, and store results.
- Data processing and quantitation is automated for reliable assay monitoring.
- With software managing your information, decisions can be made faster and with more confidence to support bioanalysis activities through the discovery, development, and manufacturing pipeline.

HOW YOU WORK WITH YOUR INFORMATION IS JUST AS IMPORTANT AS ACQUIRING THE RIGHT DATA

When science means more than great results, Waters software solutions help you manage your information on a day-to-day basis.

	IntelliStart	TargetLynx	QuanOptimize	OpenQuan	NuGenesis SDMS
Single compound assay	✔	✔			✔
100s of compounds per week			✔	✔	✔
Regulated environment		✔			✔
Expert users		✔	✔		✔
Routine or novice users	✔			✔	✔

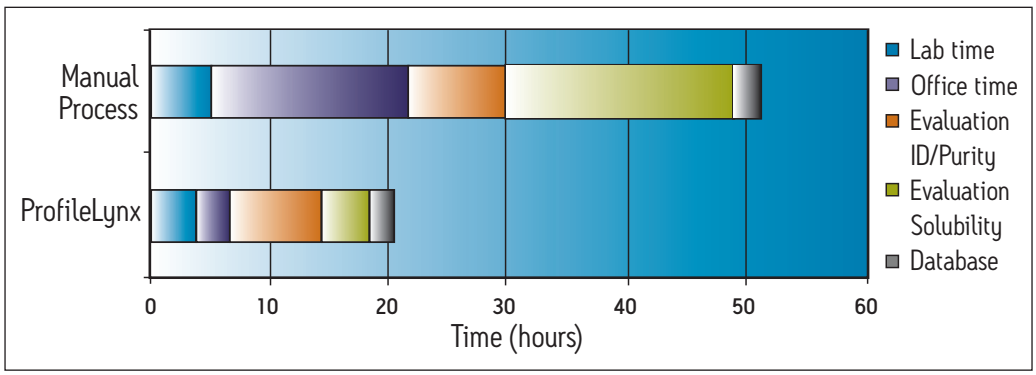
No matter your data analysis challenge, Waters has the solution to address it	
You need to have your data processed and quantitated both quickly and reliably. You need the results in an easy-to-understand format for fast decisions.	With TargetLynx™ Software, the process of quantitation is simpler than ever. The results browser and report generator clearly indicate when samples contain residues that are above minimum reporting levels. Reporting includes automated QC and confirmatory checking, so thousands of calculations and comparisons are done to improve your laboratory workflow.
You have multiple operators running various methods on the same samples. How can you maintain ISR compliance?	TargetLynx's QuanPedia is a secure, extensible, and searchable database for quantitative LC/MS methods information. Each entry in QuanPedia is populated with information that associates a compound name with details of optimal SIR/MRM acquisition methods, acceptable confirmatory ion ratios, appropriate LC methods, and expected peak retention times. For fast-paced, multi-user environments, you have a simple and convenient way to rapidly create complete UPLC/MS data and acquisition methods.
You need to know right away if something is amiss with your samples or with the system.	TargetLynx's QCMonitor is an automated tool that provides quantitative data quality monitoring to determine whether a QC or blank sample is within tolerances specified by the user. It will decide if following samples should be injected or if more checks are required, ensuring the best use of your resources.
Once you've collected all your data, you need to securely store it, while still having easy access to it.	Waters NuGenesis SDMS seamlessly interacts with existing data products for maximum productivity in a secure environment. Experimental details can be recorded in an efficient, legible manner to create a secure, shareable and searchable environment for present and future use.
You have 100s of new compounds coming to your discovery labs every week. How do you quickly and automatically generate MRM methods for them? Once you have the MRM methods, what about quantitation?	QuanOptimize™ Software performs unattended MRM method development on plates of samples. It carries out comprehensive automation of the entire process of quantitation (setup, acquisition, processing, and reporting).
You have many samples coming in but would like to reserve your experts' time for the more complicated problems. Is there any way to open your quantitative UPLC/MS systems to less experienced users?	OpenQuan™ brings the power of QuanOptimize MRM method development and TargetLynx processing to everyone. Anyone can have their compounds quantitated, with reports sent directly to their email account.

Streamlined data management in discovery bioanalysis

Managing the acquisition, processing, and interpretation of data resulting from the analysis of large numbers of compounds provides a significant hurdle to ADME analysis in drug discovery laboratories. Being able to get sample information into the analytical system as well as transferring data and results for downstream processes is critical.

With the advent of high-speed data acquisition by UPLC has come the need to rapidly process that data, including peak detection, integration, quantification, and reporting. This can often be a very time-consuming activity requiring the laborious transfer of data from one software package to another. ProfileLynx™ Software eliminates the need for this data transfer, and any transcription errors, by processing results within MassLynx™ Software. ProfileLynx also handles sample set management, results browsing, and data exporting.

Whether you're doing experiments based on single data points, such as logP, or ones where you need a calibration curve, such as stability, or even ones based on retention time, such as chromatographic hydrophobicity index, ProfileLynx streamlines the process, allowing you to get more compounds analyzed in less time. Compounds can move through discovery to development more quickly.



Chemist's time distribution for solubility screen test (for a set of 48 compounds). ProfileLynx significantly reduces the time taken to process and report ADME screening data, resulting in a faster return of results to the project team.

"By using new tools, including MassLynx templates and the ProfileLynx Application Manager, the chemists are able to reduce the amount of time it takes to do solubility evaluation down from 51 to just 20 hours. The office time was reduced from 17 to 2.5 hours. Because of the improved reporting capabilities of ProfileLynx, the solubility evaluation takes just 4 hours instead of 19."[4]

Physical chemistry group, major pharmaceutical company

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2. UHPLC – Why all the Hype? Houghton R, Grace P. Chromatography Today. 2008 Feb; (5-7): 4.
3. Systematic and comprehensive strategy for reducing matrix effects in LC/MS/MS analyses. Chambers E, Wagrowski-Diehl DM, Lu Z, Mazzeo JR. J Chromatogr B Analyt Technol Biomed Life Sci. 2007 Jun 1; 852 (1-2): 22-34.
4. ProfileLynx Application Manager for MassLynx Software: Increasing the throughput of physico-chemical profiling. Waters. 2007; 720001793en.

For additional information about Waters solutions for bioanalysis:

- A Guide to Effective Method Development in Bioanalysis. Waters. 2008; 720002710en.
- Xevo TQ MS Pharmaceutical Application Notebook. Waters. 2008; 720002826en.

www.waters.com/bioanalysis

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