

Waters

MICROMASS QUATTRO *micro*™ API TANDEM QUADRUPOLE SYSTEM

The new analytical paradigm

Increasing throughput targets coupled with the high cost of laboratory space, scarcity of qualified staff and the quest for knowledge rather than "just" data is forcing a new analytical paradigm in scientific enterprises.

Looking for a smarter way to overcome these challenges in analytical LC-MS-MS?

- Need for intelligently optimized systems
- Pressure to meet increasing throughput targets
- Necessity to rapidly cross-train analysts
- Demand for better sensitivity and LOQs
- Requirement to operate in a 21 CFR 11 environment



*The next generation of API
LC-MS-MS... smaller,
smarter, wired.*

LC-MS-MS instruments with traditional "data systems" that efficiently converted sample mountains into raw data mountains are being superseded with networked "Sample to Knowledge" converters like the new Micromass® Quattro *micro*™ API. These new systems are a fusion of compact "intelligent" mass analyzers and client-server Mass-Informatics™ operating within the Global e-MS™ workspace.

Smaller

The Micromass Quattro *micro* API incorporates the finest high precision tandem quadrupole mass analyzer technology in only 15 3/8" (390mm) of linear bench space – 1/3 the width of existing instruments! The mass analyzer has a m/z range of 2-2000 as standard.

Quattro *micro*™ API



Quattro *micro*™ GC



Micromass LC-MS-MS and GC-MS-MS
benchtop solutions.

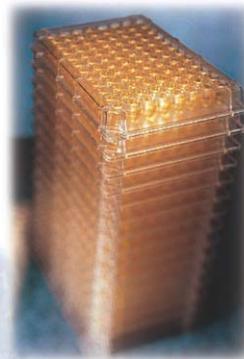
Residues
Toxicants
Impurities
Pharmaceuticals
Organics
BioPolymers
BioMarkers



The Micromass Quattro *micro* API delivers the latest evolution of the acclaimed Micromass brand of tandem quadrupole analyzer technology... enabling smarter use of space to maximize analytical power while minimizing footprint.

New features include:

- A state-of-the-art differentially pumped vacuum system featuring singular air-cooled, split-flow turbomolecular pump technology
- Vertically mounted liquid inlet probe minimizing system footprint, reducing the length of connecting tubing and the potential for peak broadening
- Integrated syringe pump with Masslynx™ control and autostop facility
- Electronically controlled injector valve
- Digital control of source gas flow rates
- Expanded diagnostic capabilities
- Ergonomic system architecture for improved serviceability
- IonSABRE™ ultra high efficiency APCI



The Micromass Quattro *micro* API design is a step change advance over the classic "triple quadrupole" concept. The traditional quadrupole collision cell is replaced with a hexapole for enhanced ion containment and transmission. Hexapole technology, used in conjunction with proprietary ion counting threshold software, delivers superior sensitivity and enhanced resolution for precursor ion scanning experiments. An example is shown in Figure 1, where a 2-3 fold increase in sensitivity is observed when scanning for precursor ions of the 156m/z fragment of a series of sulfonamide drugs.

The high performance analyzer is complemented with an optically coupled, low noise/high gain orthogonal detector that approaches 100% efficiency for the detection of single ions. In this proprietary system the conventional electron multiplier has been superseded by a photomultiplier with a 10 year lifetime - simultaneously maximizing sensitivity and minimizing the cost of ownership.

The Atmospheric Pressure Ionisation (API) source features patented **Z SPRAY**™ inlet technology for LC-MS-MS. The dual orthogonal geometry of **Z SPRAY** enables prolonged LC-MS-MS analysis of samples in complex biological or environmental matrices. **Z SPRAY** can even tolerate involatile buffers - saving time and money in HPLC method

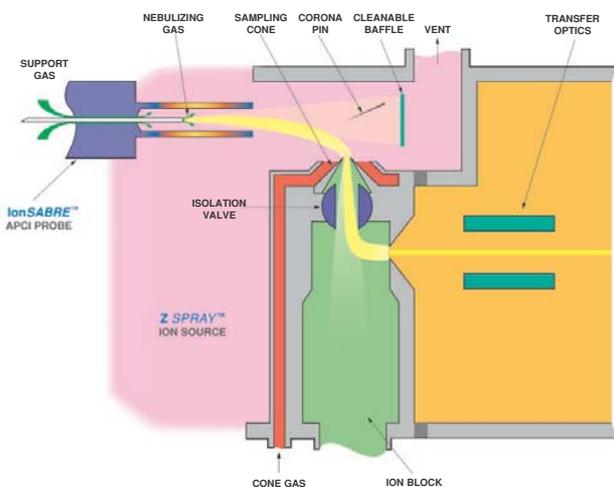
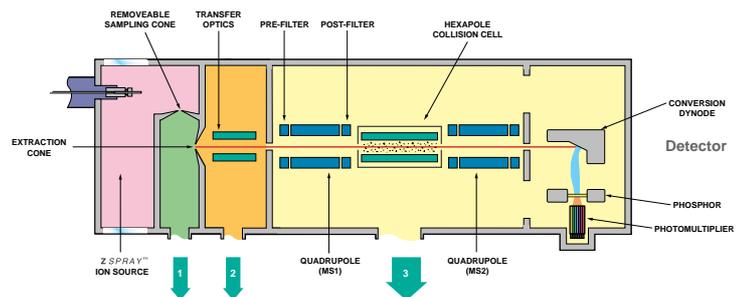
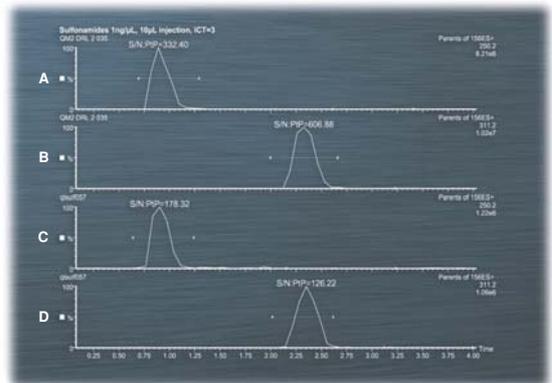


Figure 1: Precursor ion scanning of a sulfonamide mixture (Precursors of m/z 156). Traces A+B were recorded using a Micromass Quattro *micro* API and show a 2-3 fold increase in sensitivity compared with equivalent analyses on a Quattro LC (traces C+D).



redevelopment. **Z SPRAY** is the only API interface available with an in-source isolation valve allowing the sampling cone to be rapidly removed for routine cleaning without breaking vacuum – maximizing uptime. The inlet probe is mounted vertically for maximum space saving.

Over 4000 **Z SPRAY** based instruments are in MS laboratories world-wide, making it the number one LC-MS interface of choice. Figure 2 demonstrates the unrivaled robustness of the **Z SPRAY** source when dealing with complex matrices and buffer systems.

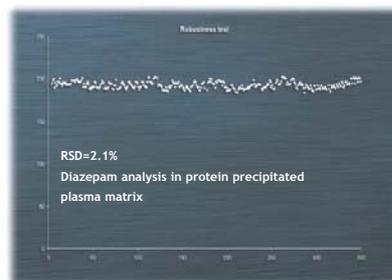


Figure 2: **Z SPRAY** Robustness.

Smarter

The Micromass Quattro *micro* API uses proprietary Embedded Personal Computer Acquisition System (EPCAS™) for intelligent data acquisition and dynamic instrument control. The tandem quadrupole system contains only the finest technology - EPCAS is also at the heart of the Micromass Q-ToF™ family^{2,3} of ultimate LC-MS-MS instruments. EPCAS technology enables unprecedented flexibility for automated analysis of complex mixtures using Data Directed Analysis (DDA™).

In automated LC-DDA-MS™ analyses, the system continuously records "survey" (typically MS) spectra throughout a chromatographic run, to dynamically identify candidates for MS-MS analysis. Ions shortlisted for MS-MS analysis can be compared with a list of known background ions (such as phthalates) to exclude redundant analyses. When a component of interest elutes, the analyzer switches from MS to MS-MS mode.

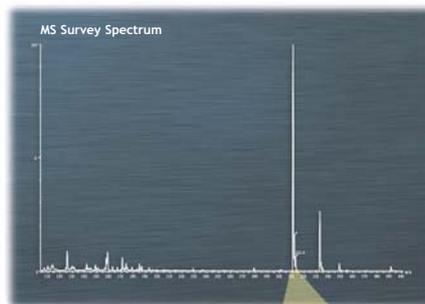
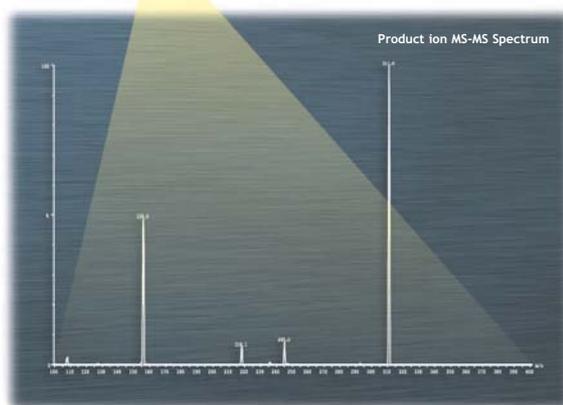


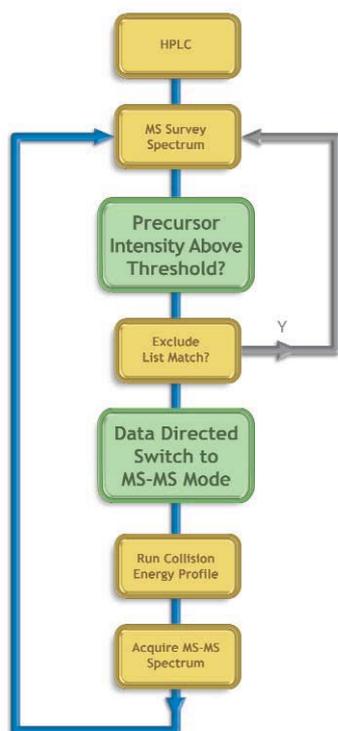
Figure 3: Data Directed Analysis (DDA).



Simultaneously, the system selects collision energy values for each targeted precursor ion and records a product ion spectrum (Figure 3). After the MS-MS analysis is completed the system returns to the selected survey mode to hunt for the next candidate. The most commonly used survey mode is full scan MS. Precursor ions that have been selected and analyzed may be dynamically appended to the exclusion list to prevent duplicate analyses.

Open Access MS-MS

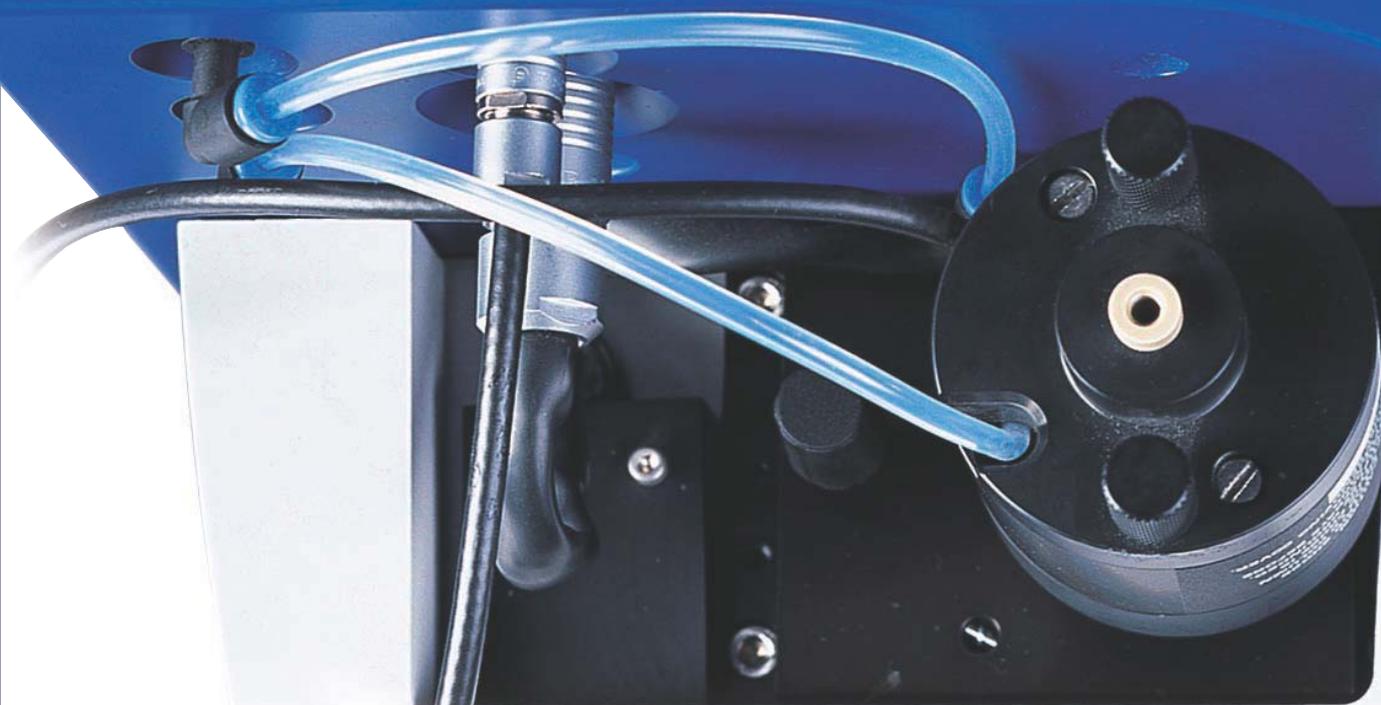
Compound identification is made accessible, as never before, with walk-up open access MS-MS on the Micromass Quattro *micro* API. Samples can be submitted through OpenLynx™ Application-Manager™ with information on molecular weight or formula to automatically generate product ion spectra by LC-MS-MS.



DDA™

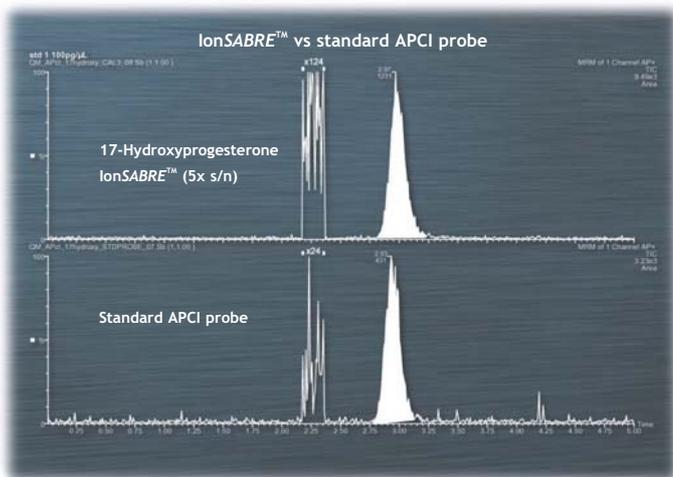


Z SPRAY ion source.



IonSABRE™ APCI

ESI is the most widely used API technique for sensitive, general analysis of polar compounds, however, APCI maintains an important role in the analysis of less polar species. The new IonSABRE high efficiency APCI inlet probe for the Micromass Quattro *micro* API delivers significant improvements in sensitivity for these analytes. The IonSABRE is a high power output APCI probe employing a new, optimized heater aspect ratio with thermally balanced vaporization and fully symmetrical heating to deliver the best LOQs in quantitative bioanalysis.



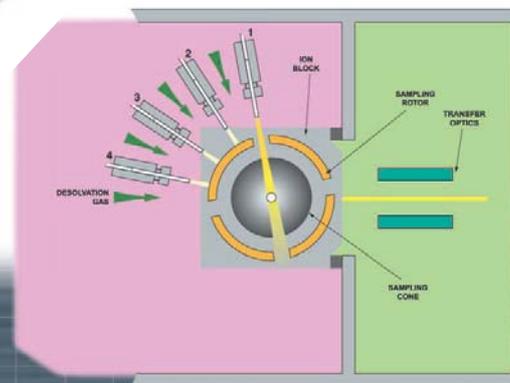
*The new IonSABRE APCI probe delivers better sensitivity for less polar compounds such as steroids. This example demonstrates a 5x improvement in signal-to-noise for 17-hydroxyprogesterone using IonSABRE on the Micromass Quattro *micro* API.*



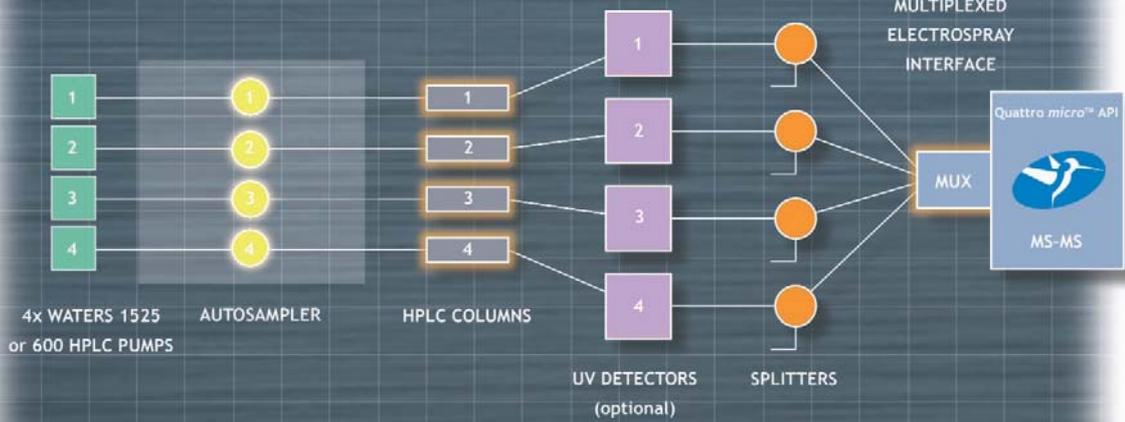
MUX-technology interface.

MUX-technology™ ...maximizing productivity

Using the proven MUX-technology option upgrades your Micromass Quattro *micro* API to a 4-channel automated parallel LC-MS-MS system for very high throughput analyses. The 4-channel multiplexed electrospray inlet allows you to interface four HPLC systems in parallel to one tandem quadrupole - leveraging system productivity by a factor of four without increasing analyzer footprint. MUX-technology is fully compatible with Metabolynx™ and Quanlynx™ Application Managers™ ...turning data into knowledge in parallel!



Quattro micro API
4 Channel MUX system



MassLynx™ 4.0

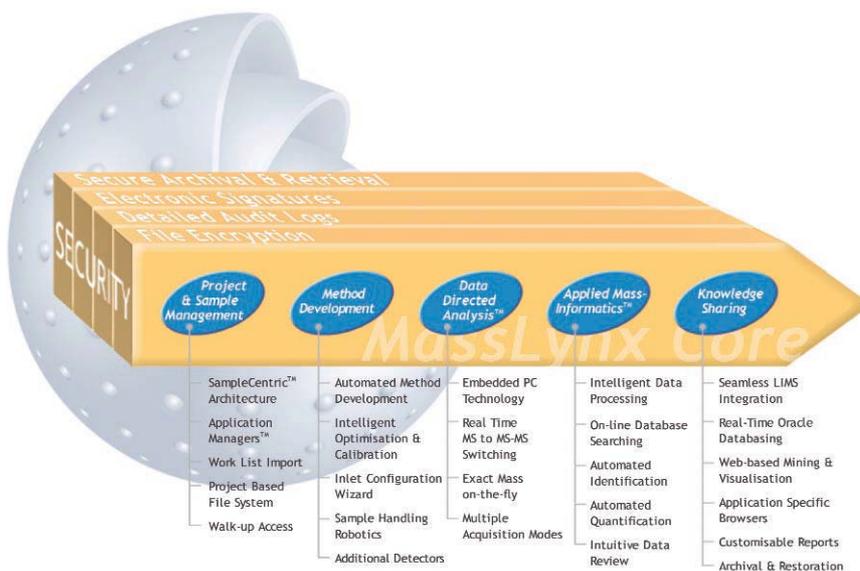
MassLynx 4.0 is the next generation of the market leading mass spectrometry software from Waters - pioneers in the science of Mass-Informatics. MassLynx 4.0 is optimized for Microsoft Windows® XP and functionally validated for Windows NT / 2000.

With over 1000 refinements, MassLynx 4.0 introduces the "targeted" Mass-Informatics concept. Featuring a ground breaking context sensitive user interface, MassLynx 4.0 makes the most powerful mass spectrometry techniques accessible - with Application-Managers optimized using simple 'customization wizards'.

Application-Managers

The "core Mass-Informatics engine" of MassLynx 4.0 can be enhanced with a range of optional "plug-in" Application-Managers for many key tasks in pharmaceutical and life science research (e.g. proteomics, walk-up LC-MS-MS, metabolism studies and quantitative bioanalysis).

The Application-Managers enable each user to effortlessly select and augment only the relevant tools from the powerful "core Mass-Informatics engine"- enabling the analysts to focus the full power of targeted Mass-Informatics on their challenge with the minimum training overhead.



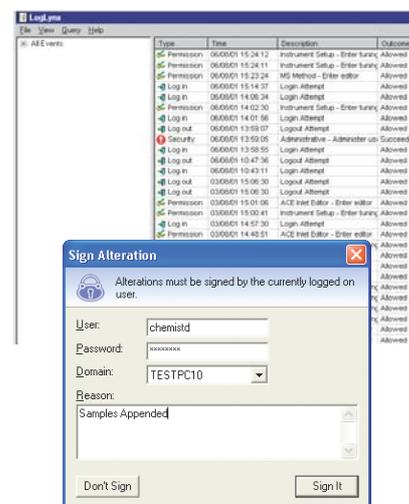
Secure quantification

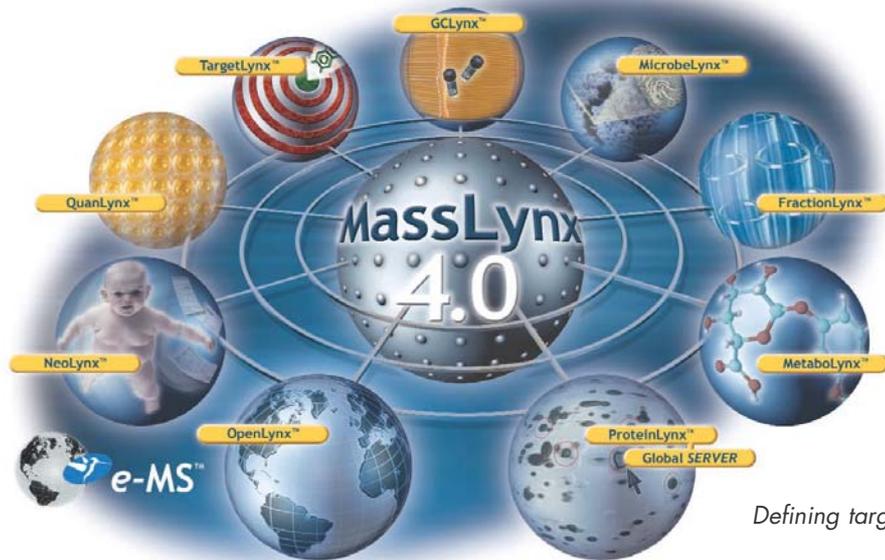
The QuanLynx Application-Manager provides an automated systematic solution for accurate and precise quantitation in 21 CFR Part 11 compliant enterprises.

QuanLynx 4.0 is the most fully featured, secure Application-Manager for quantitative bioanalyses in preclinical and clinical drug development. Security features include: user-privilege selection, checksum data and method file encryption, electronic signature support, date/time-stamped audit logs for tracking all user events/file movements, and automated utilities for secure archival and valid restoration.

Advanced metabolite ID

Metabolynx is the MassLynx 4.0 Application-Manager for metabolite identification and impurity analysis. Utilizing an advanced control comparison approach, Metabolynx is able to search complex chromatographic and spectral data for expected and unexpected metabolites. Metabolynx aggregates all of the relevant tools in a simple browser-based environment, giving you access to putative biotransformations, molecular structures and data directed MS-MS to boost your productivity.





Defining targeted Mass-Informatics.

The Global e-MS workspace

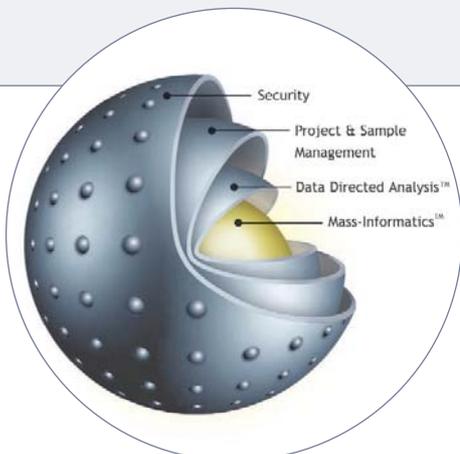
Many scientific enterprises are adopting common platforms to facilitate virtual integration of knowledge from a multiplicity of sources. Windows NT, HTML and XML are enabling this process - providing the *de facto* standard for the Global e-MS Consortium's workspace. MassLynx 4.0, Waters' groundbreaking targeted Mass-Informatics technology, provides the exclusive MS vendor portal to the Global e-MS workspace ...with the largest portfolio of compatible software platforms.

Secure LIMS access

QuanLynx now integrates seamlessly with laboratory information management systems (LIMS). Utilizing a direct electronic interface within QuanLynx, a LIMS can now access your quantitation results directly for secure transfer, ensuring full audit trail compatibility and avoiding unsecure file generation.

Secure data archival

Secure LC-MS-MS data storage is facilitated with MassLynx 4.0's integral data archival and restoration tools. Operating within a secure environment, MassLynx files and QuanLynx reports can be automatically scheduled for secure back-up to/from a remote location with tamper-proof audit trails. Additional tools for secure multi-technique, enterprise wide data management are provided by the e-MS consortium partners.



QuanLynx™ Application-Manager

Quantification does not end with the acquisition of high sensitivity LC-MS-MS data. QuanLynx is the most fully featured Application-Manager, designed to manage your quantitation projects from sample submission to secure archive ...from QuanOptimise™ automated method development to Waters' advanced Apex Track™ peak integration algorithm.

QuanLynx now produces a single, secure report file containing all of the related LC-MS-MS chromatograms, calibration plots and experimental records. The interactive browser allows rapid review in a slide show format, with full audit logging of all report editing and file movements.

Whether you want an open access early screening system or a tamper-proof advanced quantitation package for clinical development, QuanLynx's expansive functionality is easily customized to present a simple interface to suit your application.

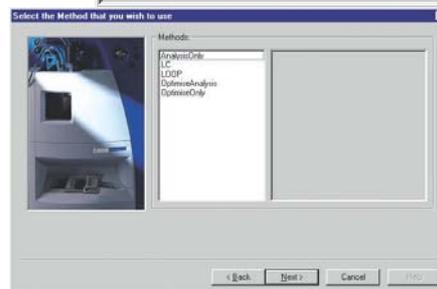
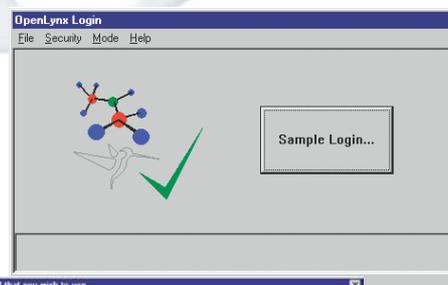
Automated quantification

With the vast range of compounds now being screened, a major bottleneck in the process is the optimization of LC-MS-MS methods for each individual compound.

QuanOptimise is in use in both high and low throughput laboratories worldwide for automating the process of method development, followed by automated calibration and quantification of samples with results presented in the QuanLynx rapid-view browser.

Open Access quantification

If you want to take things a step further, Open Access Quan now provides your laboratory with a simple walk-up LC-MS-MS system. Let your chemist choose an existing method, or simply activate QuanOptimise during sample log-in to develop a new method automatically. Results are e-mailed directly to the chemist for review in the stand-alone QuanLynx browser - no need to have MassLynx installed.



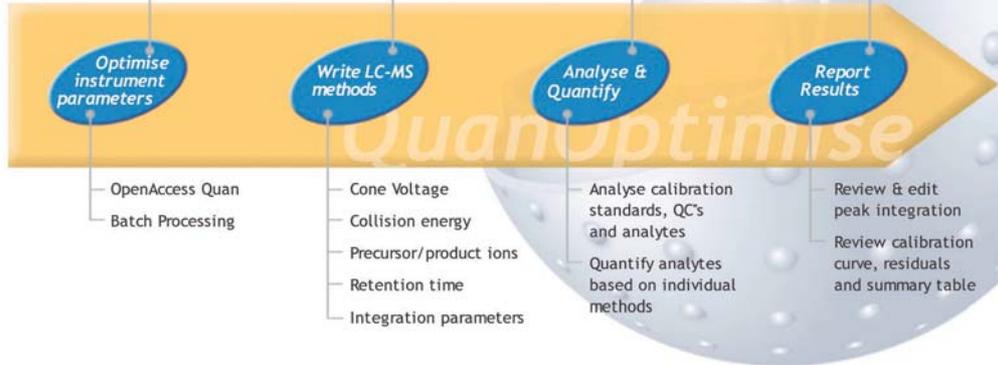
QuanLynx™	Drug Discovery			Clinical Development	
	CaCO ₂ Adsorption Studies	Clearance Profiling	In vitro metabolism screening	In vivo DMPK	Impurity monitoring
Open Access	•	•	•	○	○
Batch Processing	•	•	•	•	•
QuanOptimise™	•	•	•	•	•
MassLynx™ Quantify	○	○	○	○	○
ApexTrack Peak Detection	•	•	•	•	•
21 CFR 11 Compatible Security Tools	N/A	N/A	○	•	•
High throughput MIX-compatible	•	•	•	○	○

Automatically tune cone voltage, collision energy & select SIR or MRM ions for standard samples

Write LC-MS methods for each compound
Run standards on column
Write Quan methods

Run LC-MS-MS
Plot calibration curve
Quantify analyte samples

Rapid view
QuanLynx™ browser
Customised electronic or printed report



Sample summary table

#	Name	Sample Text	ID	Type	Std. Conc.	RT	Area	IS Area	Response	Flags	ng/ml	%Dev
1	ASSAY01	plasma blank	ID1	Blank				930.147				
2	ASSAY02	0.2pg/ml std	ID2	Standard	0.200	2.79	101.248	883.674	0.115	bb	0.2	0.8
3	ASSAY03	0.5pg/ml std	ID3	Standard	0.500	2.79	230.680	908.750	0.285	bb	0.5	4.2
4	ASSAY04	0.75pg/ml std	ID4	Standard	0.750	2.79	294.803	753.757	0.391	bb	0.7	-4.1
5	ASSAY05	1pg/ml std	ID5	Standard	1.000	2.79	415.267	759.225	0.547	bb	1.0	-1.1
6	ASSAY06	2pg/ml std	ID6	Standard	2.000	2.79	869.522	824.580	1.055	bb	2.0	-1.9
7	ASSAY07	5pg/ml std	ID7	Standard	5.000	2.79	2486.259	916.398	2.713	bb	5.1	1.3
8	ASSAY08	10pg/ml std	ID8	Standard	10.000	2.81	4258.552	822.216	5.177	MM	9.7	-3.2
9	ASSAY09	15pg/ml std	ID9	Standard	15.000	2.79	6389.434	801.626	7.971	bb	14.9	-0.6
10	ASSAY10	0.3pg/ml GC	ID10	GC	0.300	2.81	142.058	776.791	0.183	bb	0.3	9.9

Date	Time	Event	Signed	Details	User	Comments
07-Sep-01	09:39:54	Process Quantity	No		TU-DOMANI_PREECES	
07-Sep-01	09:39:54	Dataset Created	No		TU-DOMANI_PREECES	
07-Sep-01	09:40:17	Dataset Saved	No	Saved to 'C:\MassLynx\testquan01.qdt'	TU-DOMANI_PREECES	
07-Sep-01	09:40:49	Dataset Saved	No	Saved to 'C:\MassLynx\Quantify\pro\testquan01.qdt'	TU-DOMANI_PREECES	
07-Sep-01	09:41:09	Peak modified	Yes	Sample ASSAY06, Compound Parent, RT:2.805	TU-DOMANI_PREECES	Peak tilling
07-Sep-01	09:41:31	Calibration point Excluded	Yes	Compound Parent - Sample: ASSAY38	TU-DOMANI_PREECES	Exceeds allowed % deviation
07-Sep-01	09:41:59	Dataset Saved	No	Saved to 'C:\MassLynx\Quantify\pro\testquan01.qdt'	TU-DOMANI_PREECES	

Secure access system lock

Experimental record

Audit log

Interactive peak integration for internal standards & analytes

QuanLynx browser.

Active residuals plot

Calibration curve

Metabolyx™ Application-Manager

The multiple modes of operation of the Micromass Quattro *micro* API make it ideally suited to identification of a wide range of compounds. From full scan LC-MS searching for unknown components, to class-specific identification based on precursor ion and neutral loss scans, through to product ion MS-MS to aid structural elucidation.

Metabolyx Application-Manager features advanced tools to extract meaningful information from these complex data sets, distilling large LC-MS raw data files into simple, manageable reports. Using innovative control sample comparison and combined chromatographic and spectral searching, Metabolyx easily identifies new components, flagging them as potential metabolites or impurities.

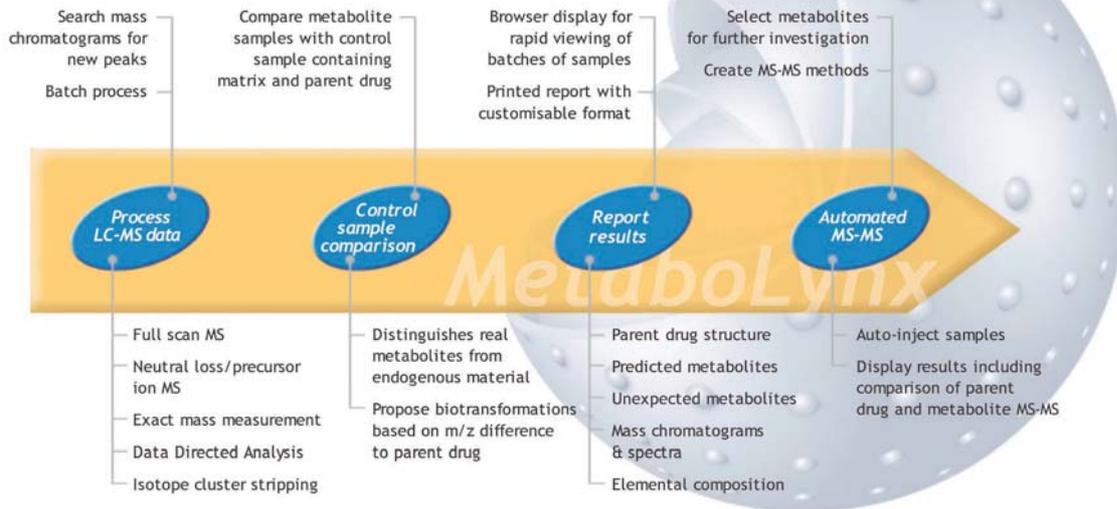
Further investigation can be carried out by automatically scheduling MS-MS analyses on flagged components. Data Directed Analysis (DDA) may also be employed to acquire LC-MS and MS-MS information from a single experiment and processed by Metabolyx to reveal structural similarities between metabolites and their parent drug.

Metabolyx works for you by:

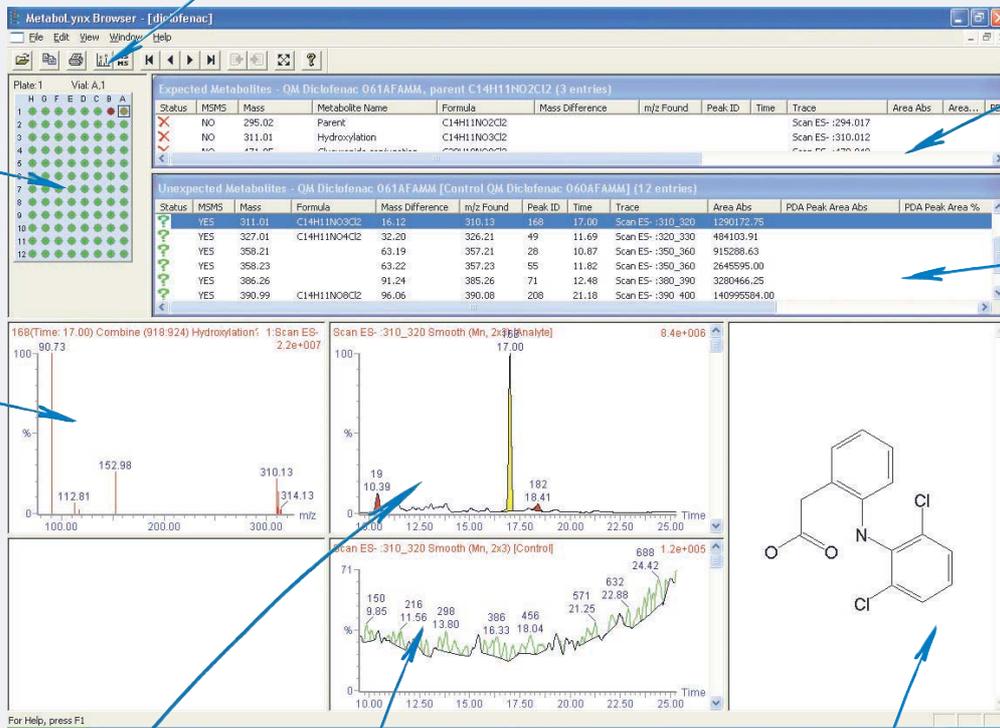
- Interrogating LC-MS data for targeted metabolites
- Correlating metabolized sample data with a control sample
- Pinpointing untargeted biotransformations using:
 - 3D LC-MS metrics - mass/intensity/retention time
 - Exact mass measurement
 - Calculated elemental composition
 - Isotopic pattern targeting for enhanced selectivity
 - PDA data
 - Up to 4 auxiliary (analog input) detectors e.g. radiochemical, fluorescence
- Generating and executing method files for automated MS-MS verification of metabolite assignments with:
 - Comparison with parent MS/MS
 - Flagging of common product ions and neutral losses
- Integrating chromatographic peaks for semi-quantification
- Electronic reporting/distribution of results.



Automated
Metabolite
Identification



View MS-MS results & parent drug comparison



Expected metabolite search results

Found unexpected compounds

Selected metabolite mass chromatogram

Control sample comparison - no compound detected at similar retention time

Active molecular viewer

TargetLynx™ Application-Manager

Since the results of quantitative analyses may have environmental, health or legal implications, regulatory bodies often require the implementation of a range of Quality Control checks. These checks provide confidence that the results are correct but are time consuming to perform.

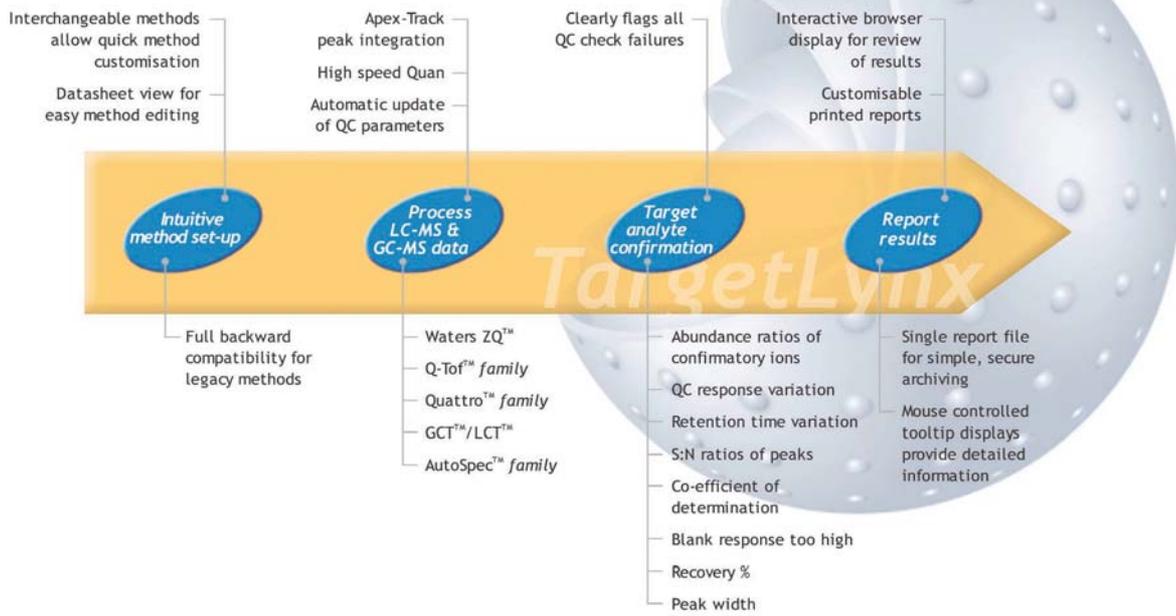
TargetLynx is a dedicated Application-Manager that offers all of Masslynx's advanced quantitative functionality, together with a complete range of QC checks that are performed automatically. The data may be reviewed and processed from a single browser report. An overview table shows the analytical data and clearly flags any QC failures. Detailed information is easily accessed for each result by the use of tooltip displays and customized printed reports may be generated.

TargetLynx is able to rapidly identify:

- Samples where analytes are above a specified Maximum Reporting Level
- Samples where analyte confirmatory ions are outside abundance ratio limits
- Samples where analyte signal-to-noise ratios are below a threshold
- Samples where analyte retention time or relative retention time is outside limits
- Samples where analyte concentration is below LOD and LOQ thresholds
- Analytes where the standard deviation of response for QC standards is too large
- Samples where the blank response is too high
- Samples where the recovery percentage is out of limits
- Samples where the peak width (at half height) is out of limits



Quality Control Confirmation



Sample summary table

#	Name	Type	Std. Conc	RT	Area	IS Area	Response	Flags	ppb	%Dev
9	CAP-spike_009	Standard	0.500	4.31	1224.194		1224.194	bb	0.5	3.8
10	CAP-spike_010	Standard	0.500	4.31	1170.179		1170.179	bb	0.5	-0.9
11	CAP-spike_011	Standard	1.000	4.34	2318.855		2318.855	bb	1.0	-0.7
12	CAP-spike_012	Standard	1.000	4.31	2414.737		2414.737	bb	1.0	3.4
13	CAP-spike_013	Standard	1.000	4.33	2483.662		2483.662	bb	1.1	6.4

	Cap_D5	CAP
CAP-spike_008	0.991588	0.508449
CAP-spike_009	0.982612	0.516832
CAP-spike_010	1.023777	0.495442
CAP-spike_011	0.970450	0.992856
CAP-spike_012	0.982618	1.034376
CAP-spike_013	0.996915	1.064223

Chromatogram: CAP peaks at 4.31, 1170.18, 68911, 4.33, 561.80, 34281. MRM of 4 channels, ES- 320.6 > 194.15, 3.569e+003.

Calibration curve: $2309.3 \cdot x + 26.0571$
 Response type: External Std, Area
 Curve type: Linear, Origin: Include, Weighting: 1/x, Axis trans: None

Residuals plot showing data points and a linear fit line.

QC parameters flagged when out of limits

Out of range tooltip

Interactive peak integration

Residuals

Calibration curve

Targetlynx browser.

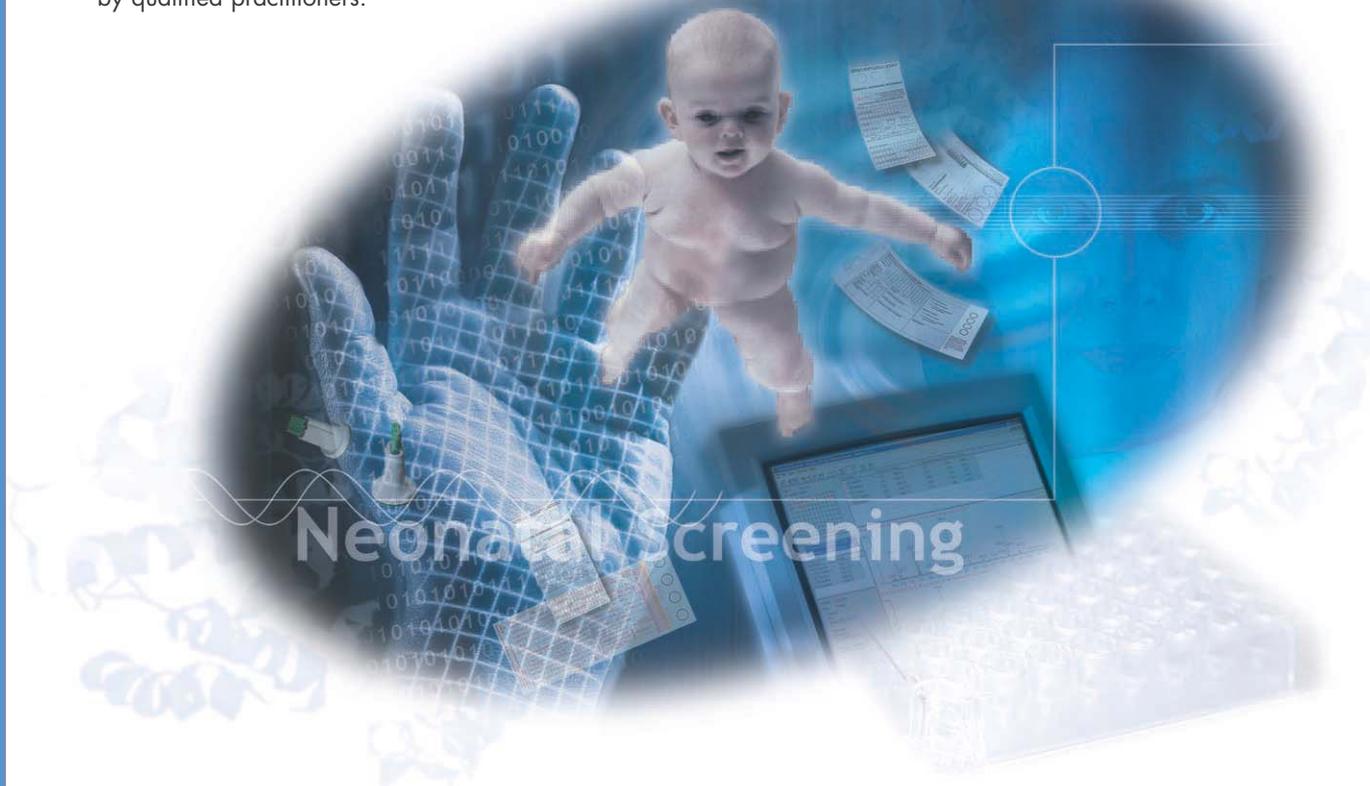
NeLynx™ Application-Manager

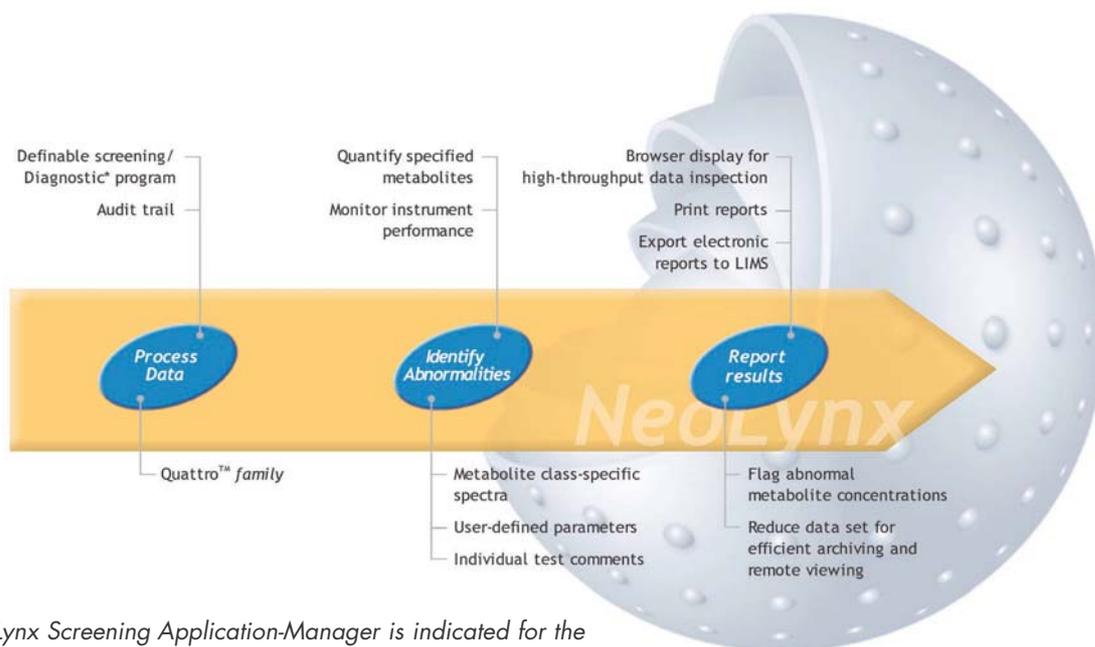
The NeLynx Screening Application-Manager is indicated for the quantitative measurement of phenylalanine and tyrosine in neonatal blood samples by tandem mass spectrometry using the Micromass Quattro *micro* API.

This automated approach for the rapid and specific detection of phenylketonuria was developed in collaboration with leading neonatal research laboratories. Measurements of phenylalanine are used in the diagnosis and treatment of inherited phenylketonuria. Additionally, measurements of tyrosine can be used as an adjunct to the measurement of phenylalanine in reducing the number of false-positive results with NeLynx Screening Application-Manager.

NeLynx Screening Application-Manager software coupled with a Micromass Quattro *micro* API mass spectrometer offers the simplest solution for integrated sample management, ESI MS-MS data acquisition and data analysis to rapidly provide clear metrics for interpretation by qualified practitioners.

The NeLynx Screening Application-Manager is used to efficiently schedule the acquisition of ESI MS-MS data and its reduction to metrics that can readily be displayed and assimilated with an intuitive results browser. A simple-to-program test file causes NeLynx to flag samples that are out-of-range, and the NeLynx Browser allows the user to interrogate individual results with a single mouse click. The NeLynx Screening Application-Manager is an enhancement option for MassLynx Mass-Informatics software - with over 8000 users world-wide. MassLynx integrates easily with laboratory information management systems (LIMS) to import worklists and export results. Processed data and results are stored in a file structure that enables simple archiving/retrieval and extensive customization of both electronic and printed reports. The NeLynx Screening System is backed with an extensive range of application support services and training options co-ordinated through facilities in Manchester UK, and Beverly MA., USA.





*The Neolynx Screening Application-Manager is indicated for the measurement of phenylalanine and tyrosine in neonatal blood samples for the purposes of screening for inherited phenylketonuria.

Neolynx Browser - [Pku_mrm_001.nrf; Report Scheme - test.nrs]

Test Name	Calculated Conc	Units	Result	High Conc	Low Conc
X Phe	455	umoles/L	High Phe	200	20.00
X Phe/Tyr	7.80	-	High Phe/Tyr	2.50	0.00

Autosample plate map

Results summary

Sample and testing information

Metabolite concentrations

Mass spectrum

Sample elution profile

Neolynx browser.

Figure 4.

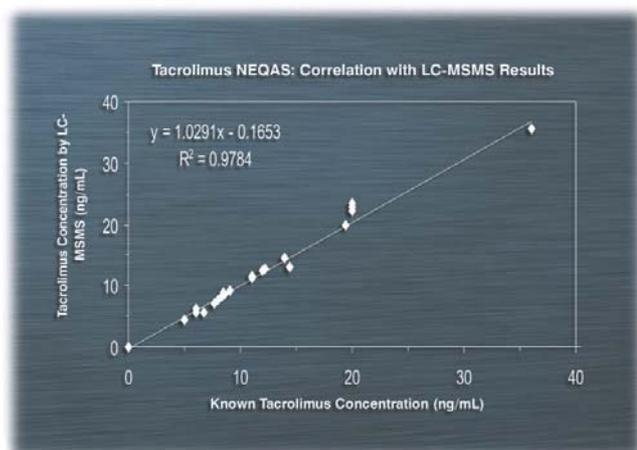


Figure 5.



Therapeutic Drug Monitoring

Mass spectrometry is beginning to make an impact in the clinical chemistry laboratory as a cost-effective research tool. A typical example is the treatment of patients undergoing transplant surgery, where immuno-suppressant drugs such as Tacrolimus (FK506) will be administered to prevent organ rejection. Failure to maintain the drug concentration within the narrow therapeutic window can lead to organ rejection or toxicity. For the Micromass Quattro *micro* API, determination of low levels of Tacrolimus is a simple task that is achieved with a minimum of sample preparation, negligible consumables costs and a level of selectivity that cannot be matched with current immunoassays.

Protein precipitated whole blood samples are analyzed by on-line solid phase extraction with a total analysis time of less than 2 minutes per sample. Multiple reaction monitoring (MRM) is used to specifically detect Tacrolimus and the internal standard. Quantitation is by peak area integration and comparison to a range of standards (protein precipitated blood), a fully automated process within MassLynx. The accuracy of this method was verified by analyzing a series of QC standards issued by the UK National External Quality Assurance Scheme (NEQAS). The results demonstrate excellent correlation with the expected values (Figure 4).

The flexibility of LC-MS-MS allows a single instrument to monitor a range of different drugs with a concomitant reduction in consumable expenditure and training requirements whilst providing the flexibility to adapt to the introduction of new therapies. This assay is currently undergoing validation.

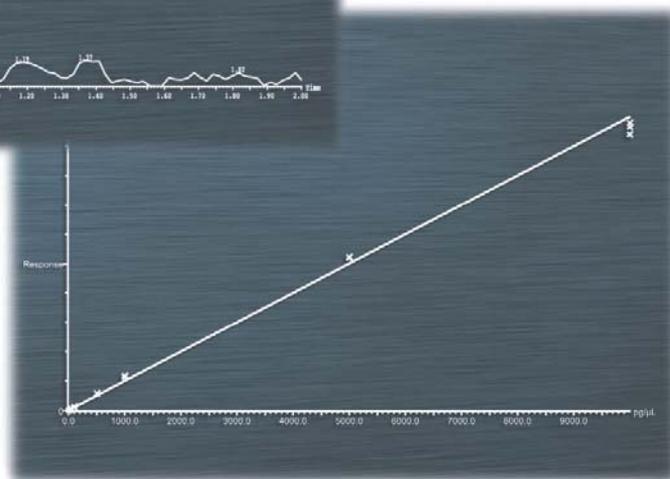
Automated metabolite identification

The Metabolyx Application-Manager was used in conjunction with the Micromass Quattro *micro* API to aid automatic identification of metabolites of dichlofenac from samples of rat urine. Using comparison with a control sample, and with no prior knowledge of the expected metabolic pathways, Metabolyx successfully identified the four major metabolites - hydroxy dichlofenac (+16 Da), hydroxy sulfate (+96 Da), dihydroxy sulfate (+112 Da) and ether glucuronide (+192 Da), Figure 5.

Figure 6.



Figure 7.



Only a few minutes of automated processing were required to identify the unknowns from a 25 minute LC-MS run. The combination of Metabolyx with the sensitivity and linear dynamic range of a tandem quadrupole creates a powerful tool for both identification and quantification in metabolism studies.

Performance

The Micromass Quattro *micro* API offers superior performance for a benchtop tandem quadrupole mass spectrometer – fitting the performance of the distinguished Quattro LC™ into only 1/3 of the footprint, whilst delivering greater functionality and ease-of-use. Figure 6 shows a mass chromatogram for sulfadimethoxine, demonstrating sensitivity from only 500fg on column with a signal-to-noise ratio of greater than 10:1 (Peak to peak; RMS s/n >30:1). An unrivaled 5 orders of magnitude linear dynamic range are available, illustrated in Figure 7, over the concentration range 0.1 pg to 10000pg, producing a coefficient of determination of 0.9975 for sulfadimethoxine injected on column, eluted in 50% aqueous acetonitrile.

The reproducibility of analysis across multiple injections is evident from 350 repetitive injections of diazepam in protein-precipitated plasma, yielding an RSD of 2.1%, despite the direct flow of plasma impurities into the **Z** SPRAY source (Figure 2).

The Micromass Quattro *micro* API incorporates the finest tandem quadrupole technology, Targeted Mass-Informatics and e-MS integration -

maximizing data excellence, knowledge generation and your return on investment like no other LC-MS-MS system.

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