Advancing your Quantitative Capabilities

TSQ Plus Series

Thermo Scientific's 2022 LCMS Product Portfolio
Food Safety Seminar Bangkok

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Regional Application Leader – SEA & Taiwan

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The world leader in serving science

TSQ Plus triple quadrupole mass spectrometers

Innovative hardware and software delivering next-level performance for targeted quantitation

Acquisition rate	600 SRMs/sec
Maximum quadrupole resolution	TSQ Fortis Plus MS 0.4 Da FWHM TSQ Quantis Plus MS 0.4 Da FWHM TSQ Altis Plus MS 0.2 Da FWHM
Polarity switching speed	5 msec
Linear dynamic range	TSQ Fortis Plus MS > 5 orders TSQ Quantis Plus MS > 6 orders TSQ Altis Plus MS > 6 orders
Operating software	TNG

Notable Improvements

Active Reaction Collision Cell II (ARC II) for improved low-mass product ion transmission and improved sensitivity

Advanced power supply to enable 5 ms polarity switching to maintain accurate quantitation using UHPLC/HPIC separation

QR5 Plus quadrupole mass filters (Thermo Scientific™ TSQ Altis™ Plus MS) to improve ion transmission stability to ensure superb sensitivity, selectivity, and reproducibility over time

Integrated system check and calibration consolidated instrument performance evaluation and calibration for simplified maintenance

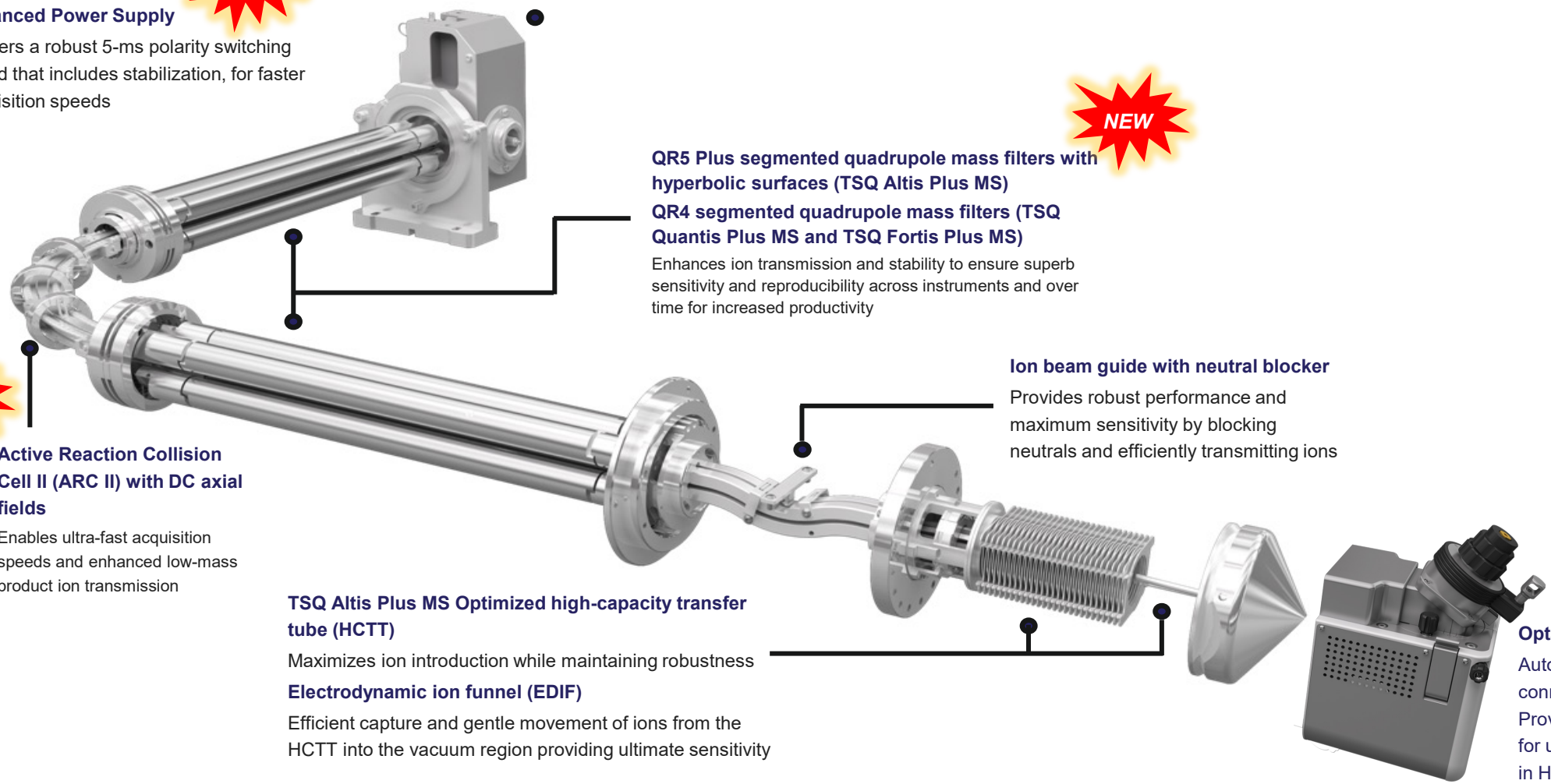
Thermo Scientific™ mzCloud™ database integration to access over 19,000 curated selected reaction monitoring (SRM) transitions for direct inserting into new or existing instrument methods

Global dwell time determination to automate dwell time settings based on chromatographic performance

Dwell time prioritization to quickly modify dwell time settings based on SRM response

Thermo Scientific™ FAIMS Pro Duo interface compatibility with automated CV determinations

Instrument schematic



NEW

Advanced Power Supply

Delivers a robust 5-ms polarity switching speed that includes stabilization, for faster acquisition speeds

NEW

QR5 Plus segmented quadrupole mass filters with hyperbolic surfaces (TSQ Altis Plus MS)

QR4 segmented quadrupole mass filters (TSQ Quantis Plus MS and TSQ Fortis Plus MS)

Enhances ion transmission and stability to ensure superb sensitivity and reproducibility across instruments and over time for increased productivity

NEW

Active Reaction Collision Cell II (ARC II) with DC axial fields

Enables ultra-fast acquisition speeds and enhanced low-mass product ion transmission

Ion beam guide with neutral blocker

Provides robust performance and maximum sensitivity by blocking neutrals and efficiently transmitting ions

TSQ Altis Plus MS Optimized high-capacity transfer tube (HCTT)

Maximizes ion introduction while maintaining robustness

Electrodynamic ion funnel (EDIF)

Efficient capture and gentle movement of ions from the HCTT into the vacuum region providing ultimate sensitivity

OptaMax NG Ion Source

Automated gas and voltage connections for ease-of-use. Provides optimizable spray position for ultimate and robust performance in HESI or APCI modes

Improving Haloacetic acids analysis

Providing a single-vendor solution to improve HAAs and DBPs analysis for today and tomorrow

Thermo Scientific™ Dionex™ ICS-6000 Capillary HPIC™ system coupled to the TSQ™ Fortis™ Plus triple quadrupole mass spectrometer for increased productivity for polar compound detection and quantitation

- Disinfection by-products (DBPs) and the subset haloacetic acids (HAAs) are generated during drinking water purification
- DBPs and HAAs have been associated with elevated health risks spurring government regulatory agencies to establish detection and minimal reporting levels for individual and collective DBPs/HAAs compounds
- Traditional LC-MS methods often require costly derivatization to effectively separate compounds
- Incorporating high-performance ion chromatography (HPIC) with MS/MS increases instrument detection limits, robustness, and minimizes cost
- Predefined workflows are established with sample preparation, chromatographic separation, SRM detection, and Thermo Scientific™ TraceFinder™ data processing master methods

https://www.thermofisher.com/order/catalog/product/ICS6000-007#/ICS6000-007

Improved performance for low-mass transitions

ThermoFisher SCIENTIFIC

New ARC II active collision cell increases performance for routine analytical methods

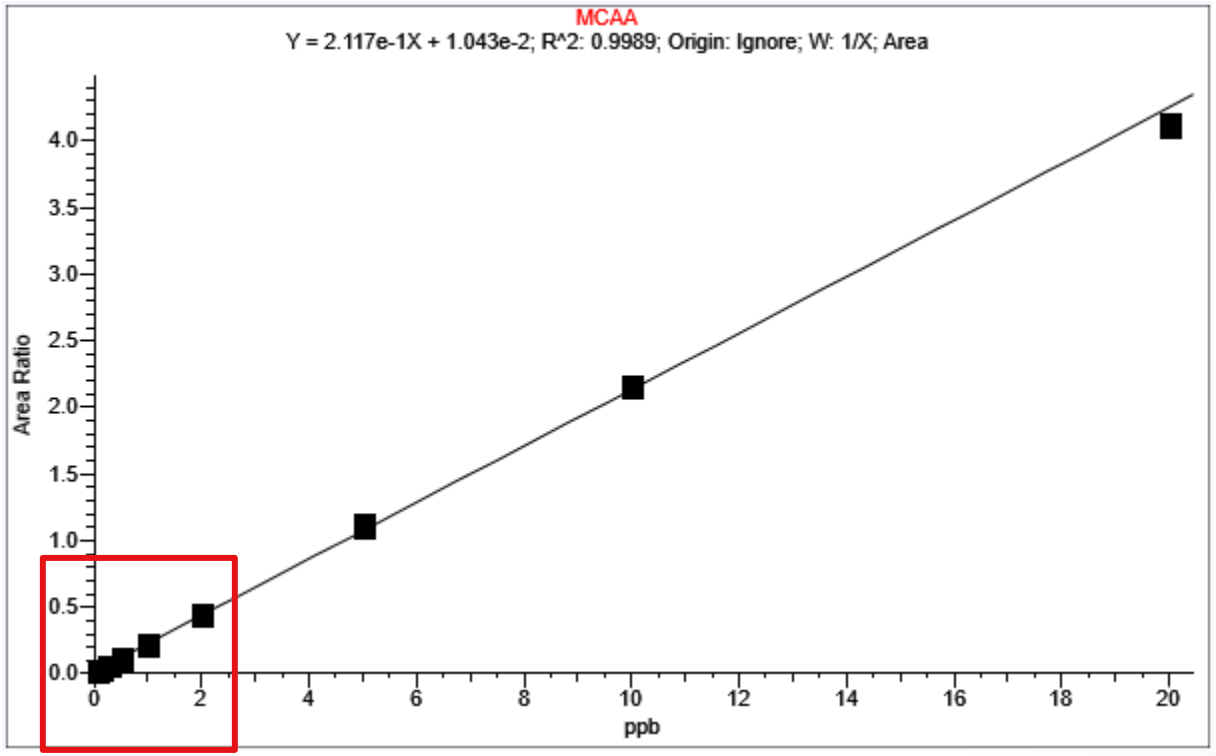
- Regulated methods in environmental and food safety dominated by small molecules
- Small molecules typically have low-mass product ions that require greater detection capabilities
- The new ARC II active collision cell improves mass stability and transmission that can increase detection limits and reproducibility
- Future-proof instruments for greater regulatory requirements

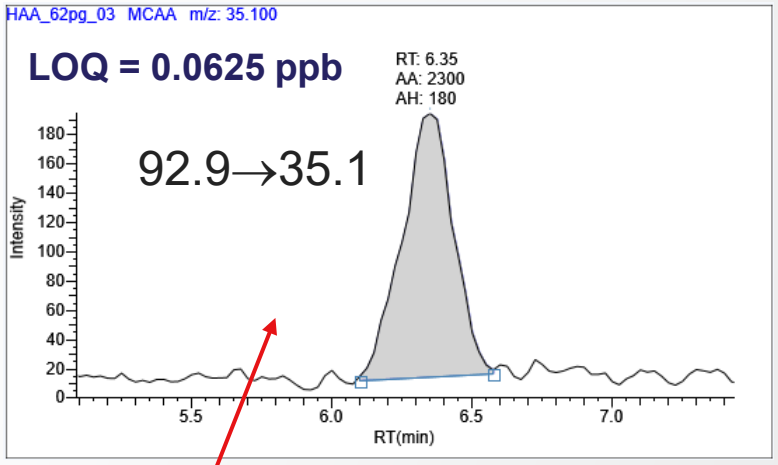
Compound	SRM Transition	EPA LLOQ µL/L	TSQ Fortis Plus MS LLOQ (µL/L)	EPA 557 Method MDL (µL/L)	TSQ Fortis Plus MS MDL (µL/L)
BCCA	172.8→128.9	0.25	0.06	0.11	0.01
BDCAA	162.8→80.9	0.25	0.06	0.05	0.02
Bromate	126.8→79.0	0.25	0.06	0.02	0.01
Dalapon	140.4→96.9	0.25	0.06	0.04	0.01
DBAA	216.7→172.7	0.25	0.06	0.02	0.01
DBCAA	206.7→78.9	0.25	0.06	0.04	0.05
DCAA	126.8→83.0	0.25	0.25	0.06	0.01
MBAA	136.8→78.9	0.25	0.06	0.06	0.01
MCAA	92.9→35.1	0.25	0.06	0.20	0.01
TBAA	250.7→78.9	0.25	0.25	0.07	0.05
TCAA	162.8→118.9	0.25	0.13	0.09	0.02

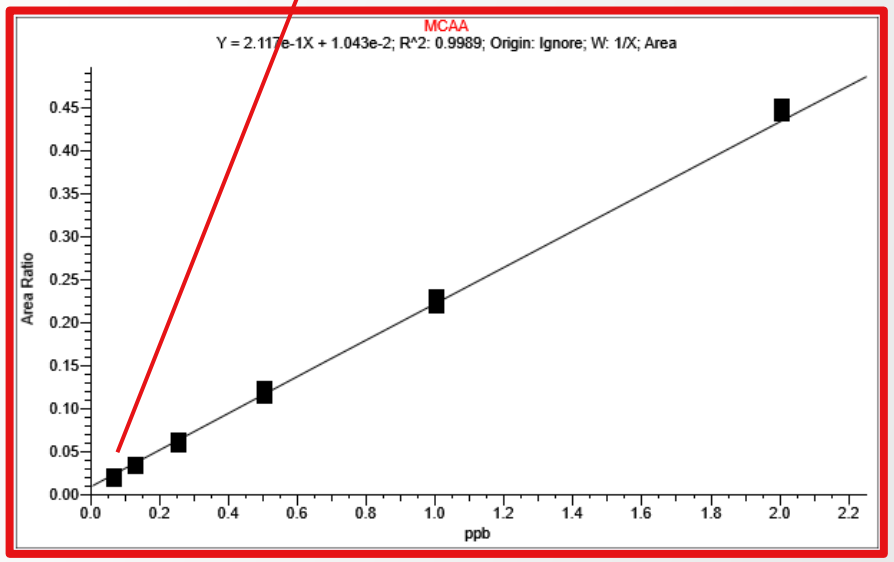
4x LLOQ improvement for 8/11 compounds without any method optimization

Quantitative response for MCAA

Leveraging the improved low-mass transmission of the ARC II cell for increased quantitative performance



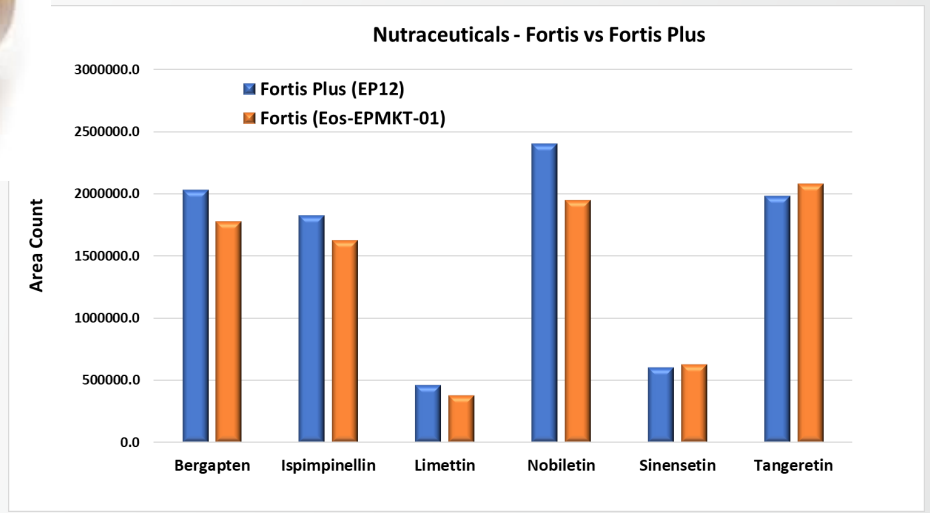




Nutraceuticals direct method transfer for immediate acquisition

Instrument methods can be directly imported from TSQ Fortis MS to TSQ Fortis Plus MS for scalability

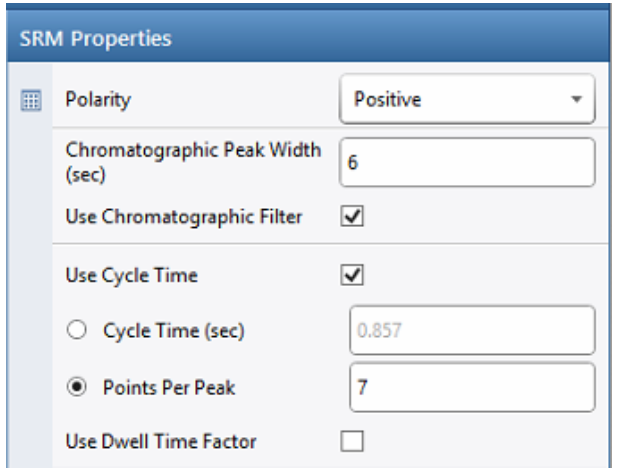
- LC-MS/MS method for nutraceuticals was created and optimized on the TSQ Fortis MS
- The method was transferred to the TSQ Fortis Plus MS and implemented without further optimization
- **Seamless method transfer with equivalent or better response for all 9 nutraceuticals ion orange juice covering 3 orders of magnitude**
- Nutraceutical is a term derived from “nutrition” and “pharmaceutics.” The term is applied to products that are isolated from herbal products, dietary supplements (nutrients), specific diets, and processed foods such as cereals, soups, and beverages that other than nutrition are also used as medicine.

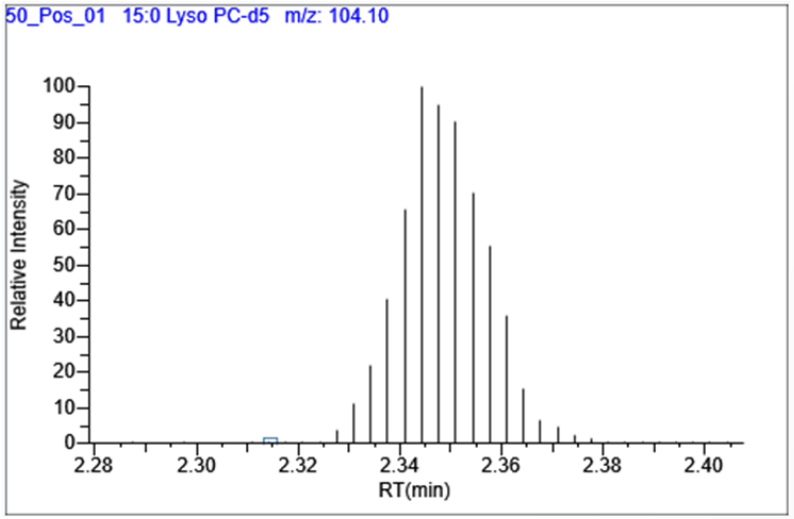


Nutraceuticals	Polarity	Transition	Fortis Plus (EP12)	Fortis (Eos-EPMKT-01)	Ratio
Arbutin	-	317 > 271	4309.0	4104.7	1.05
Bergapten	+	217 > 201	2034222.7	1777627.0	1.14
Ispimpinellin	+	247 > 216.9	1827096.0	1628804.7	1.12
Limettin	+	207 > 192	463638.7	382245.3	1.21
Limonin	+	471 > 425	26604.0	22996.0	1.16
Nobiletin	+	403 > 373	2402430.7	1948724.7	1.23
Phloridzin	-	435 > 273	15311.7	14291.3	1.07
Sinensetin	+	373 > 312	605139.7	630524.3	0.96
Tangeretin	+	373 > 343	1983801.333	2080280.7	0.95

Enabling automated dwell time determination

Simplifying instrument method creation for large panel detection and quantitation





Criteria to determine dwell times

- Leverage chromatographic peak width and either desired cycle time consideration or minimum number of data points per compound elution profile
- Sets the dwell time for all compounds in the unscheduled or per scheduled time window in the experimental method

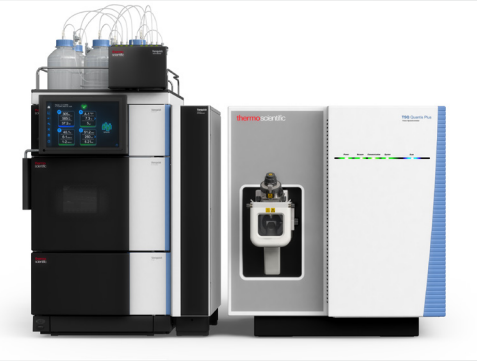
Additional tools for targeted quantitative workflows

The TSQ Plus MS portfolio delivers versatility, confidence, and productivity

Requirements for targeted analyses are increasing in terms of number of compounds within each method, number of samples to be analyzed, and limits of detection required. To address these ever-changing demands, Thermo Fisher Scientific has a portfolio of tools from hardware to software to maximize the productivity of your laboratory

- The 3-tiered TSQ Plus mass spectrometer portfolio delivers superior performance to address specific challenges scientists and technicians face on a daily basis
- Integrated single-vendor market-leading workflows including:
  - ✓ Online sample preparation
  - ✓ High-performance chromatographic solutions
  - ✓ Optional ionization interfaces
  - ✓ Data processing software

Ion chromatography mass spectrometry



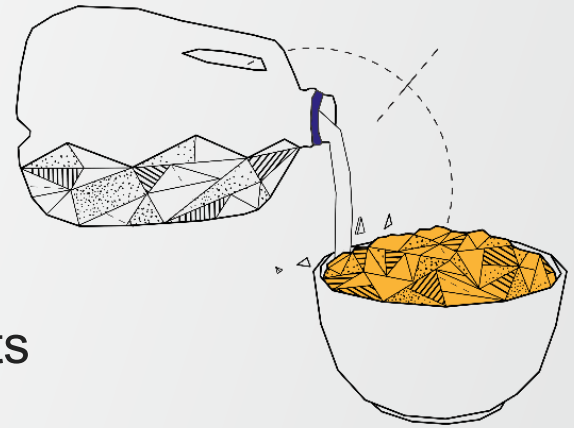
Liquid chromatography mass spectrometry

Thermo Scientific™ TriPlus™ RSH autosampler for online sample preparation mass spectrometry

Thermo Scientific™ VeriSpray™ PaperSpray mass spectrometry

Challenges of Multi-Residue Methods

- Generic enough to apply to several different matrices - e.g. meat, fish, dairy…..
- Stability of Matrix Extracted Spikes (MES) and spiking standards
- Chromatography - Column must handle wide polarity range; be rugged
- Sample preparation must minimize loss of analytes, be simple and cost effective
- Need sufficient sensitivity for all compounds
- Need for polarity switching
- Avoid reporting residue result not actually in sample (False +ve)
- Avoid missing residue result in a sample from not being detected (False -ve)
- Results need to be in compliance with regulations & accreditation requirements

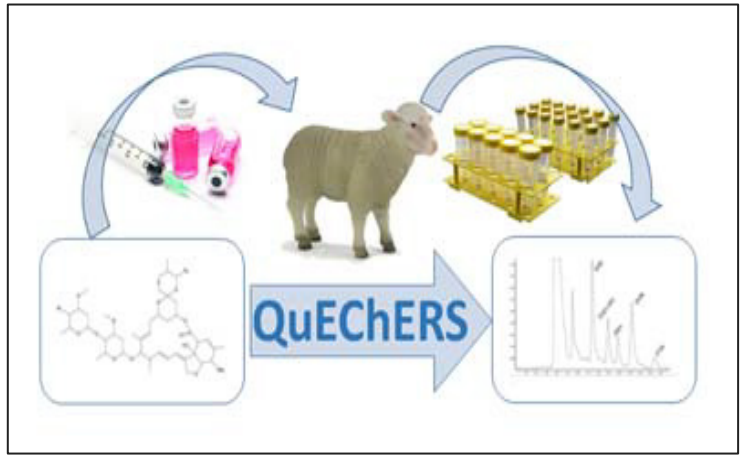


Can we solve these challenges in a single workflow?

Multi-Class Veterinary Drugs

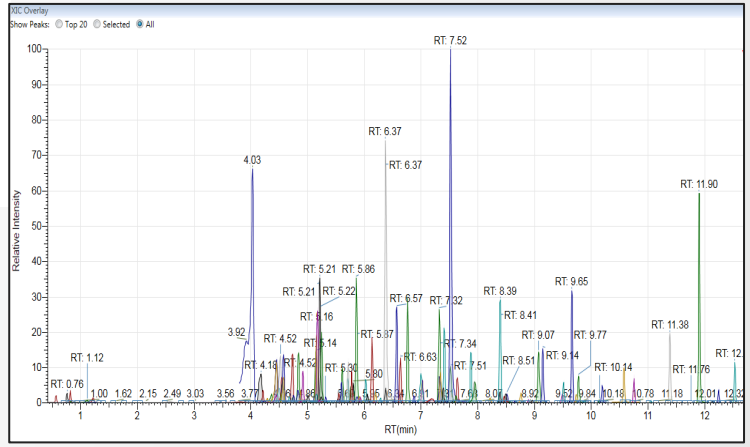
Several single-class methods → One multi-class method

Stability of multi-component mixtures



Generic sample prep with good recoveries + RSDs

Wide range of chemical classes+ MRLs

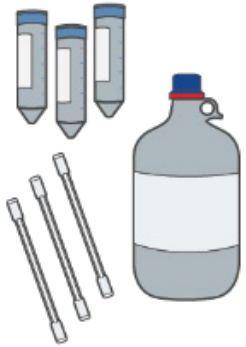


Inert LC system and column for wide pKa range and good peak shape

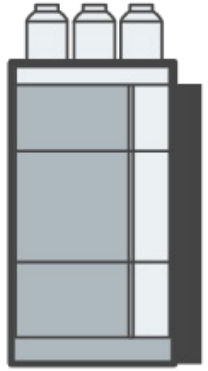
VetDrugs Explorer Collection-

The VDX Product

QuEChERs Sample Prep & Columns



Vanquish Flex Pump



TSQ Altis Plus QQQ

TraceFinder with methods, compound database

QuEChERS Sample Preparation
(Includes detailed methods, consumables)

UHPLC Chromatographic Separation
(Vanquish Flex, columns, HW, SW)

QQQ Detection
(TSQ Altis Plus – robust methods, HW, SW, seamless integration w/ front end)

Data Processing & Reporting

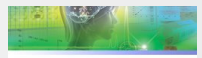
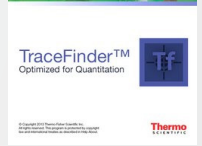
VetDrugs Explorer Technical Highlights

Feature	Detail	Comment
# of Compounds	170+ Analytes with acquisition and master processing method	Compound data base contains extra analytes (250 total) for labs wanting to add more compounds
Matrices	Muscle meat (cattle), milk, and salmon (fillet)	Demonstrates broad applicability of the multi-class method approach
QC and Analytical Standards	QC Check-20 cmpds Standards- 170 compounds	**Both Included** in the kit
Sample Preparation	Generic QuEChERs extraction w/simple clean-up	Detailed procedure using included Thermo reagents
Column	Accucore™ VDX 100mm x 2.1 x 2.6 um	Special Thermo column for optimal chromatographic performance
UHPLC-MS system	TSQ Altis Plus with Vanquish Flex Binary pump	Includes detailed User guide for proper installation and system check-out
Software	TraceFinder	Master method and acquisition methods, CDB all ready-to-go





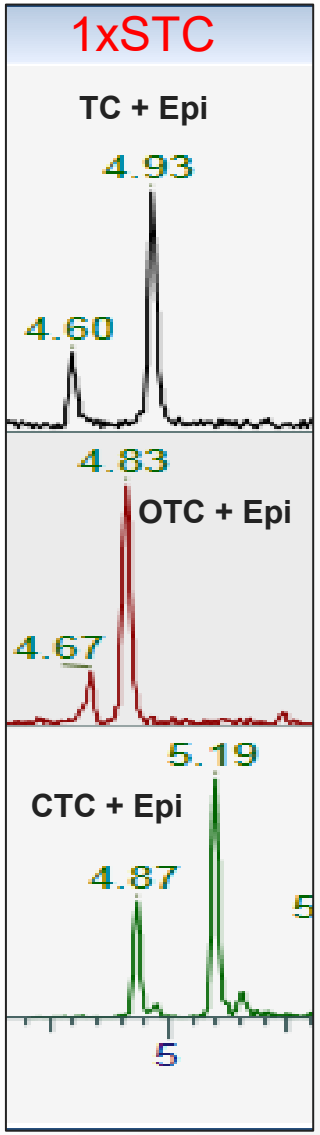


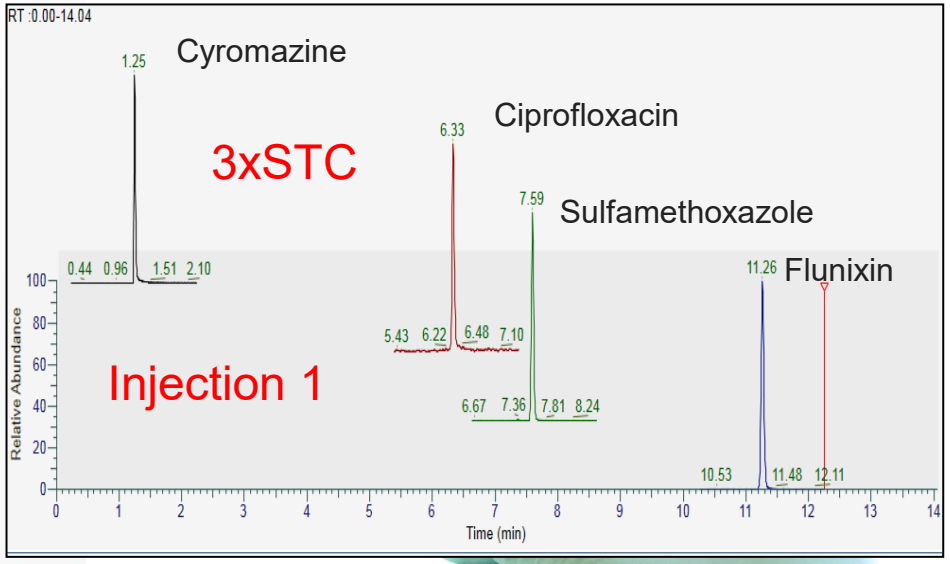




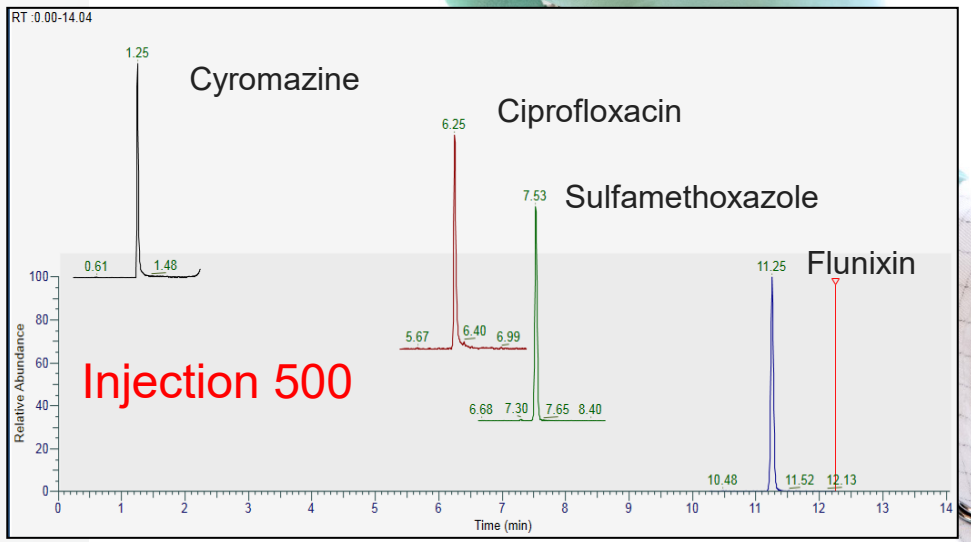
Column-Accucore VDX- Robust and Selective for VetDrugs

Features

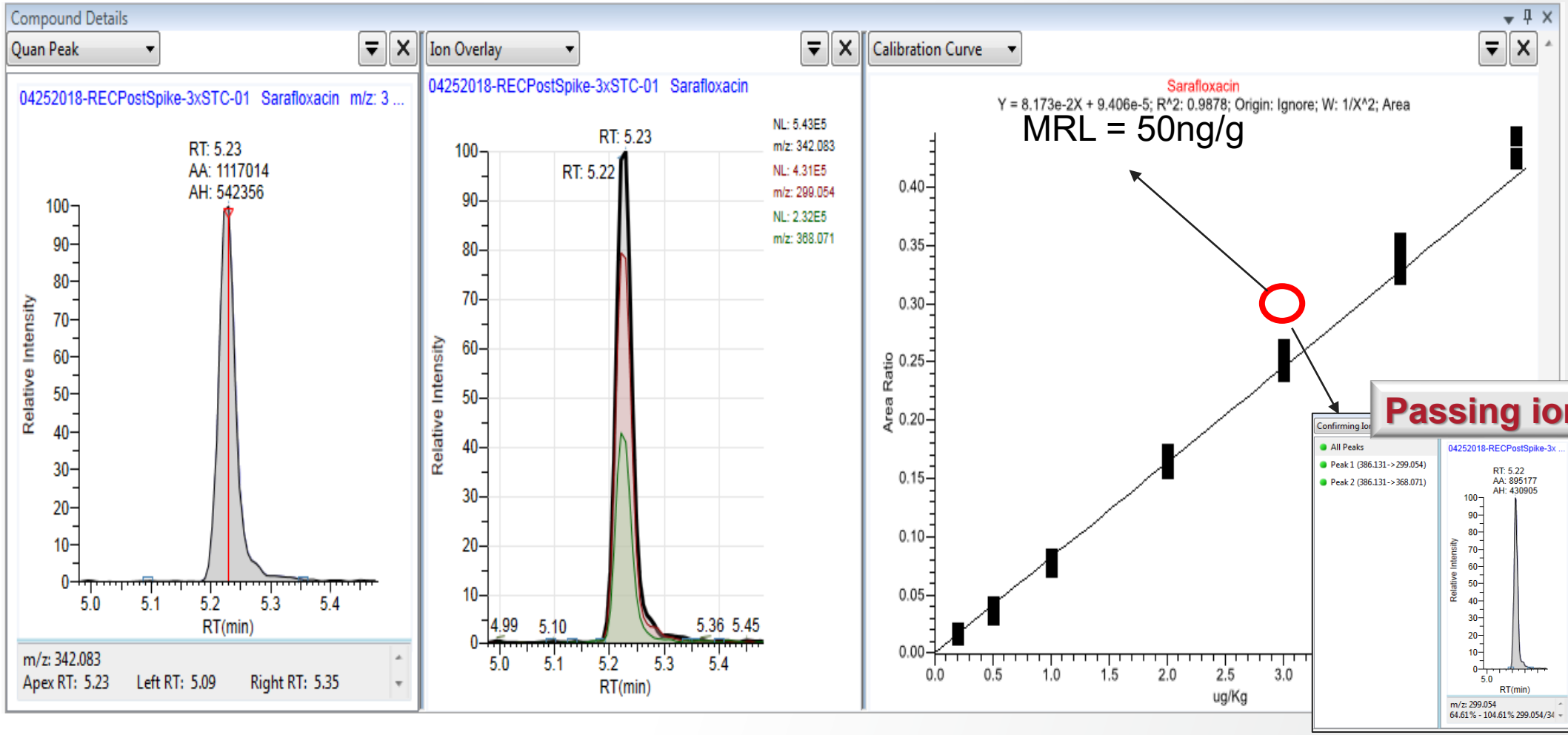
- Solid core particle- high resolution separations
- Column chemistry selectivity similar to C18 columns
- Optimized for MS detection
- Low column bleed
- Optimized for low tailing
- ***Robust against matrix extracts***
- Particle size: 2.6 µm







Quantitative Results- 0.2 to 5 x STC-Bovine Matrix Extracted Spike (MES)

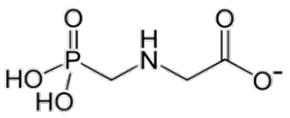


Passing ion ratios

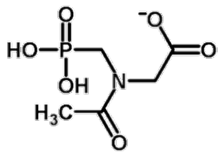
3 matrices
- **Bovine**
- **Salmon**
- **Milk**

Sarafloxacin in bovine extract at 3× STC, with screening range from 3-75 ng/g.

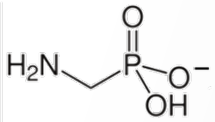
Anionic Pesticides Widely Used in Agricultural Production



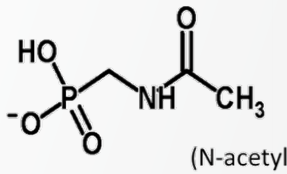
Glyphosate
(*m/z* 168.0067)



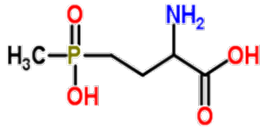
N-acetyl glyphosate
(*m/z* 210.0173)



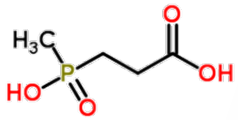
Aminomethyl phosphonic acid
(AMPA)
(*m/z* 110.0012)



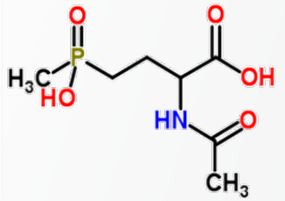
(N-acetyl AMPA)
(*m/z* 152.0118)



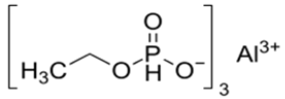
Glufosinate
(*m/z 180*)



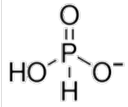
3-MPPA
(*m/z* 151)



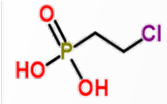
N- acetyl Glufosinate
(*m/z 222)*



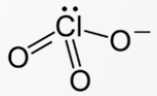
Fosetyl-aluminium
(*m/z* 109.0060)



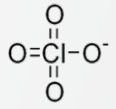
Phosphonic acid
(*m/z* 80.9747)



Ethephon
(*m/z 143*)



Chlorate
(*m/z* 82.9541)



Perchlorate
(*m/z* 98.9491)

- Residues do occur:
  - Glyphosate in cereals and cereal products (beer, breakfast cereals), and recently in honey
  - Ethephon in grapes and pineapple
  - Chlorate (from use of biocidal solutions in food preparation facilities) in fruits, dairy products and baby foods

EU MRLs & Residue Definitions for Commodities Selected for Validation

Analyte	EU MRL Residue Definition	Wheat	Leek	Baby Food
		MRL (mg/kg)	MRL (mg/kg)	MRL (mg/kg)
Bialaphos		#	#	0.01
Cyanuric acid		NA	NA	0.01
Chlorate	Chlorate ion	0.01	0.1*	0.01*
Ethephon	Ethephon - (**HEPA**) not considered to be a relevant metabolite	1	0.05*	0.01*
Fosetyl-AL	Sum of Fosetyl and phosphonic acid and their salts expressed as Fosetyl	2*	30	0.01*
Glyphosate	Glyphosate only (**N-acetyl Glyphosate, AMPA** and **N-acetyl AMPA** are not included	10	0.1*	0.01*
Glufosinate	Sum of glufosinate, it's salts, **N-acetyl glufosinate** and **MPPA** expressed as glufosinate	0.03* (effectively 0.01 or lower for each component	0.03*	0.01*
Perchlorate ion		0.1*	0.1*	0.01*

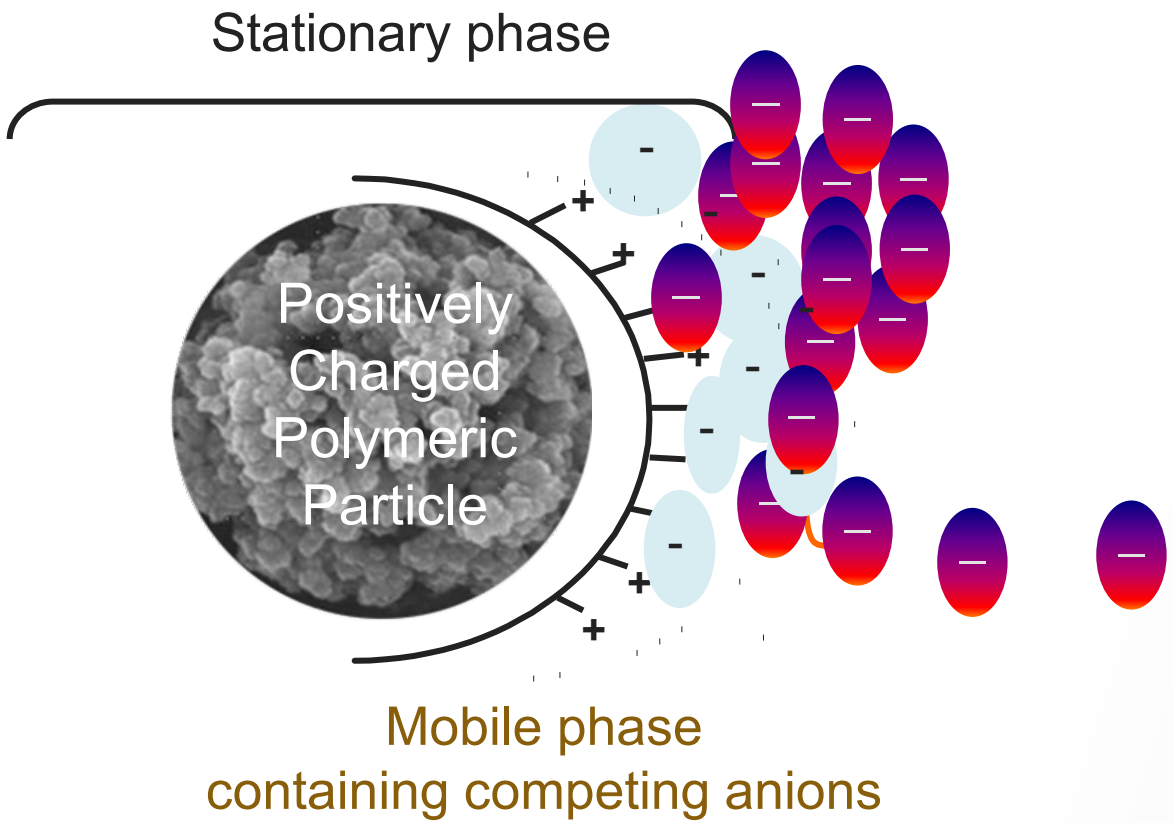
Notes:

- *MRL set at the limit of Determination, # natural herbicide not in MRL database, NA (not applicable)
- Most labs target reporting limit = 0.01mg/kg, irrespective if the MRL is a higher value

Analytical Challenges for the Determination of Anionic Pesticides

- Small water soluble molecules with poor chromatographic retention using reversed phase chromatography
- Not included in conventional multi-analyte LC-MS methods resulting in the need for additional methods and increased cost
  - Monitoring of residues of anionic pesticides in food is inadequate creating potential for misuse
  - EFSA & the European Commission have requested laboratories to develop improved method in order to generate more data
- EFSA has also indicated the residue definition for glyphosate analysis for risk assessment studies should be the sum of glyphosate, N-acetyl glyphosate, AMPA and N-acetyl AMPA
  - This would make a difficult analyses even more challenging
- Variation in Maximum Residue Levels for different commodities – most set at the Limit of Determination (LoD MRLs)

Anion Exchange Ion Chromatography – the Basis of the Anionic Pesticides Explorer



Advantages of ion chromatography

- ✓ High capacity of IC columns
- ✓ High sensitivity
- ✓ Increased retention of polar pesticides
- ✓ Gradient elution
- ✓ Excellent selectivity
- ✓ More control of separation
- ✓ Proven technology
- ✓ Direct analysis
  - – No chemical derivatization

High Performance Ion Chromatography (HPIC) provides many benefits

Dionex Ion Chromatography Pumping Component of the Anionic Pesticides Explorer

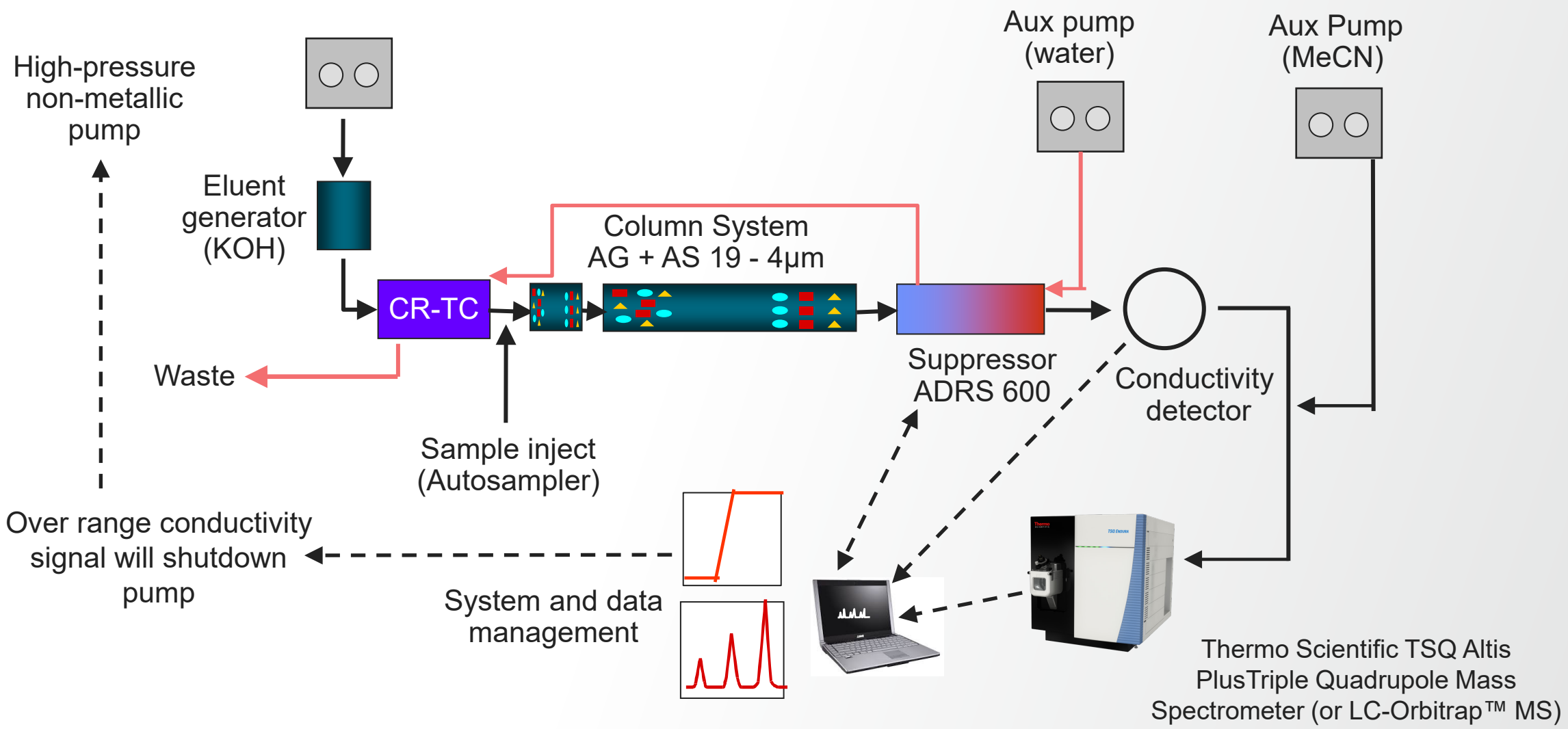
Benefits of the Dionex Ion Chromatography System

- ✓ PEEK–no metals
- ✓ No metals contamination of column
- ✓ No chelation of analytes
- ✓ Electrolytic eluent generation
- ✓ Reproducible KOH gradients
- ✓ Reagent free–just add water
- ✓ Post column AERS (Anion Electrolytic Regenerating Suppressor)
- ✓ Enables use of high ionic strength mobile phase
- ✓ Desalting of mobile phase
- ✓ Compatibility with MS (HRAM or QQQ)

Thermo Scientific™ Dionex™ Integrion™ HPIC™ (single-channel system)

Thermo Scientific™ Dionex™ ICS-6000 (two-channel system)

The Fully Integrated IC-QQQ MS/MS System



The Anionic Pesticides Explorer Product

- Method developed and validated with representatives commodities



- Polar pesticide quantitation and identification
  - Consolidated 2-3 methods into a single IC-MS/MS workflow
  - High sensitivity QQQ–“Dilute to Win”
  - Robust separation of anionic polar pesticides and metabolites in 18 minutes
  - Validated with SANTE/11813/2017 guidance

Everything included: software, consumables, user guide, system QC check solution, sample prep procedures

Modified QuPPe Extraction- Analysis of Wheat

Wheat samples (5 ± 0.1 g)

Spike blanks with native and ILIS for recovery experiments

Add 10 mL water, shake vigorously for 1 min and stand to soak for 10 min

Add 10 mL methanol, shake vigorously for 10 min

Freeze in -20 ℃, 15 min

Centrifuge, 8000 rpm 8 min

Dilute×10 with water

Push-through SPE-OnGuard RP cartridge and filter

Spike blanks with native and ILIS for preparations of matrix-matched standards

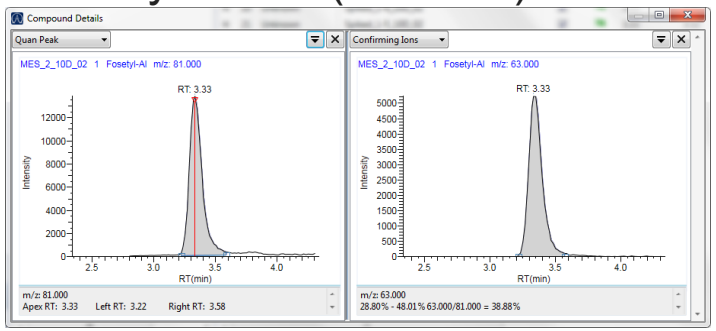
IC-MS/MS-Inj 25μL

SPE and Filtration

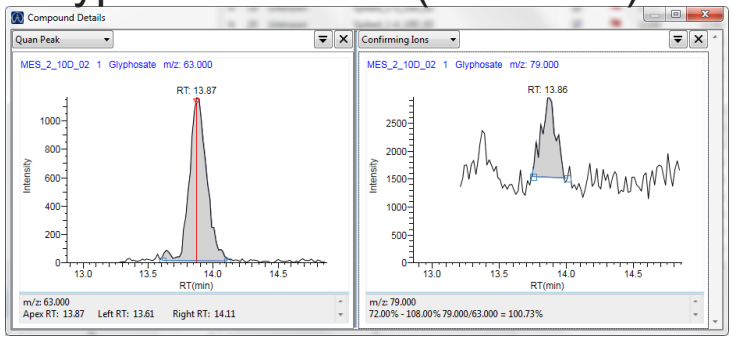
ONGuard RP SPE step removes precipitate in highly aqueous final solvent

Polar Anionic Pesticides Explorer – Extracts at 10 ng/g

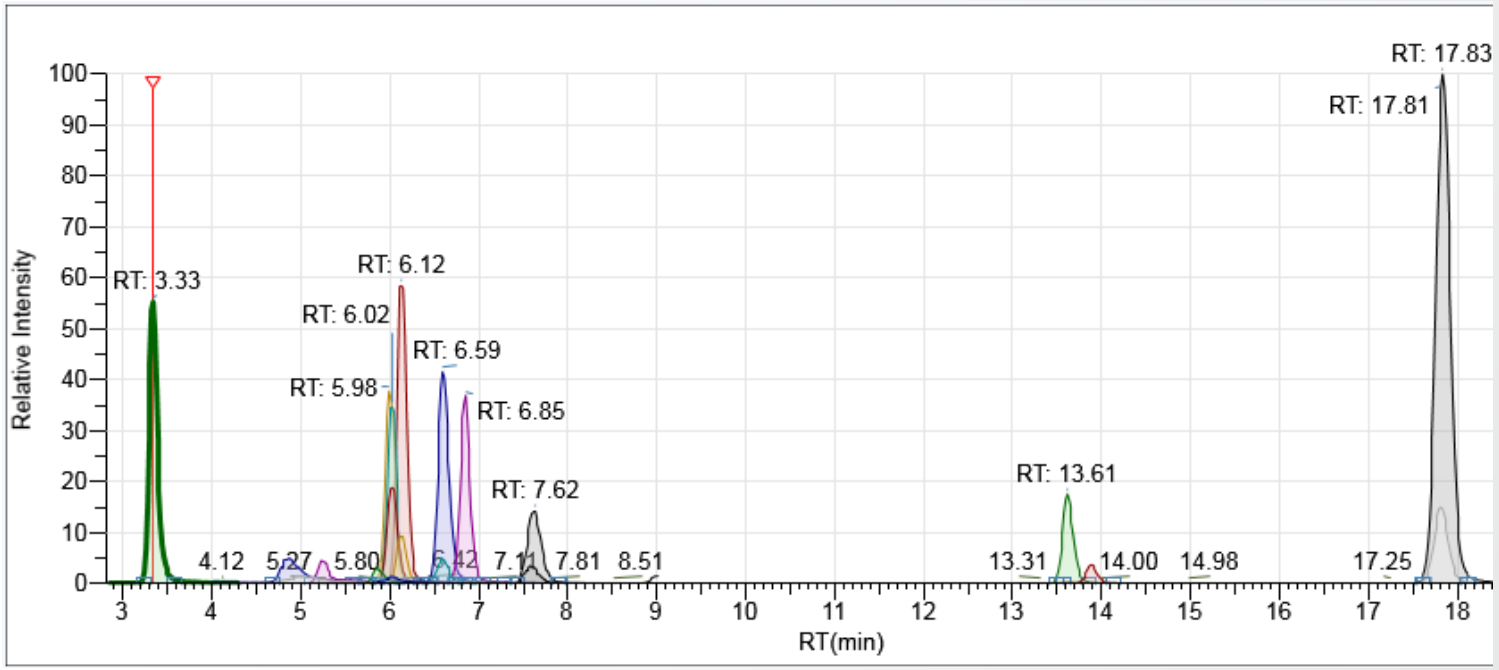
Fosetyl 81/63 (RT 3.33)



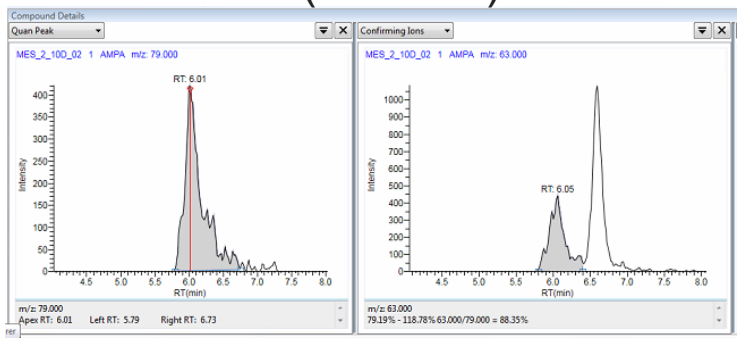
Glyphosate 63/79 (RT 13.87)



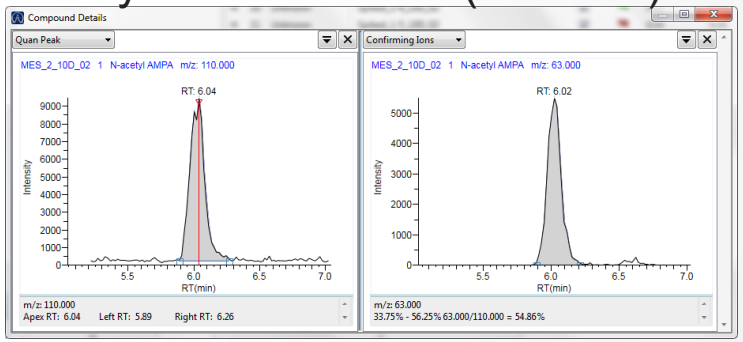
TIC in wheat flour (15 anionic pesticides) at 200 ng/g



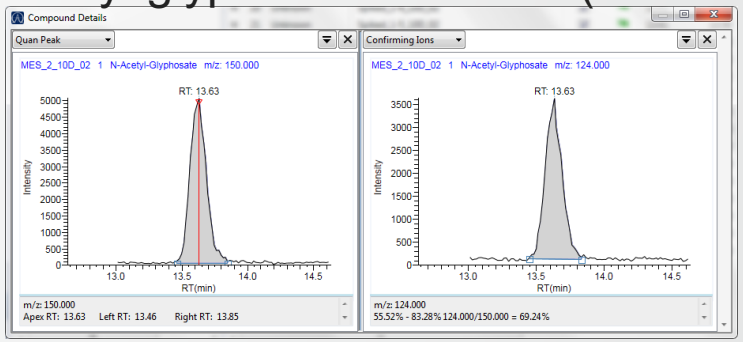
AMPA 79/63 (RT 6.01)



N-acetyl AMPA 110/63 (RT 6.04)



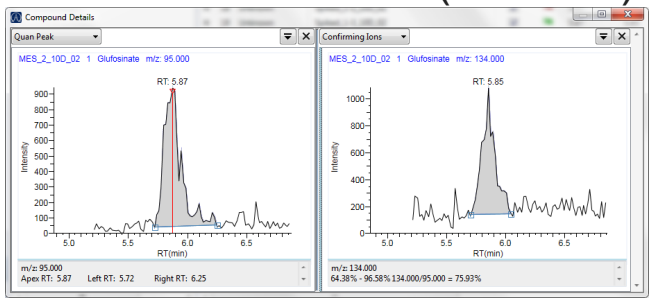
N-acetyl glyphosate 150/124 (RT 13.63)



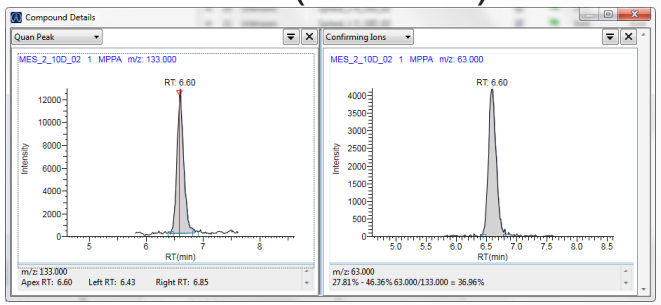
Response for Analytes Spiked at 10 ng/g in Wheat

ThermoFisher SCIENTIFIC

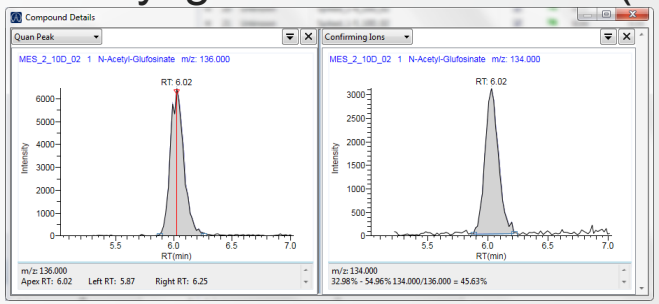
Glufosinate 95/134 (RT 5.87)



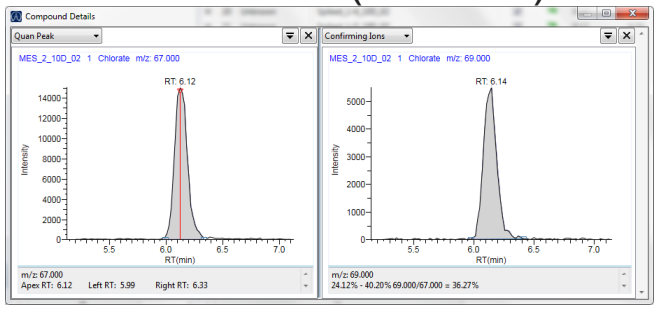
MPPA 133/63 (RT 6.60)



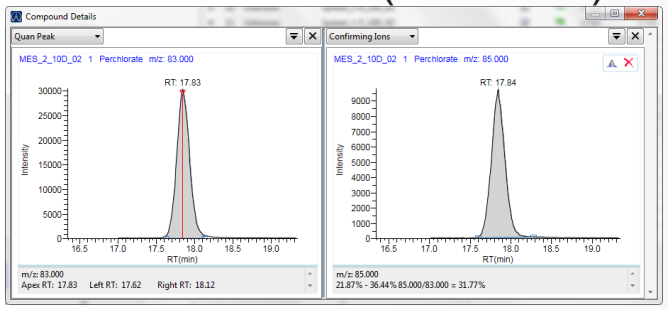
N-acetyl glufosinate 136/134 (RT 6.02)



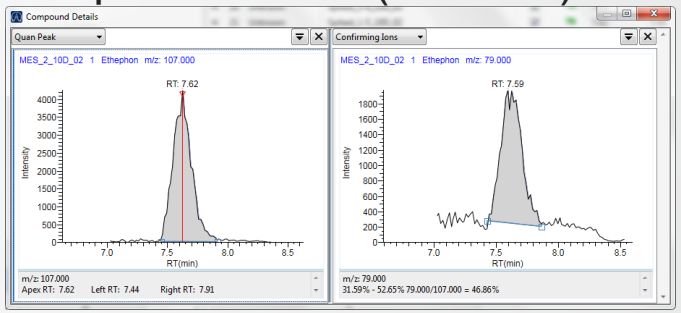
Chlorate 67/69 (RT 6.12)



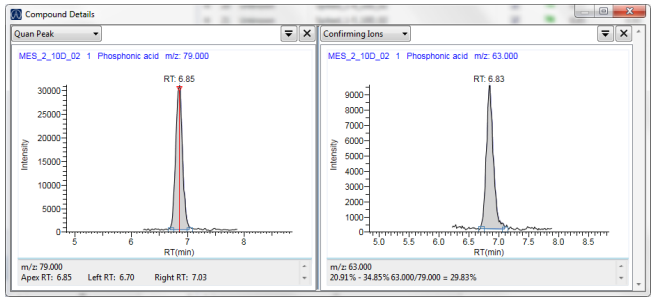
Perchlorate 83/85 (RT 17.83)



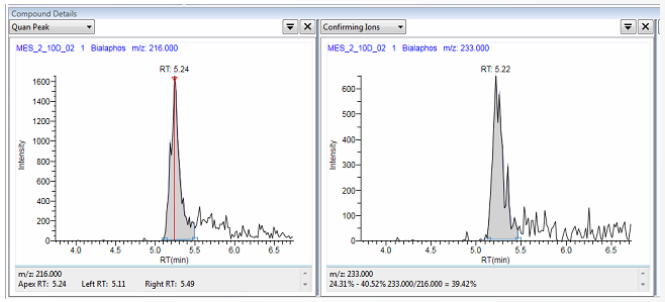
Ethephon 107/79 (RT 7.62)



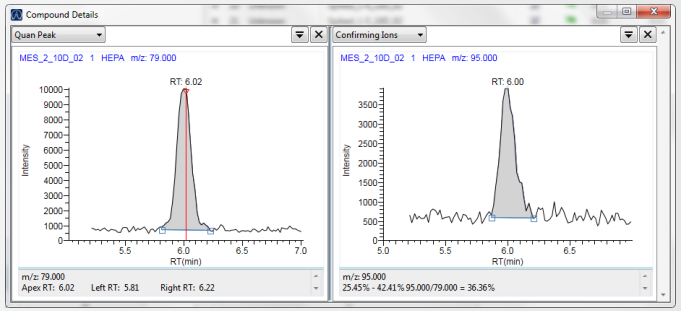
Phosphonic acid 79/63 (RT 6.85)



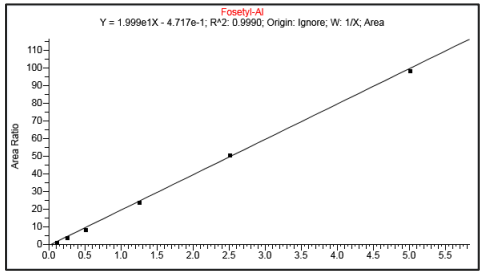
Bialaphos 216/233 (RT 5.24)

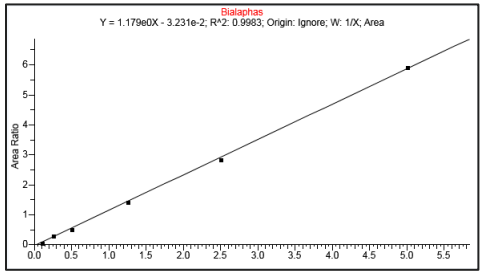


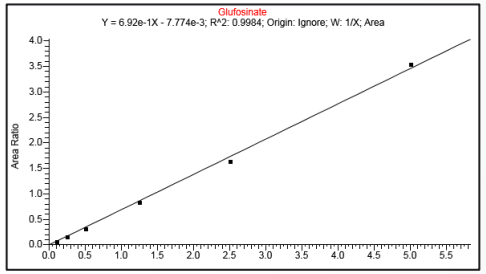
HEPA 79/95 (RT 6.02)

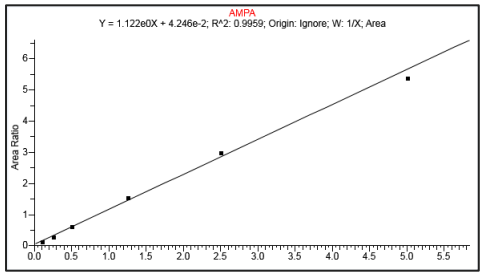


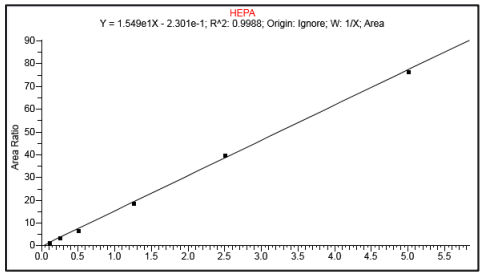
Linearity Check Six Levels–MES

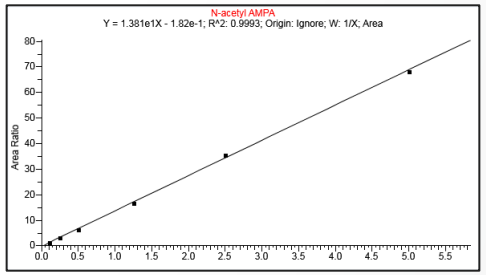


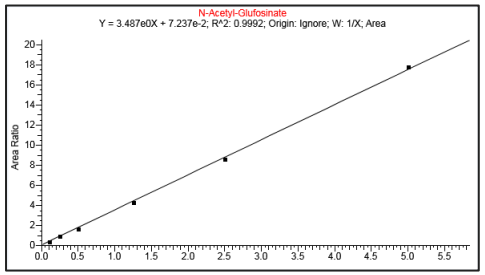


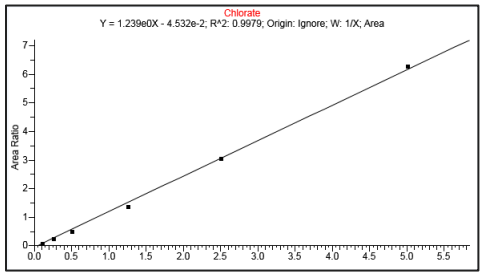


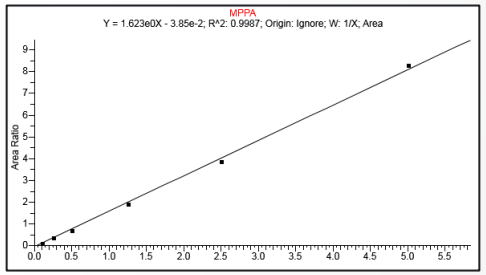


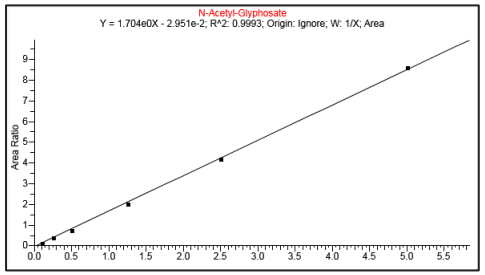


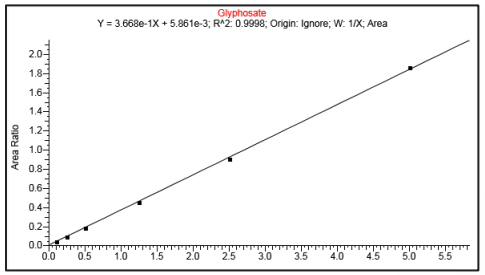


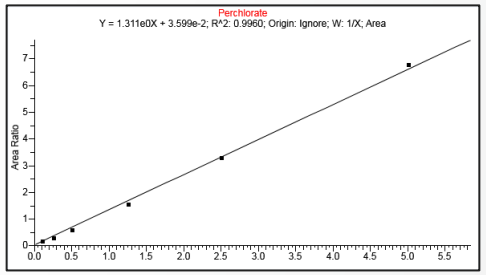












Compounds	R^2
Fosetyl-Al	0.9990
Bialaphos	0.9983
Glufosinate	0.9984
AMPA	0.9959
HEPA	0.9988
N-Acetyl-AMPA	0.9993
N-Acetyl-glufosinate	0.9992
Chlorate	0.9979
MPPA	0.9987
Phosphonic acid	0.9983
Ethephon	0.9989
Cyanuric acid	0.9982
N-Acetyl-Glyphosate	0.9993
Glyphosate	0.9998
Perchlorate	0.9960

Questions?