QTRAP 6500+ and SelexION+- Improving the Sensitivity, Speed and Selectivity in Food, Clinical Research and Pharmaceutical Applications

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Agenda

- 6500+ LC/MS System Hardware Improvements
- 6500+ LC/MS System Features and Application Benefits
- Application Data Examples

The New SCIEX 6500+ Series with HED+ Detector Technology

Industry proven performance: IonDrive™ Turbo V™ ion source and QJet® ion guide

New -Sensitivity boost with "***new HED+ detector technology***" in negative mode

New -Enhanced SelexION performance with ***"new jet injector DMS cell"*** without compromising resolution

New **-Fast polarity switching speed** (5 msec)

New **-Audible noise reduction**

New Feature	Benefit	Application
New HED^{+} detector technology	**Neg Mode**: Significant improvement in signal intensity Q3 fragment mass < 100 Da	**Oligonucleotide quant** in neg. mode with low mass Q3 fragments; **Low M.Wt. biomarkers**
New jet injector DMS cell	**Increased transmission efficiency** (up to 2X increase in signal intensity)	**Compounds with poor MS/MS or non specific fragments-** Steroids, Cyclic peptides Reduce matrix background & chemical interference
Fast polarity switching speed	**As low as 5 msec**	Biomarker discovery and multi target quant with sMRM pro algorithm

Technology Improvements

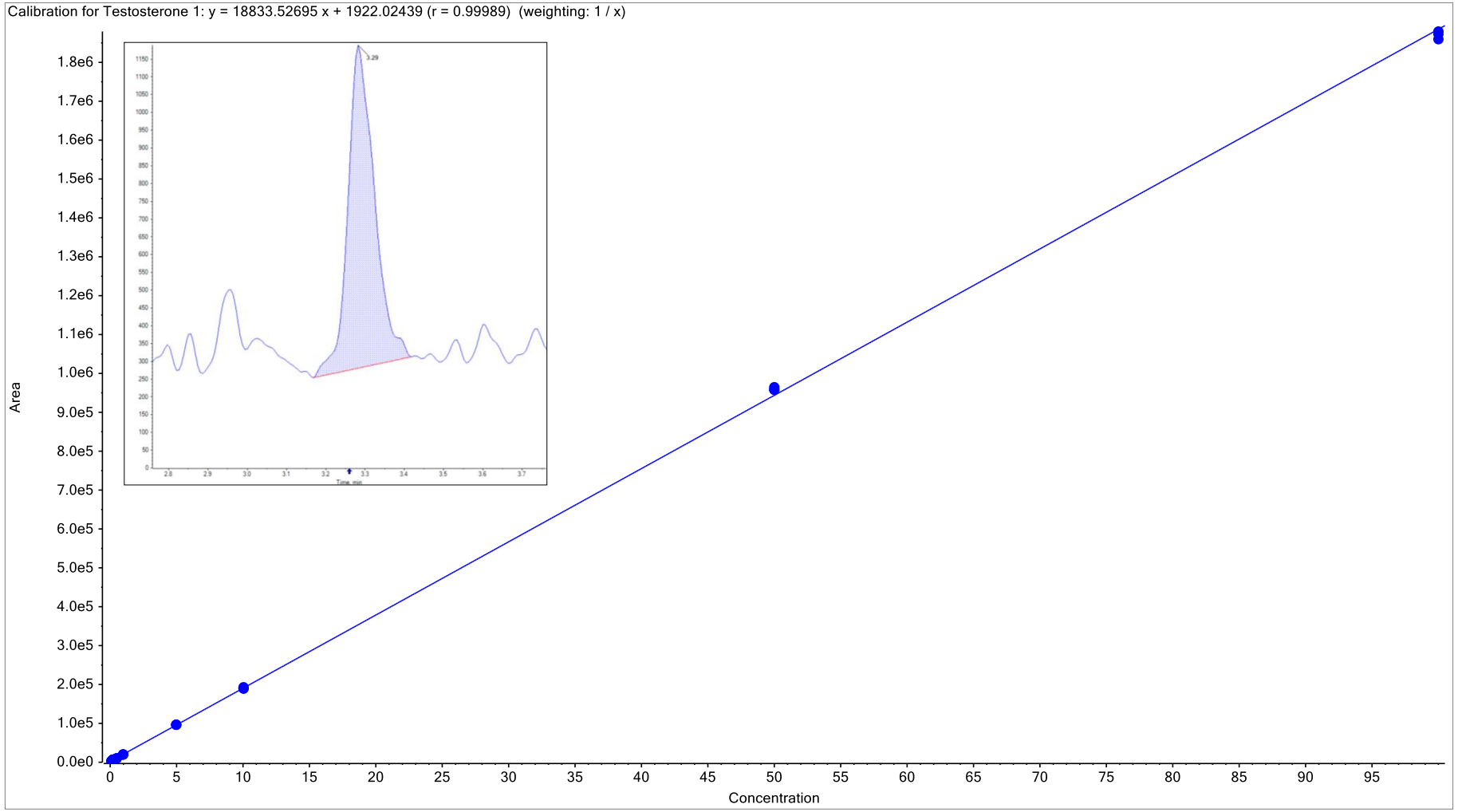
HED+ Detector Technology

- **Larger detection area**
- **New power supply**
  - High energy dynode at 15 kV improves sensitivity
  - Enables faster polarity switching
- **“Floated” design**
  - Ions in negative polarity directed straight into the detector
  - This benefits low mass ions which are detected much more efficiently

Contributes to significant signal gains in neg. mode Q3 fragment <100 Da and modest improvements in pos. mode

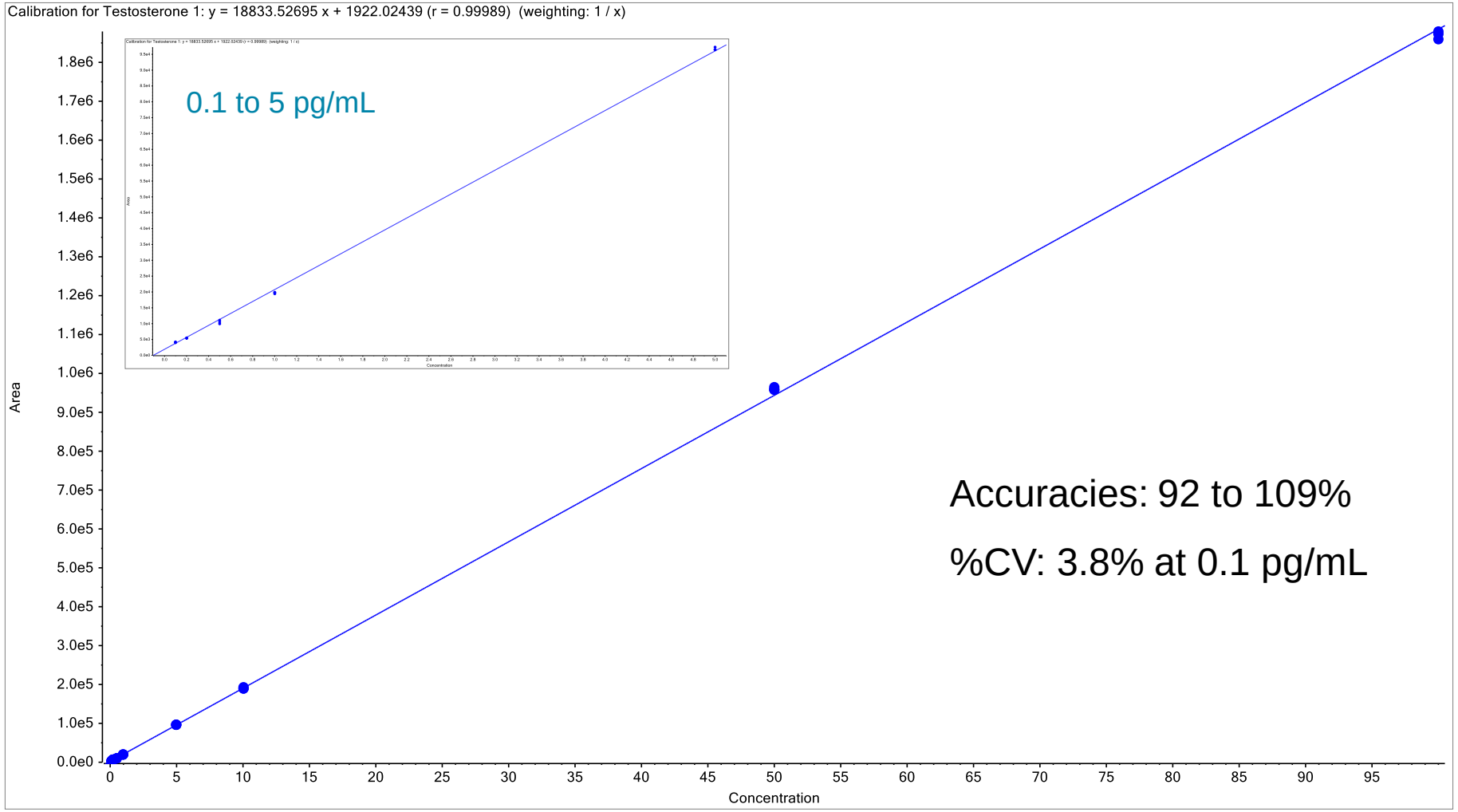
Sensitivity of 6500+ System in Positive Polarity

0.1 pg/mL Testosterone (with SelexION®+ Technology, 50 µL Injection)



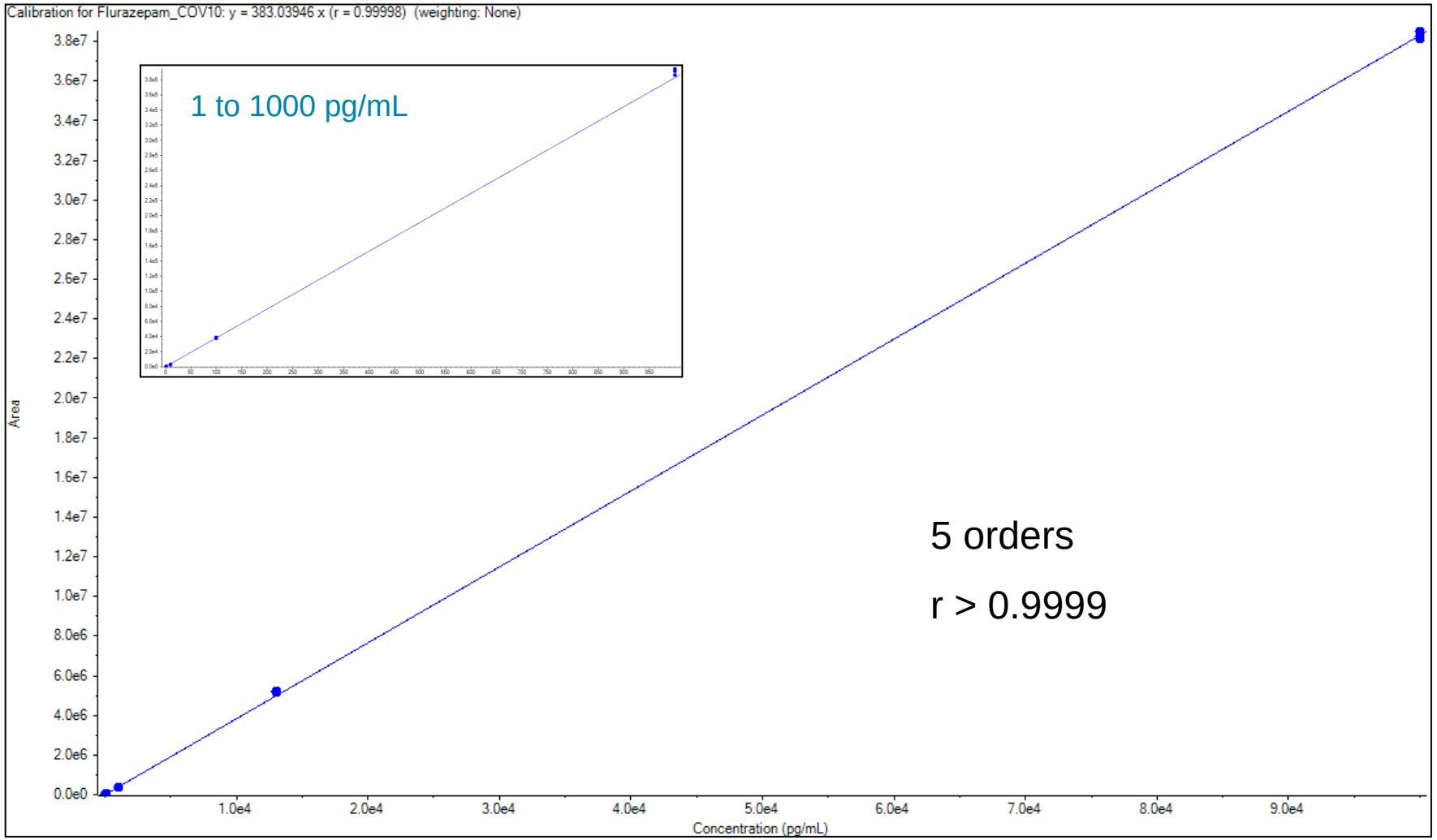
Linearity of 6500+ System in Positive Polarity

0.1 to 100 pg/mL Testosterone (with SelexION®+ Technology)



Linearity of 6500+ System in Positive Polarity

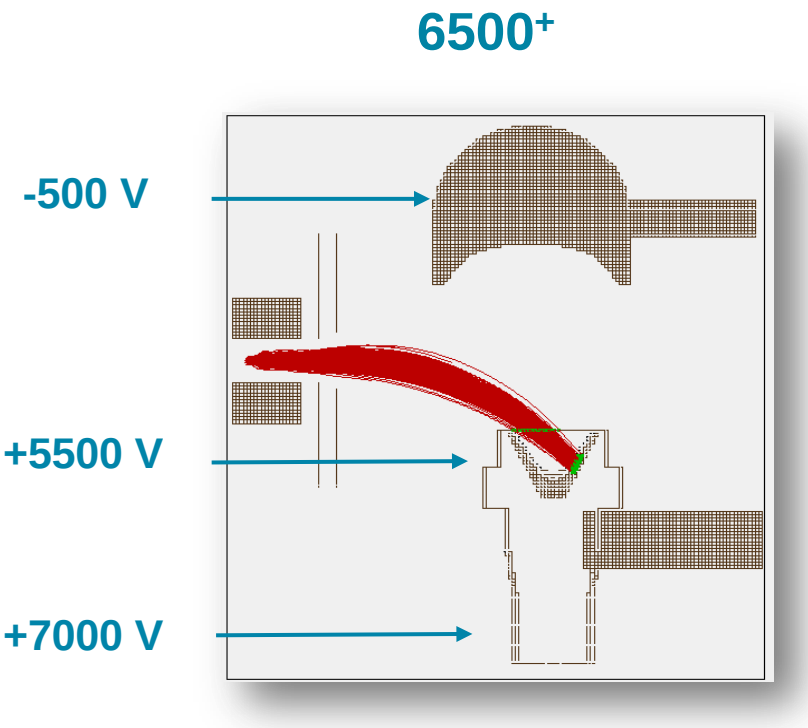
1 to 100,000 pg/mL Flurazepam (with SelexION®+ Technology)



HED+ Detector Technology in Negative Mode

Capture more negative ions and increase ion conversion

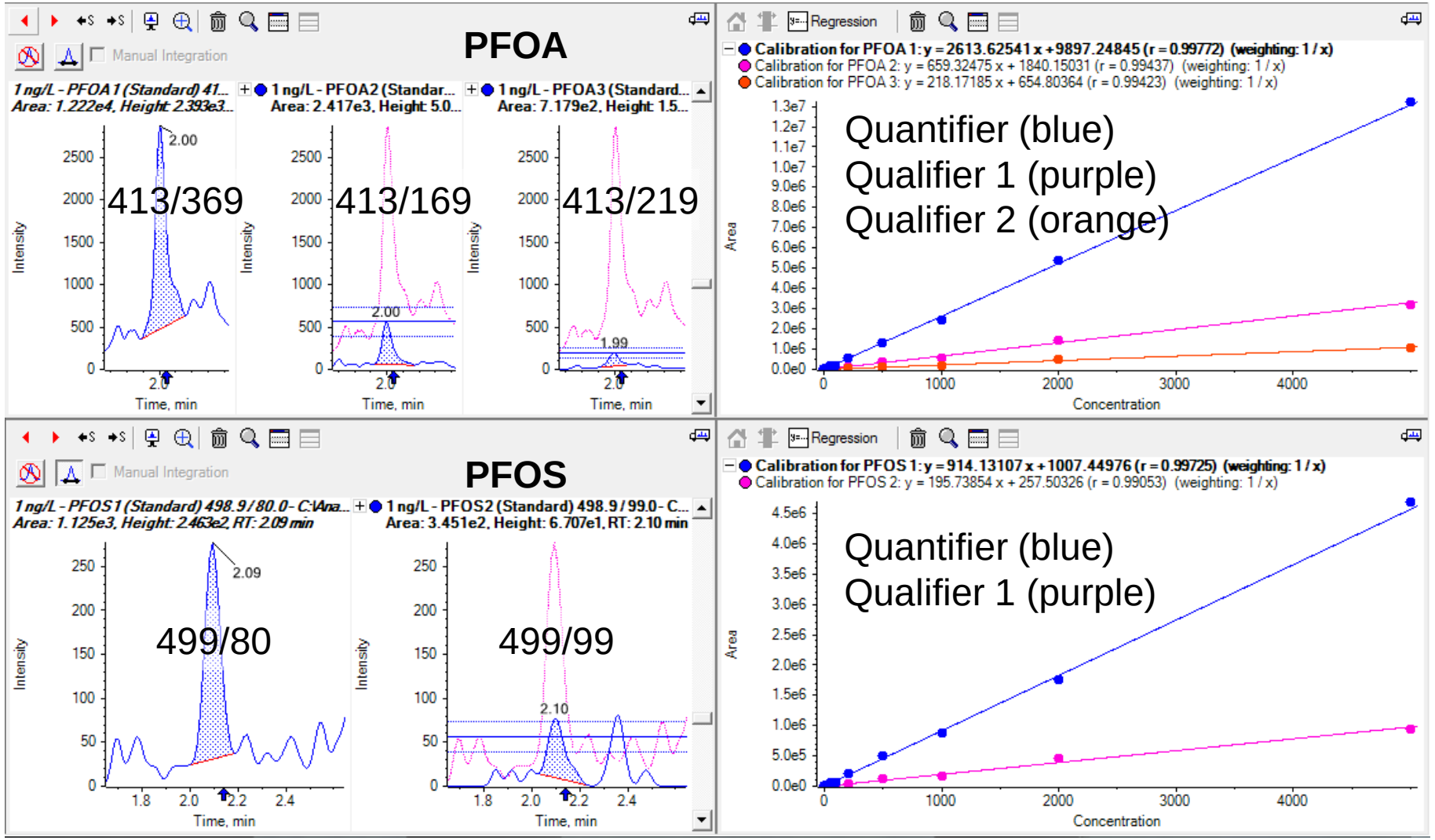
- In 6500+ negative ion mode, the ions are directed straight into the detector
- Use HED+ to deflect the negative ions to the detector
- Increase overall detector voltage to pull in negative ions



Larger detection area helps to capture wide spread of ions

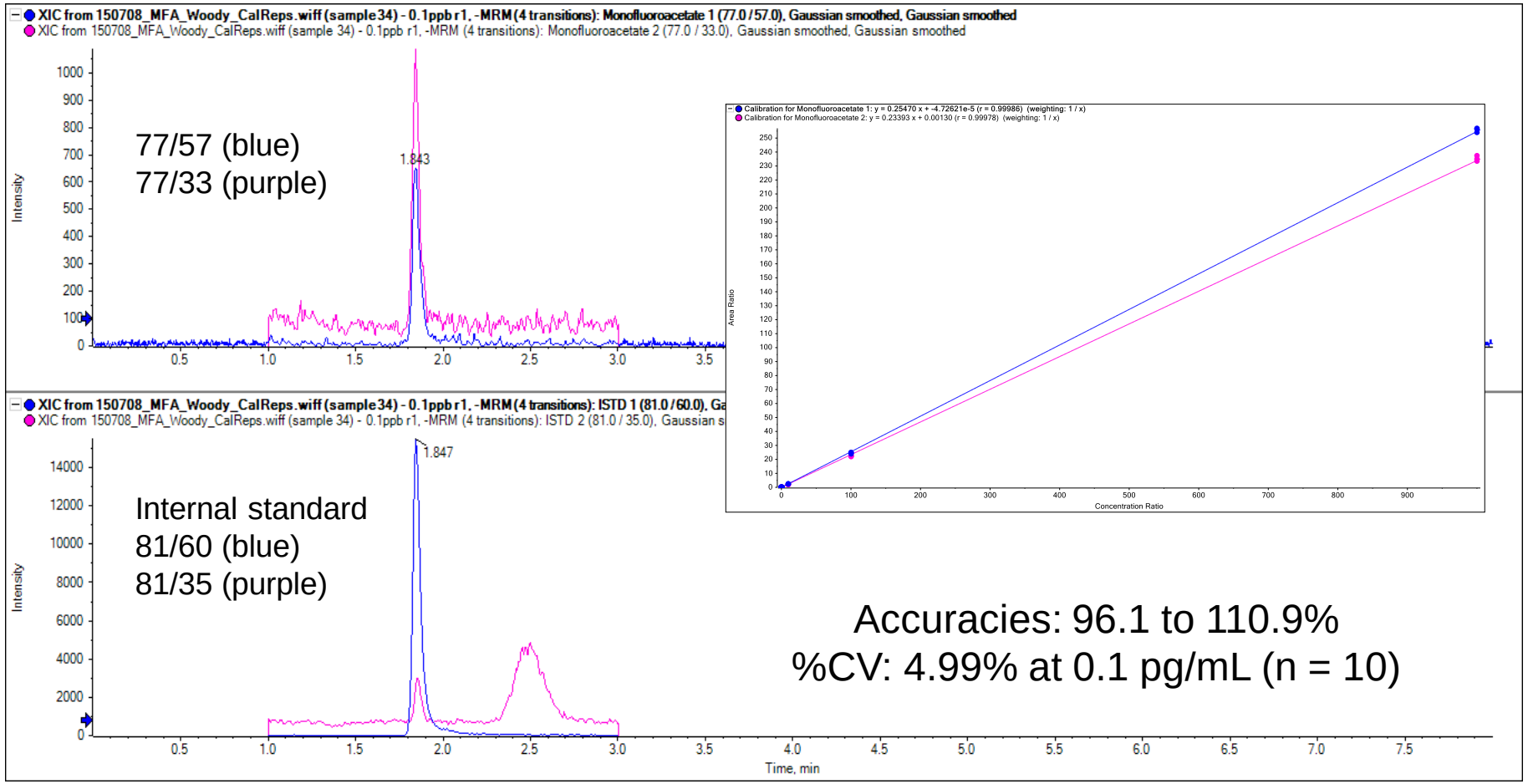
Sensitivity of 6500+ System in Negative Polarity

1 ng/L (1 part-per-trillion) PFOA and PFOS (Linearity 0.5 to 5000 ng/L)



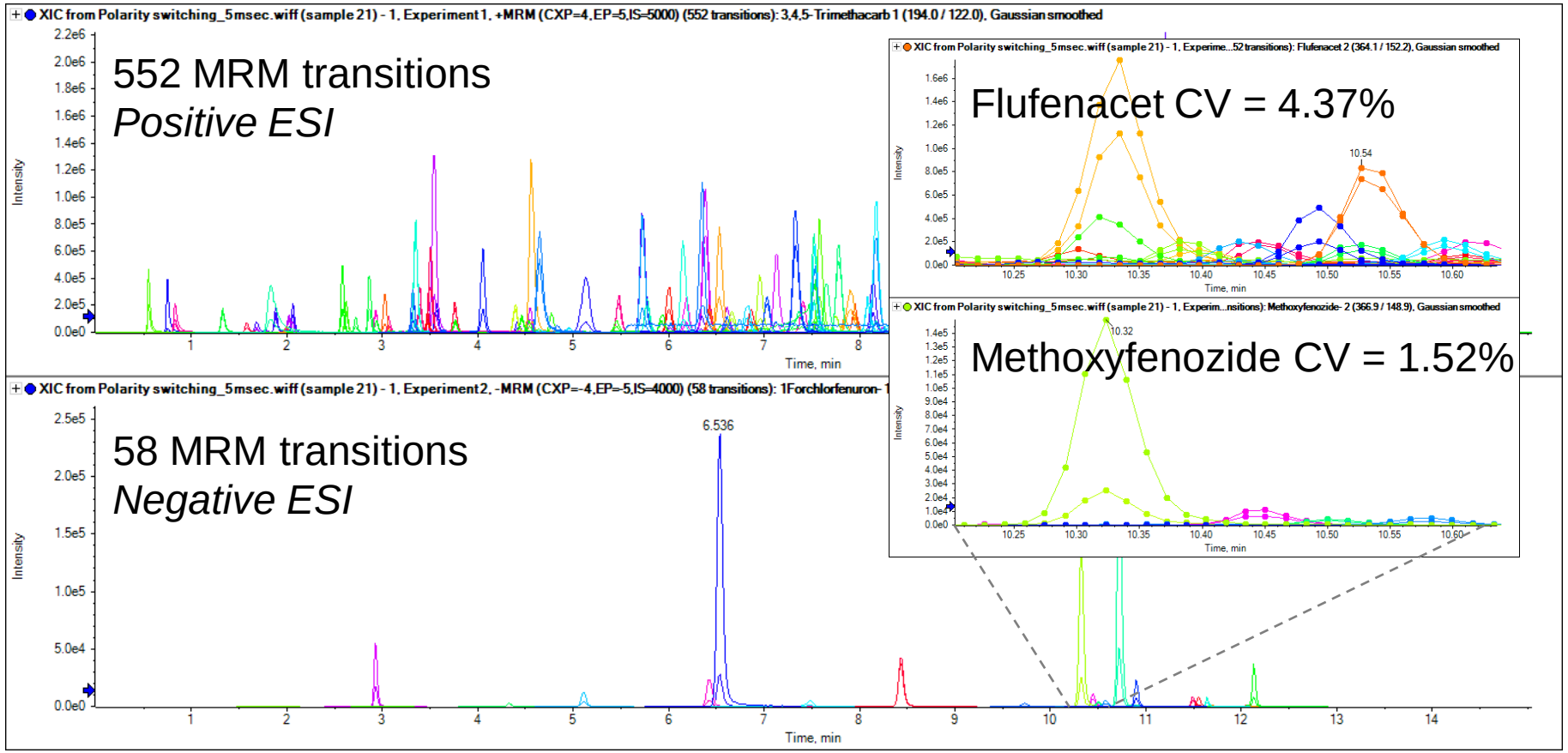
Sensitivity of 6500+ System in Negative Polarity

0.1 ng/mL (100 ppt) Monofluoroacetate (Linearity 0.05 – 1000 ng/mL)



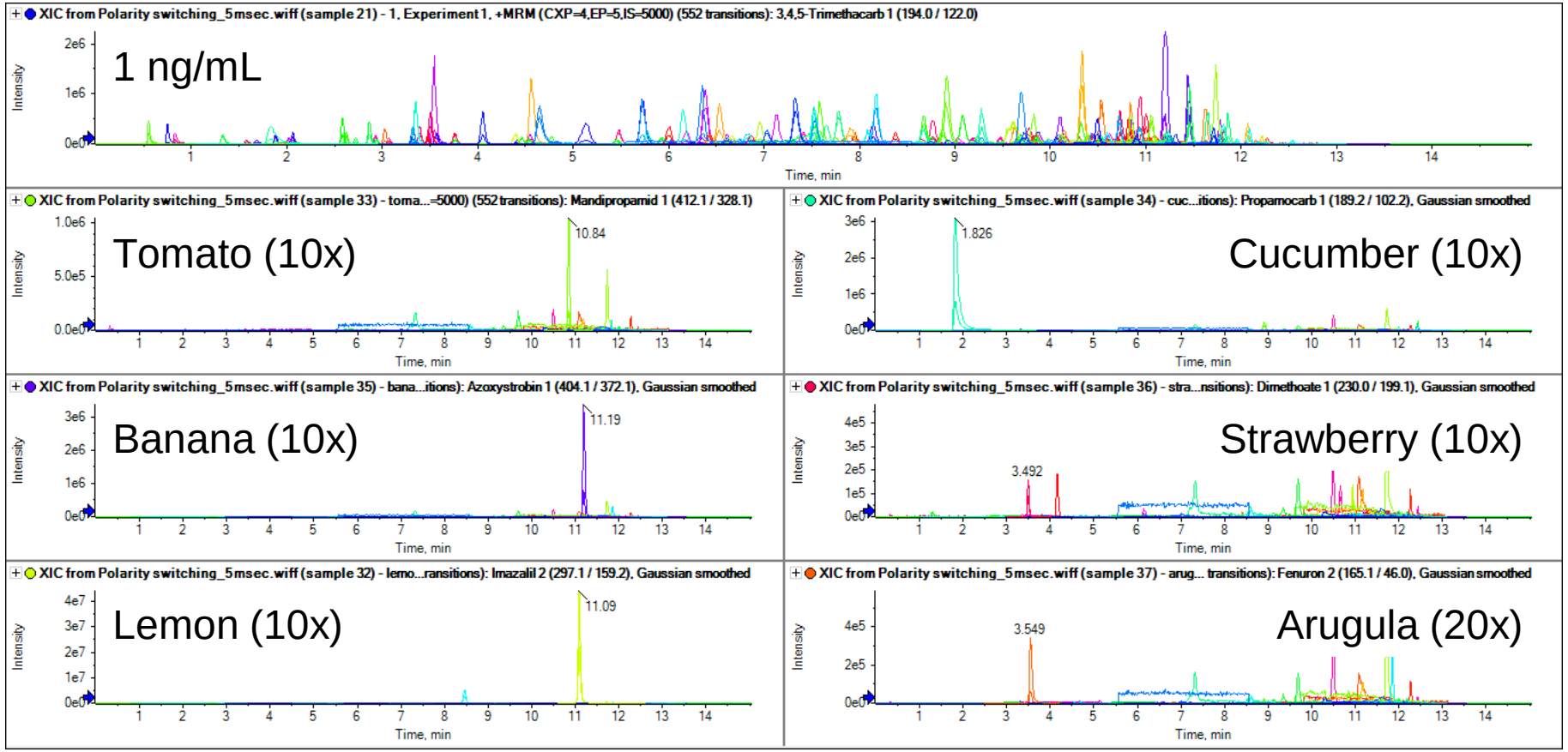
Ultra Fast Polarity Switching of 6500+ System

Multi-Pesticide Screening for ~300 Analytes with 5 msec Switching



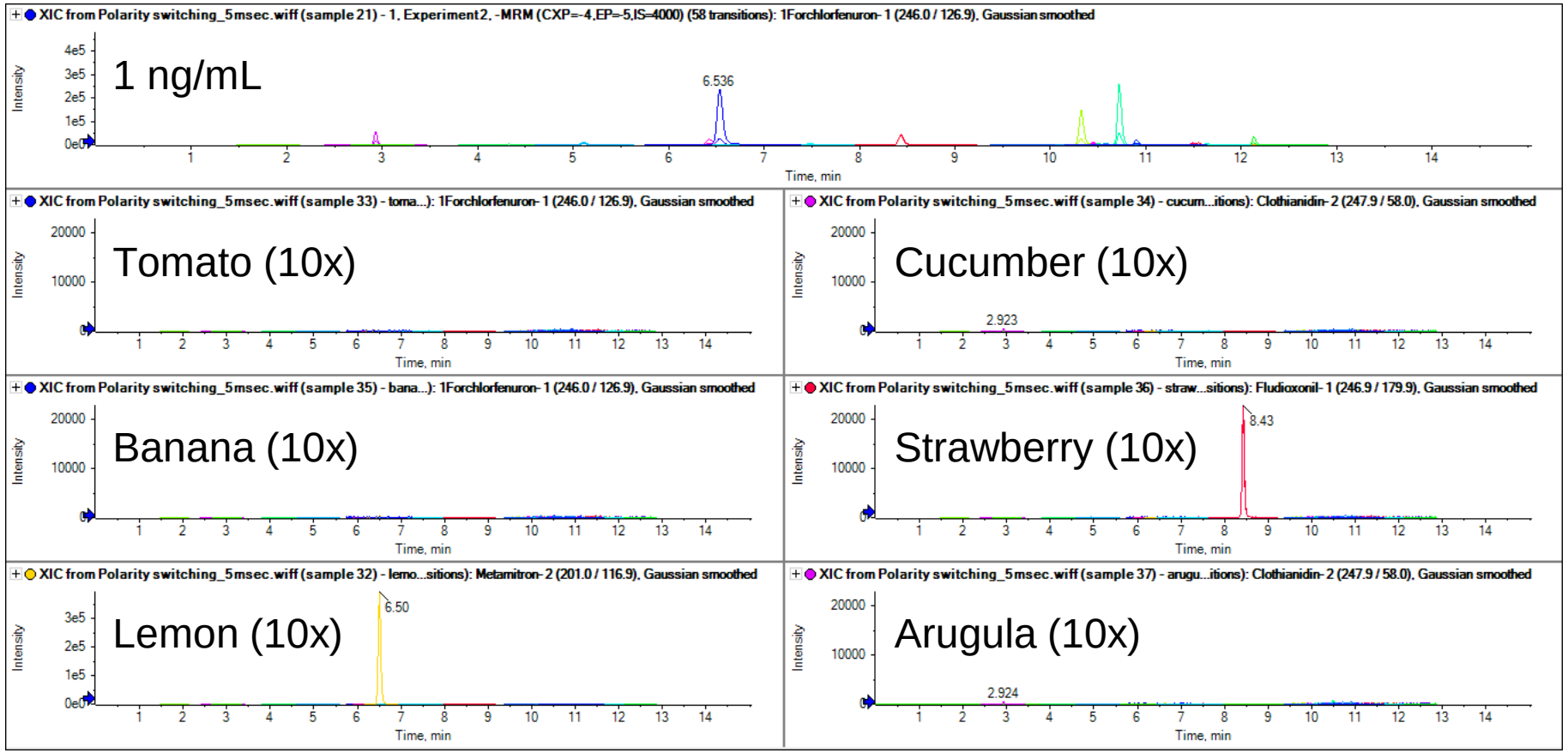
Multi-Pesticide Screening with 5 msec Polarity Switching

Pesticide Standard and Sample Extracts (Positive Polarity)



Multi-Pesticide Screening with 5 msec Polarity Switching

Pesticide Standard and Sample Extracts (Negative Polarity)

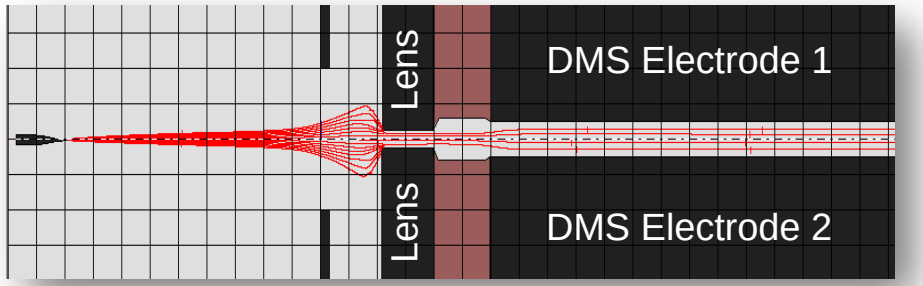


New Jet Injector SelexION®+ Technology

New Jet Injector SelexION®+ Technology

New DMS Cell Design

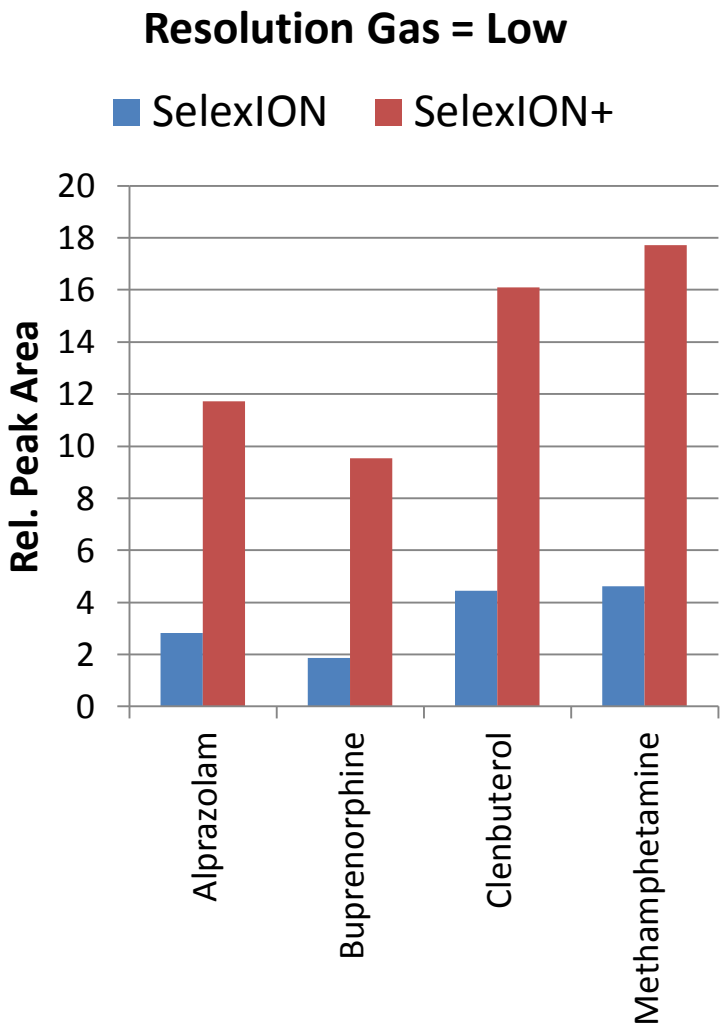
- Increase ion transmission by 2X
- Additional lens increases ion velocities into the cell
- Reduces transit time through detrimental fringing field
- ***Only available on 6500+ Platform***

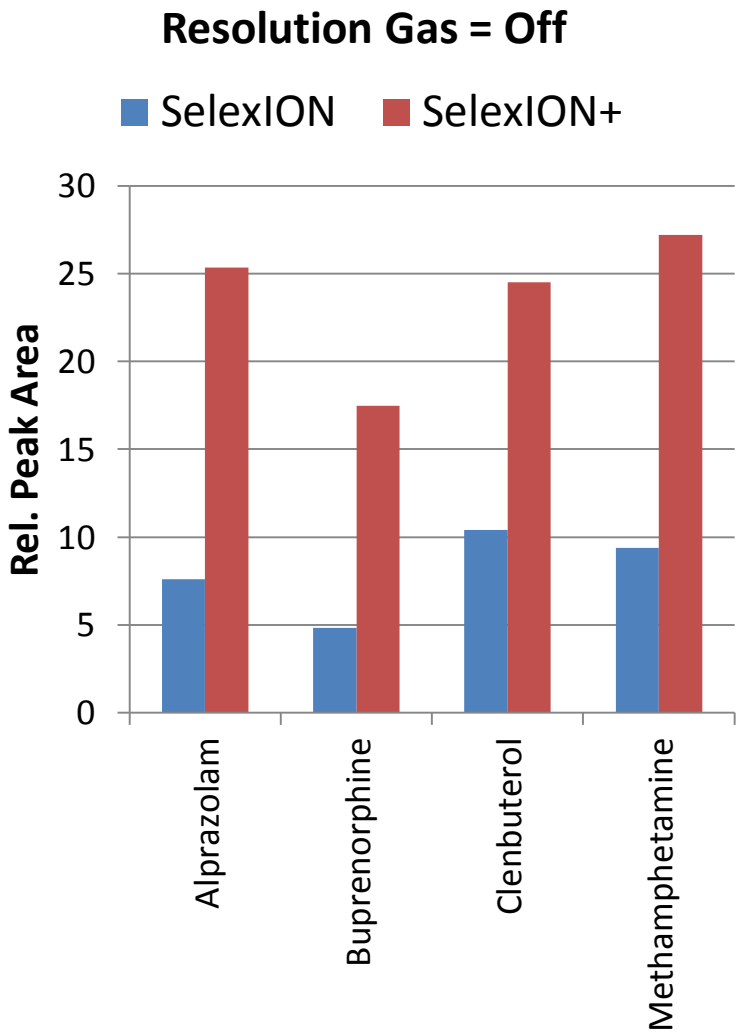


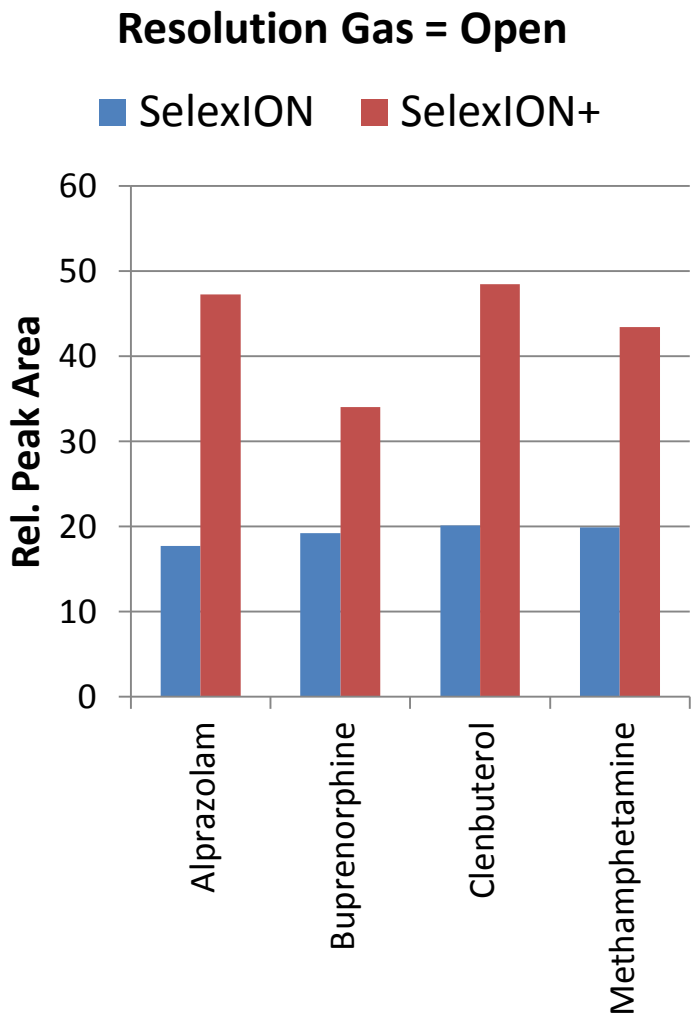
Continually driving selectivity improvements

SelexION®+ Performance Improvements

2X Increase in transmission efficiency with new jet injector



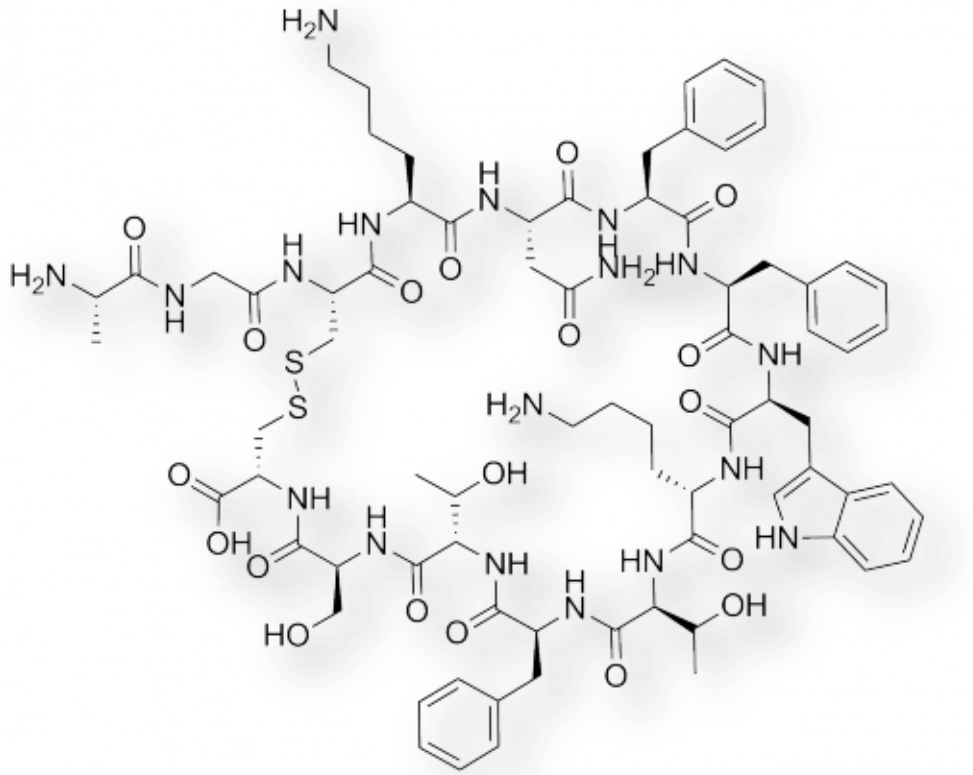




~ 2X increase in signal intensity in all DMS resolution settings

Cyclic Peptides & Peptides with Poor MS/MS Fragmentation

- Poor MS/MS-cyclic peptide
- Non specific product ions- low mass Q3 fragments



Somatostatin Cyclic Peptide

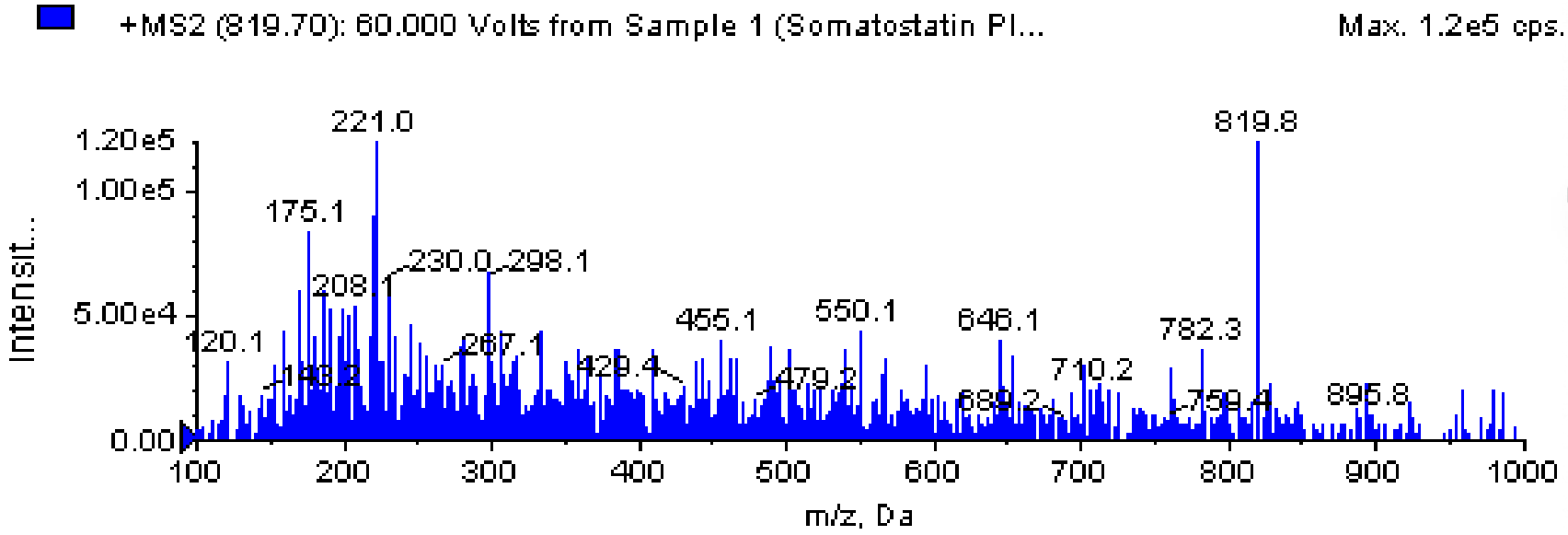
C76H104N18O19S2

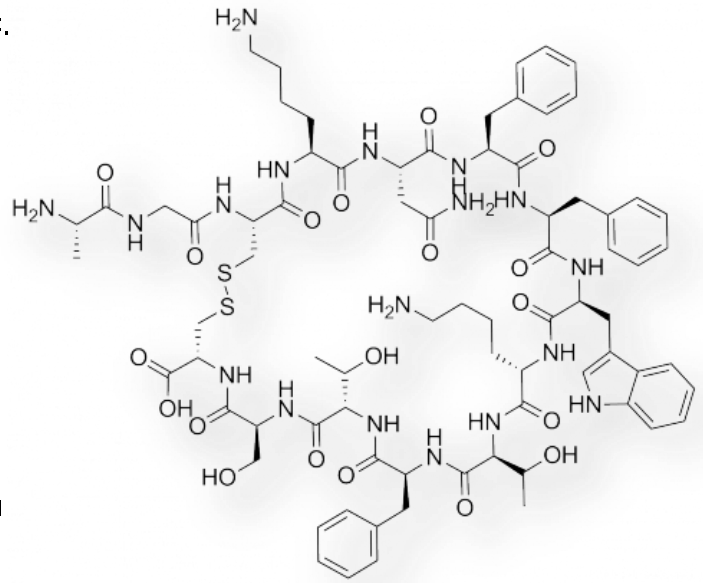
1636.7Da

+2 charge- m/z 819.7

Somatostatin Product Ion Spectrum

Product of Q1 819.7 Da

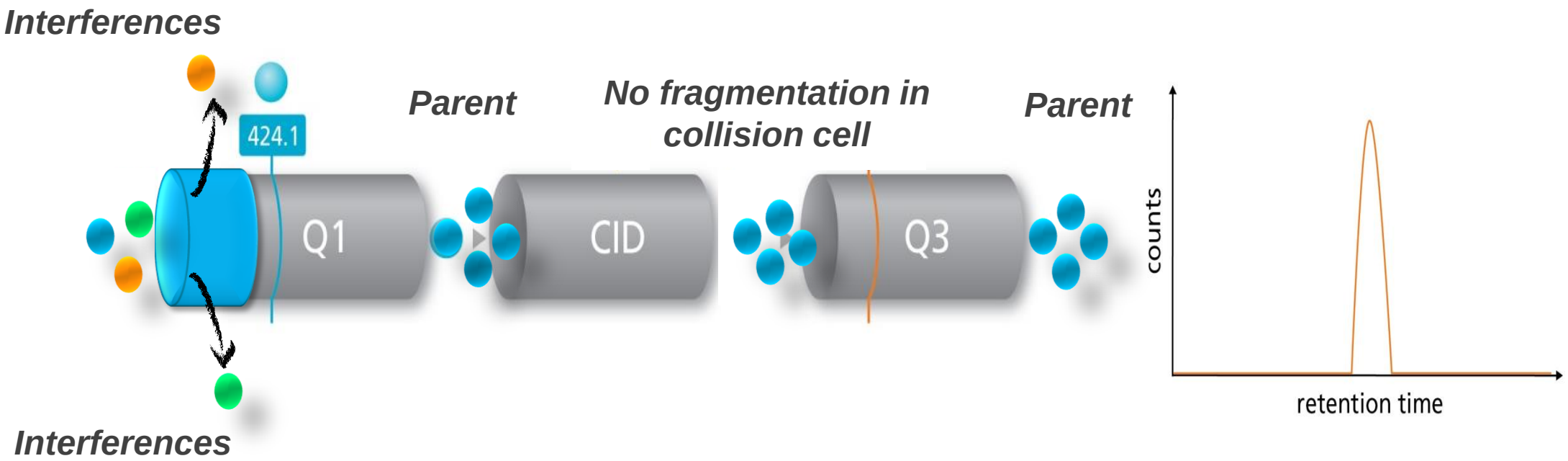




- Poor MS/MS-cyclic peptide
- Non specific product ions- low mass Q3 fragments

Best approach parent to parent quantification but limited by huge background noise

SelexION®+ Multiple Ion Monitoring (MIM) Assay



SelexION®+ Technology

Parent Ion Transmission

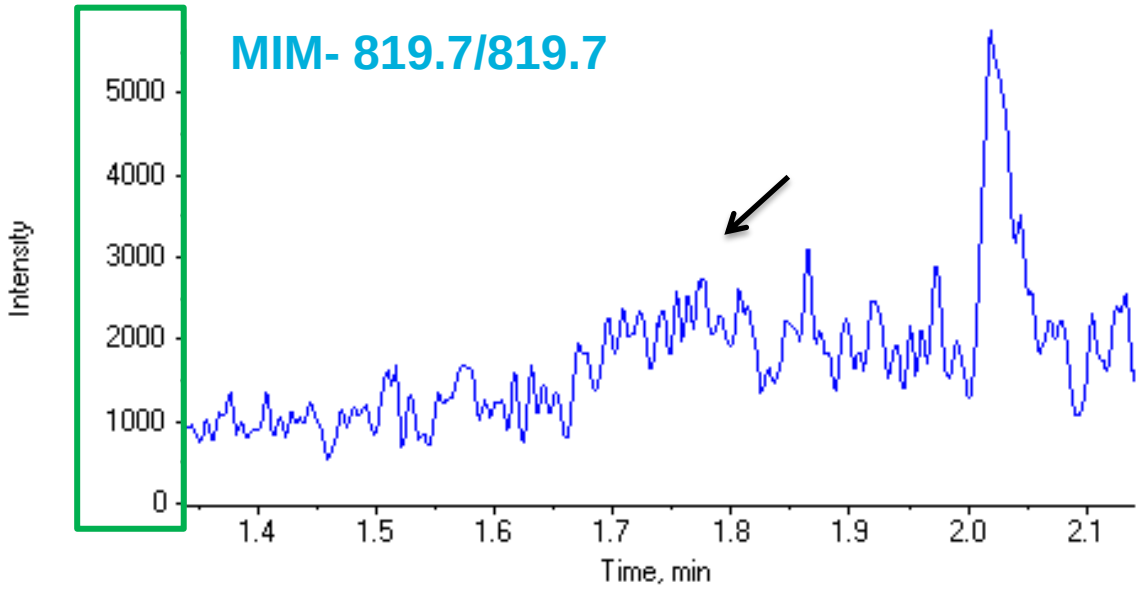
Parent Ion Transmission

Reduce Background Noise

Eliminate interferences and achieve cleaner background with SelexION®+ MIM Assay

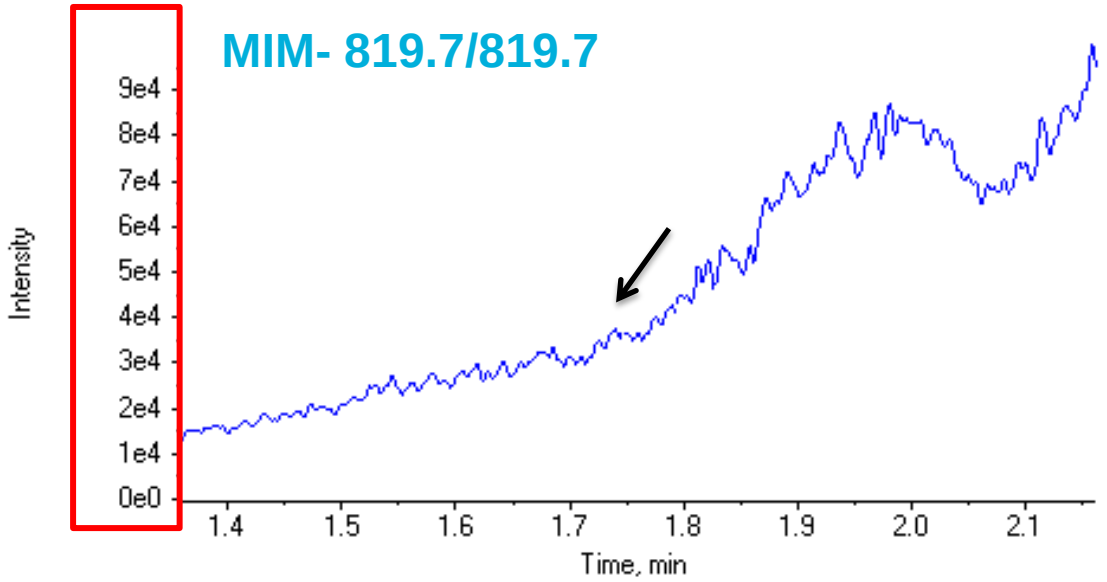
6500+ SelexION®+ MIM Assay-Somatostatin Cyclic Peptide Quant

A) Blank Plasma-*With* SelexION®+ in MIM Mode



Low background noise with SelexION+

B) Blank Plasma-*Without* SelexION®+ in MIM Mode

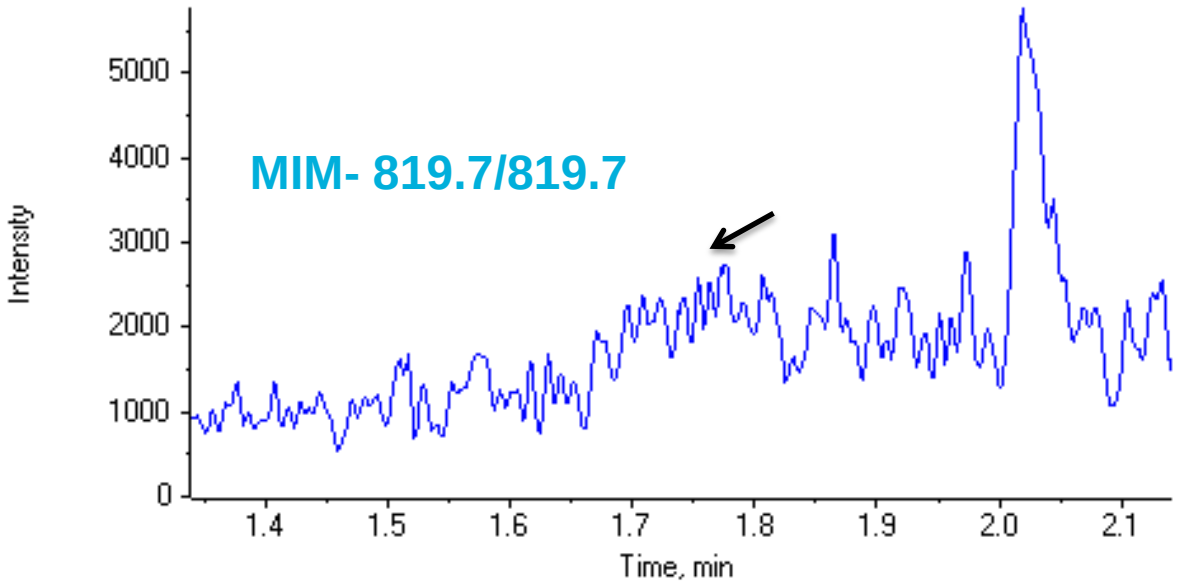


High background noise without SelexION+

Approx. 10X reduction in background noise with SelexION®+ MIM Assay

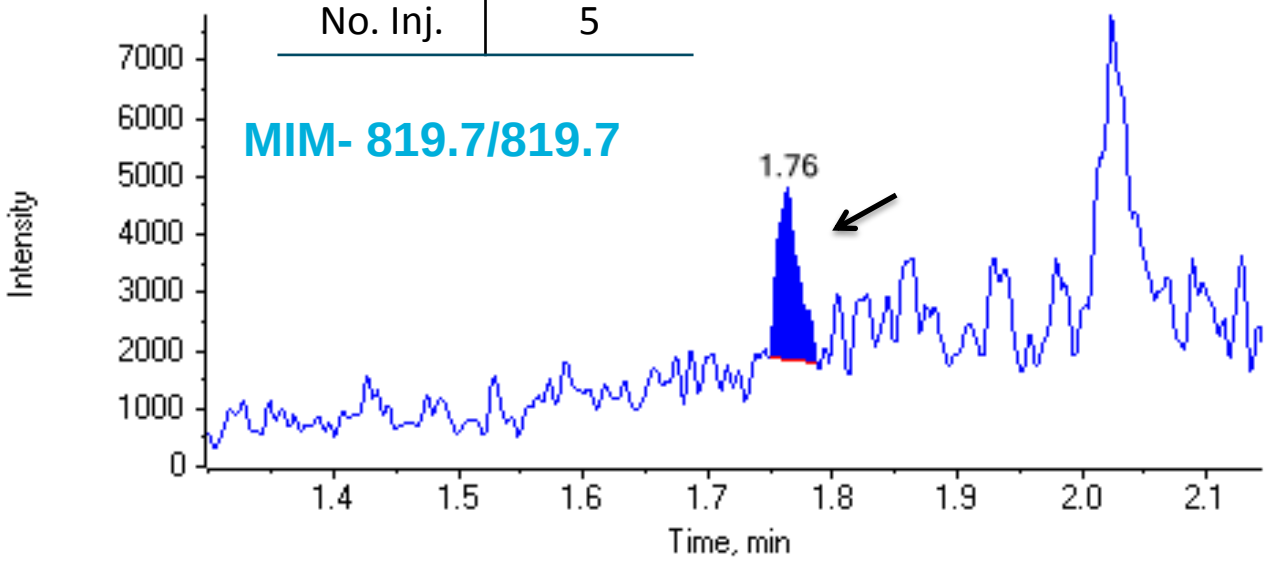
6500+ SelexION®+ Somatostatin Cyclic Peptide Quant Data

A) Blank Plasma-Somatostatin DMS MIM



B) 50 pg/mL LOQ in Rat Plasma-Somatostatin DMS MIM

S/N	9.6
Accuracy	102.7%
% CV	5.8
No. Inj.	5

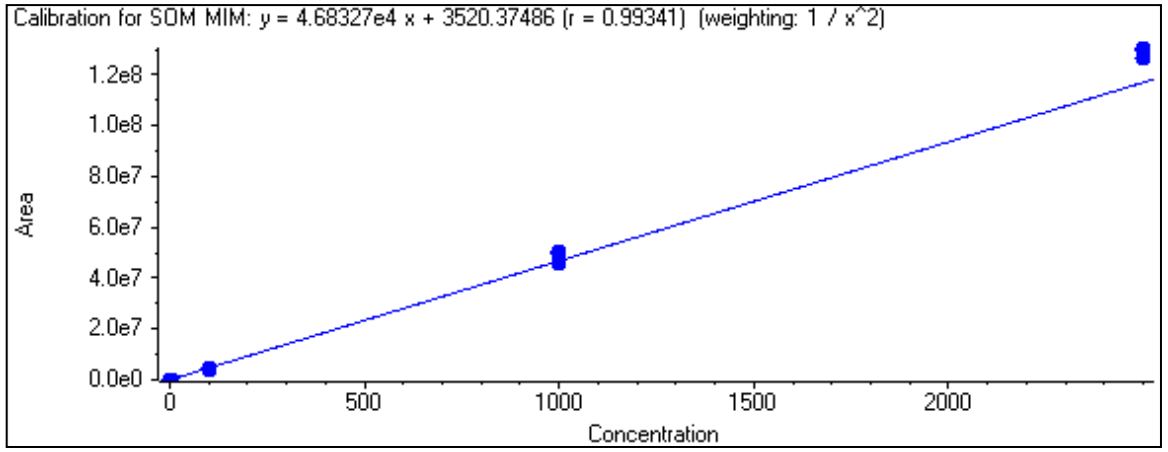


6500+ SelexION®+ Somatostatin Cyclic Peptide Quant Data

Somatostatin SelexION®+ MIM Assay in Rat Plasma

A) Calibration Curve: 0.05 ng/mL-2500 ng/mL R= 0.9934

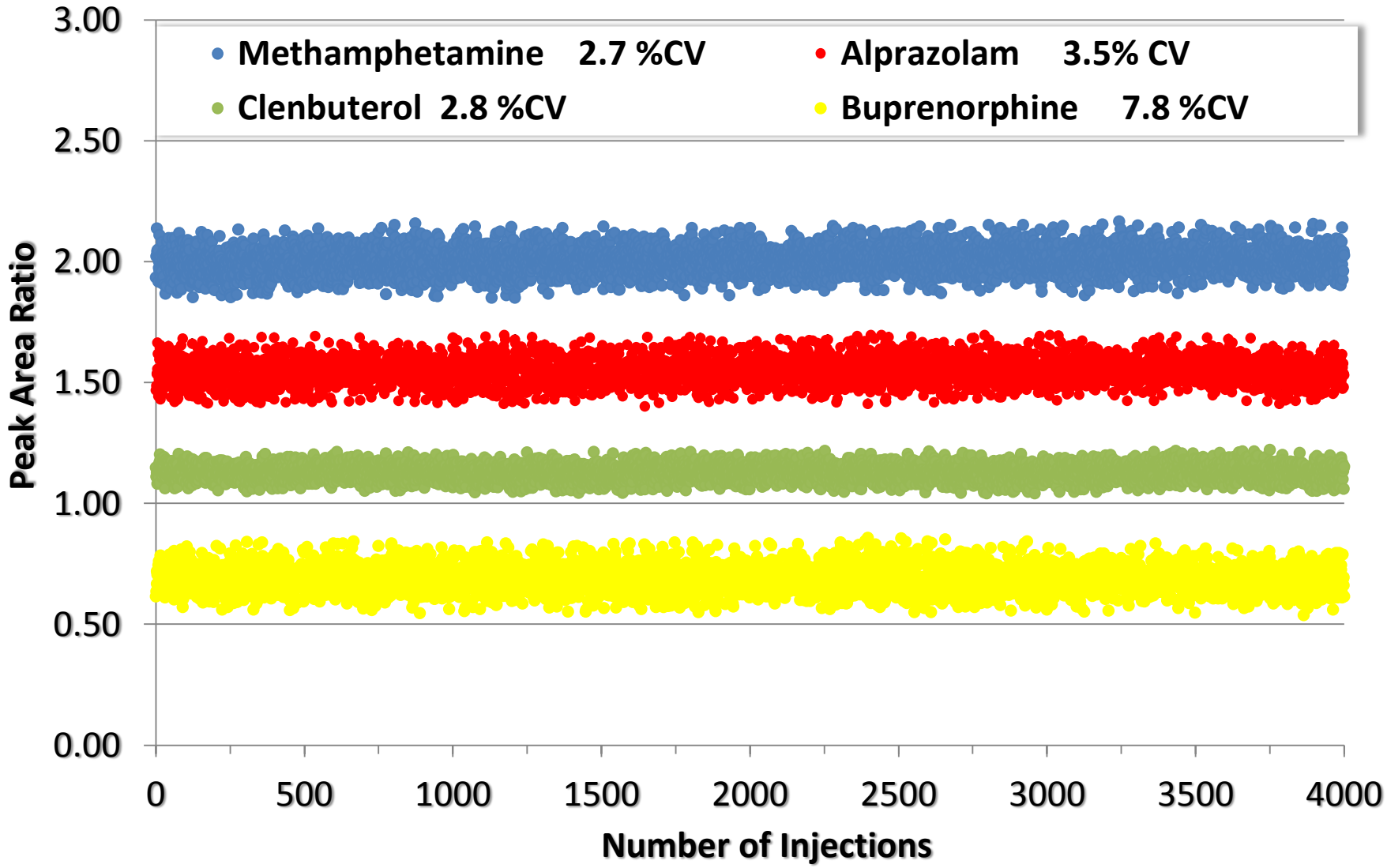
B) GLP Level accuracy: 88.9%-110.2%; Precision: <9%



ow	Compone_	Actual Co_	Num._	Mean	Stan_	Percent CV	Accuracy
1	SOM MIM	0.05	5 of 5	5.138e-2	2.99...	5.83	102.77
2	SOM MIM	0.10	5 of 5	9.664e-2	9.07...	9.39	96.64
3	SOM MIM	0.50	5 of 5	4.410e-1	1.73...	3.93	88.21
4	SOM MIM	5.00	5 of 5	5.494e0	2.06...	3.75	109.87
5	SOM MIM	100.00	5 of 5	8.895e1	5.70...	6.41	88.95
6	SOM MIM	1000.00	5 of 5	1.033e3	4.85...	4.70	103.29
7	SOM MIM	2500.00	5 of 5	2.757e3	3.23...	1.17	110.27

6500+ SelexION®+ Robustness Data in Crashed Plasma: 4000 Injections

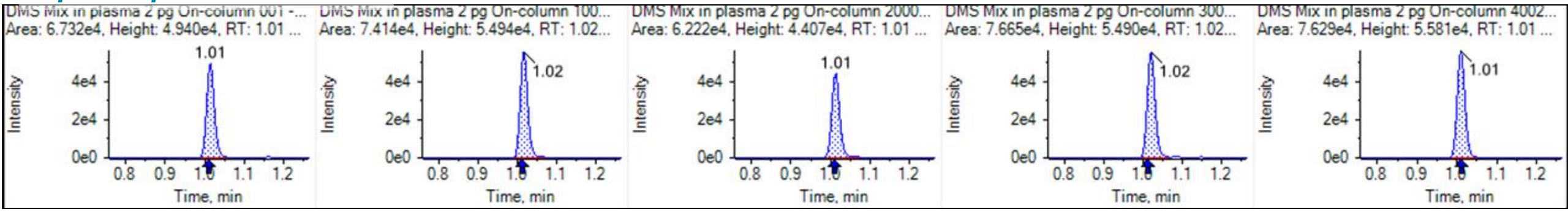
Repeatability of 4000 injections (crashed human plasma (1:3) diluted 1:2)



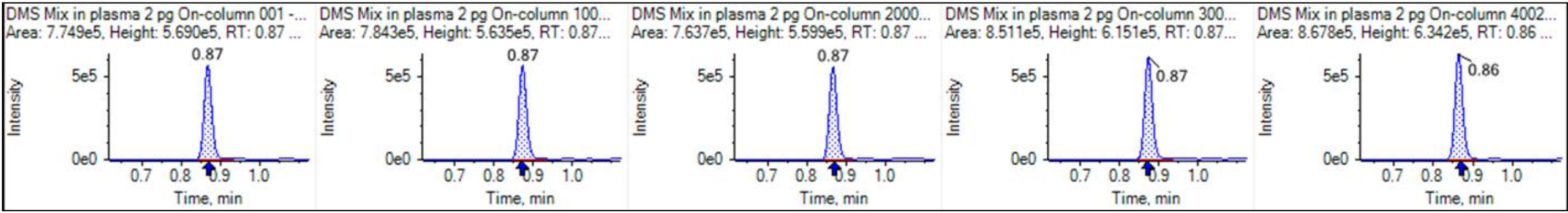
6500+ SelexION®+ Robustness Data in Crashed Plasma: 4000 Injections

1st Injection *1000th Injection* *2000th Injection* *3000th Injection* *4000th Injection*

Buprenorphine - % CV- 7.8

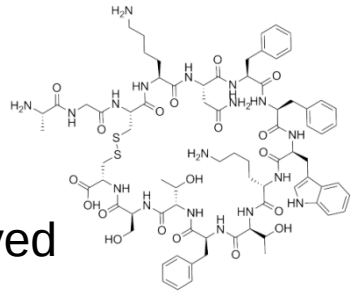


Clenbuterol- %CV-2.8

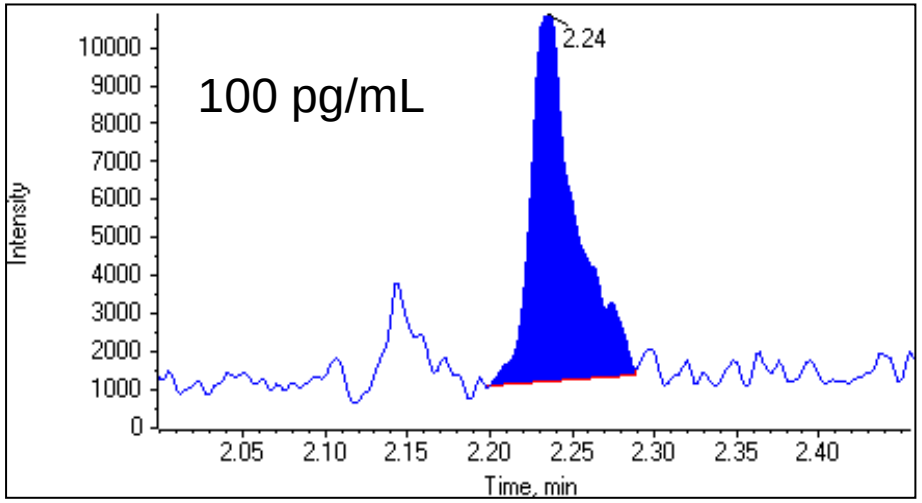


Proven Performance for Robust and Rugged Bioanalytical Assays

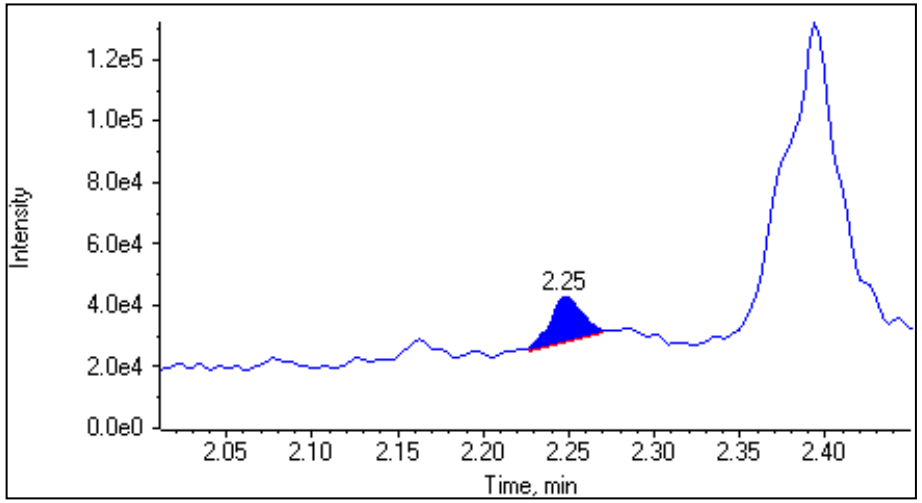
Detection of Somatostatin with and without SelexION+



6500+ with DMS



6500+ DMS removed



Somatostatin, a cyclic peptide with poor MS/MS fragmentation is acquired using MIM (819.7/819.7) assay in rat plasma showing high background noise limiting the S/N ratio and LOQ

Highly reduced background noise enabling desirable LOQ of 100 pg/mL using new SelexION+ jet injector on 6500+ System (S/N ratio = 12, accuracy = 101% and %CV < 10%)

Audible Noise Reduction

- **Active (source exhaust modifications)**
  - Source exhaust flow minimized to match gas load
- **Passive (quieter tubing)**
  - Eliminate “whistling” noise
- **Quieter system operation**
  - Noticeable under most source conditions
  - No impact on sensitivity

Decreased audible noise for a more comfortable work environment

The New SCIEX 6500+ Series with HED+ Detector Technology

Industry proven performance: IonDrive™ Turbo V™ ion source and QJet® ion guide

- Sensitivity boost with "***new HED+ detector technology***"
- Enhanced SelexION performance with ***"new jet injector DMS cell"*** without compromising resolution
- **Fast polarity switching speed** (5 msec)
- **Audible noise reduction**

Acknowledgements

- Sylvie Beaudet
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- Kelli Jonakin

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