

# High resolution MS vs Triple Quadrupole

Why aren't we all using it?

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November 2014

# High Resolution benefits

- Full scan data
- Quantitative and qualitative data
- Retrospective integration and analysis
- Minimal method development
- No optimisation between MS
- Selectivity
- Discrimination of multi-charge analytes
- Co-elution of tryptic digested peptides
- Eliminating matrix effects and “dirty extracts”
- Large dynamic range
- Remove chromatography

# High resolution MS

## Perceived shortfalls

- Sensitivity
- Instrumentation cost
- Regulatory acceptance?
- Data volume

# Triple Quad MS

## Perceived shortfalls

- Long development times
- Dedicated skilled analyst
- Matrix interference with similar m/z
- Cross talk / cross ion
- Metabolites with close m/z

# Why are we not all using it?

Review of published methods 2012 – 2014

## HRMS

1 published method

Analyte / Species	Range	Author
Aesculin in rat	10/50 – 1500 ng/mL (no LLOQ QC)	Yi Li et al 2013 (Xi'an Jiaotong University)

## TQ-MS

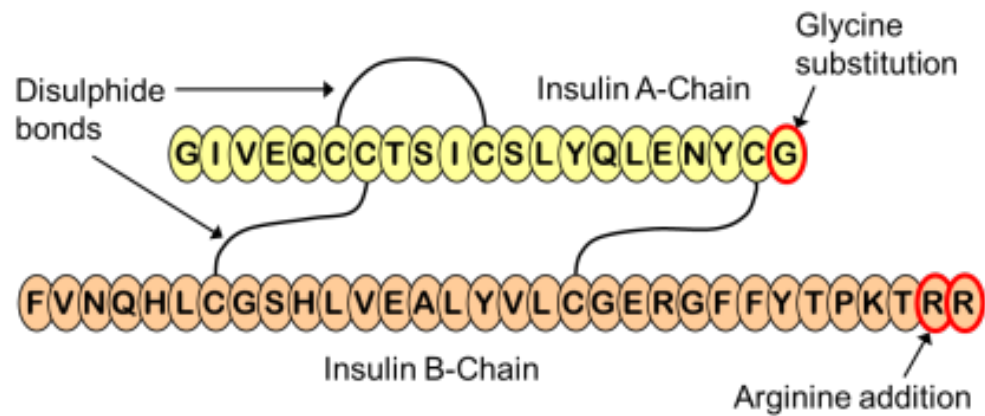
64 published methods

# Our experience

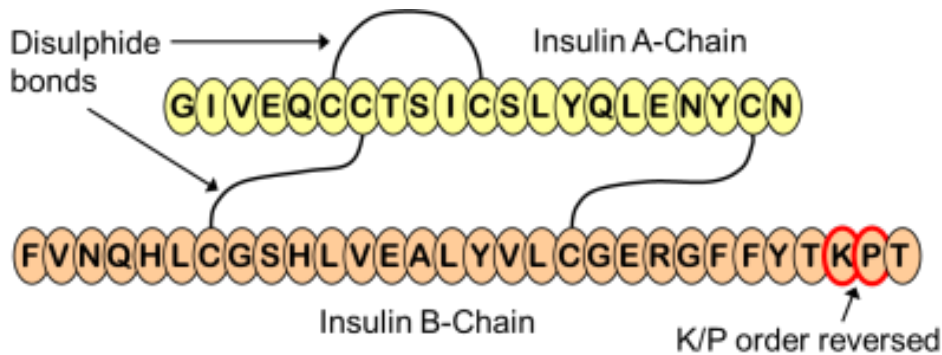
Analyte	MW (Da)	QTOF range (ng/mL)	TQ range (ng/mL)
Clobetasol	467	10 – 500	0.01 – 10
Clobetasol propionate	411	5 – 500	0.01 – 10
oligonucleotide 18-mer	5825	50 – ?	1 – 500
Insulin glargine	6063	20 – ?	0.2 – 200 0.05 – 10

# Case study: Difficult and sensitive high throughput assay

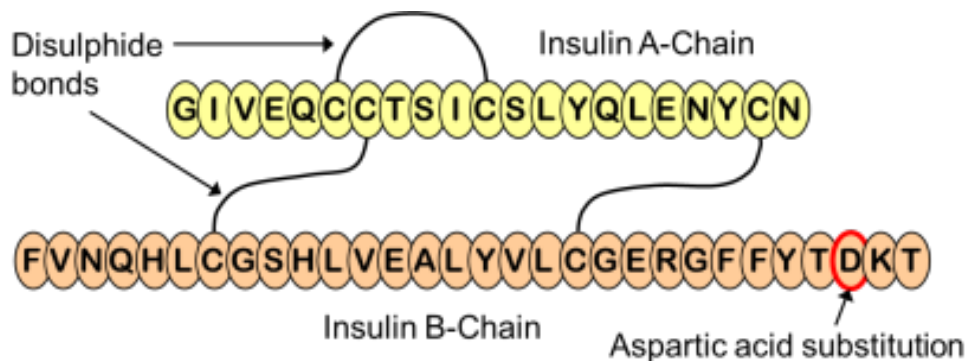
Protein analysis on TQ –  
breaking the 50 pg/mL  
barrier for insulin  
analysis



Glargine



Lispro



Aspart



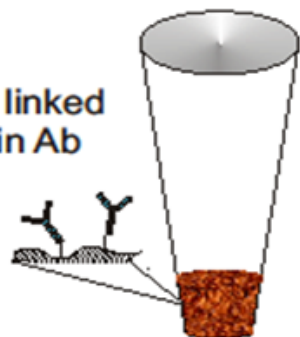
# Insulin MSIA D.A.R.T.'S



**Step 1**  
Sample Incubation  
(repetitive flow)

**Step 2**  
Washes  
(repetitive flow)


**Step 3**  
Elution  
(repetitive flow or mix within tip)

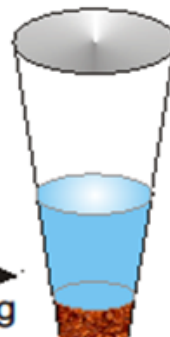
Covalently linked  
pan Insulin Ab




Insulin (internal standard) =   
Insulin Analogs = 



  
Insulin analog capture



  
Rinse & Elute



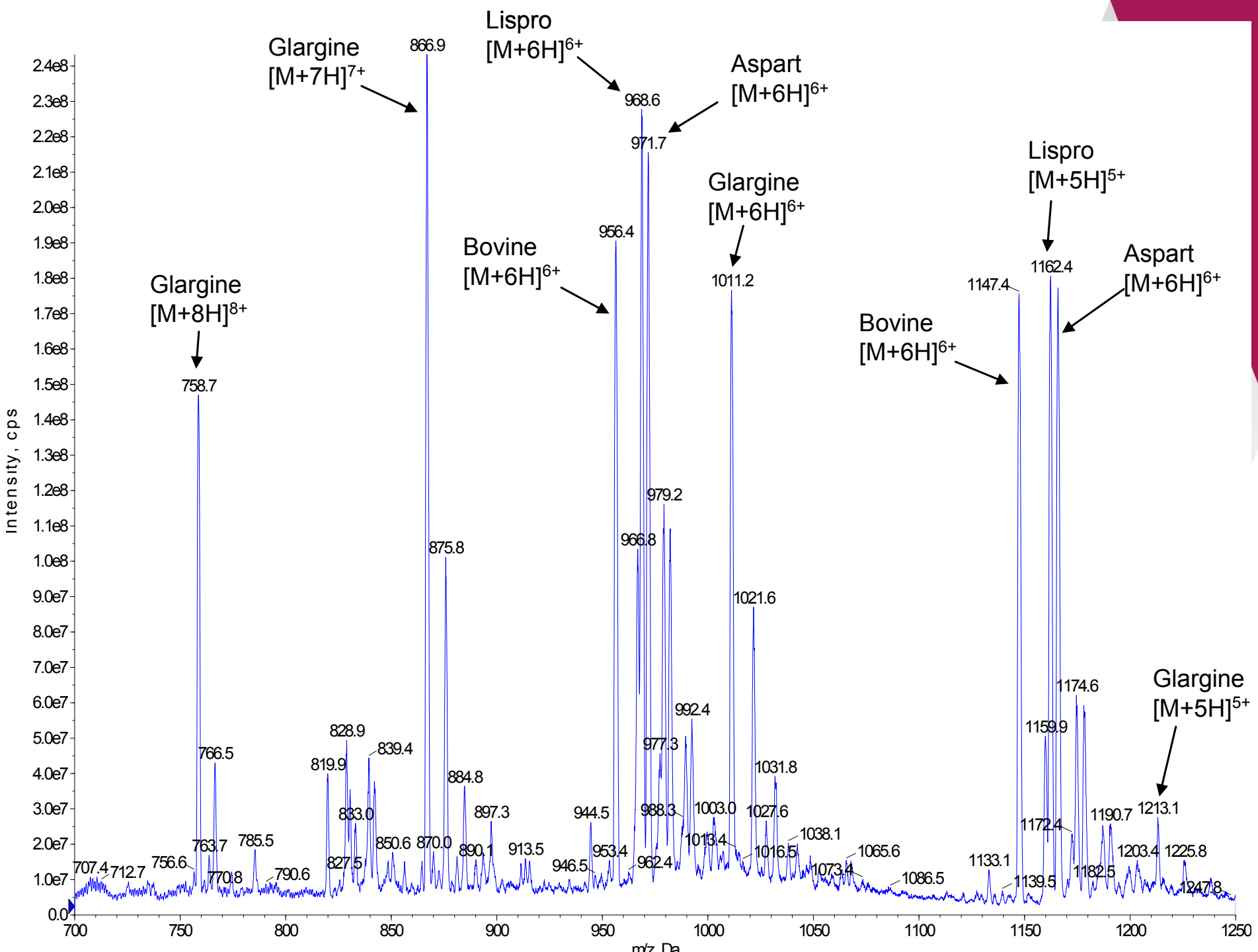
Analytical  
Sample

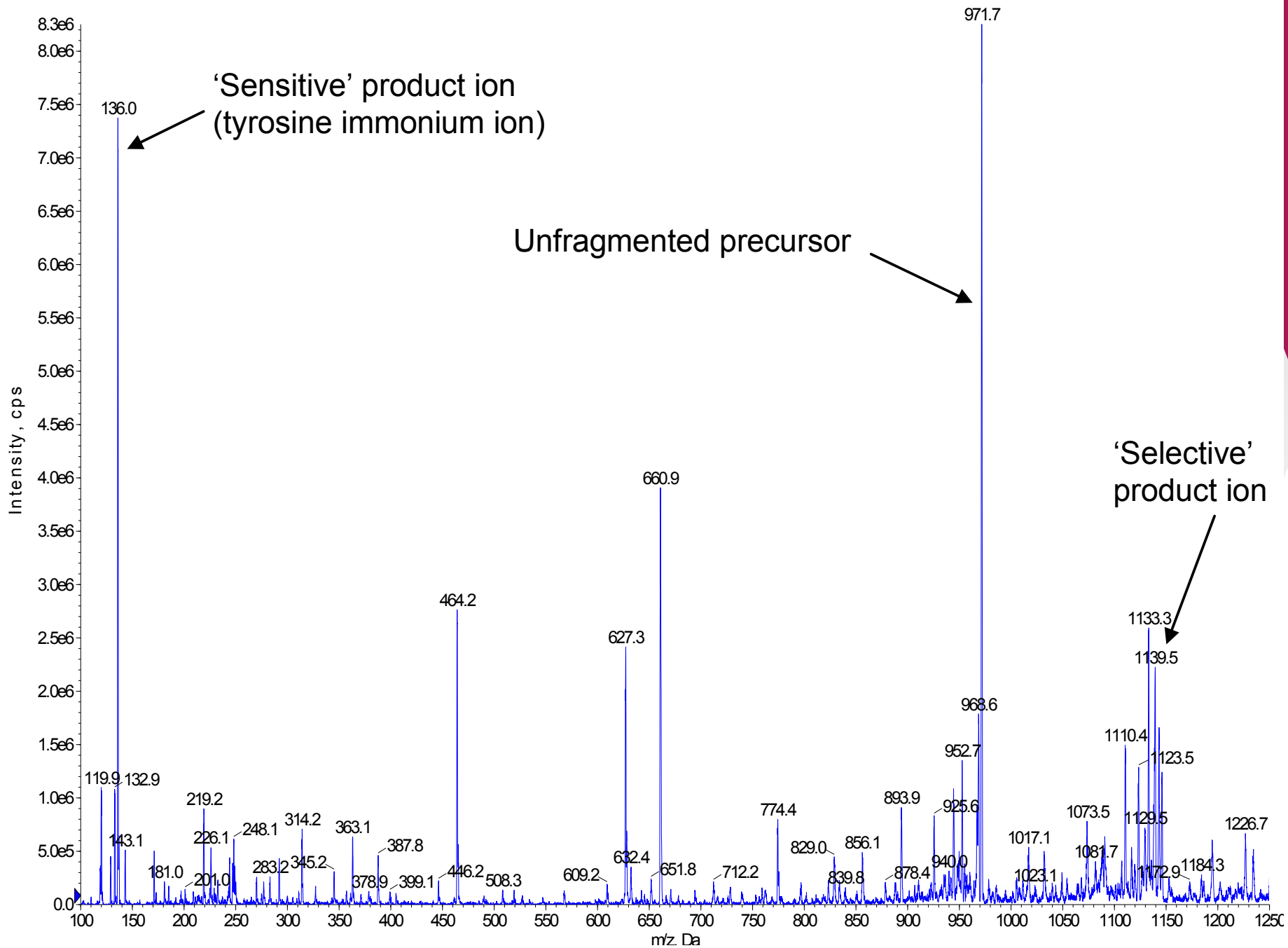


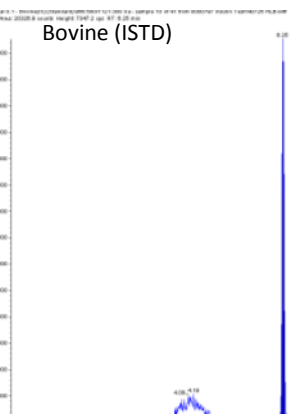
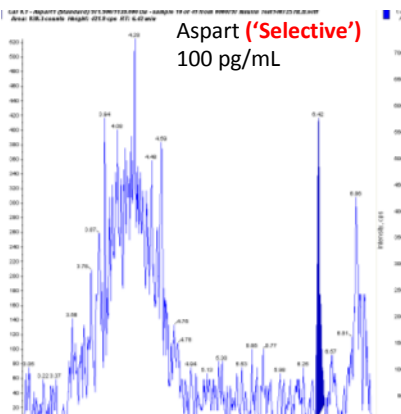
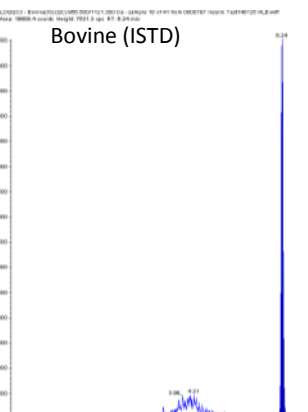
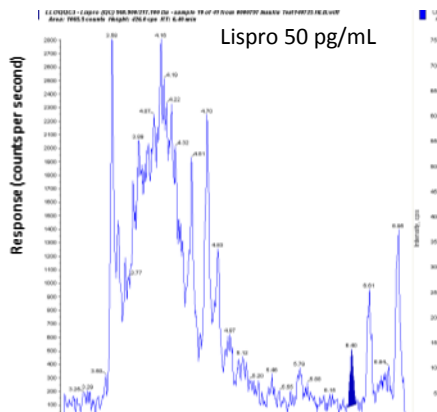
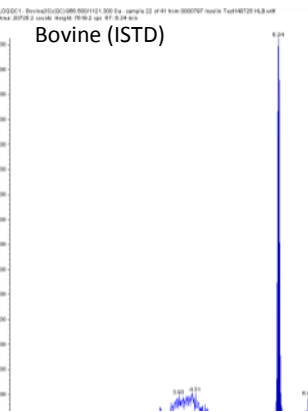
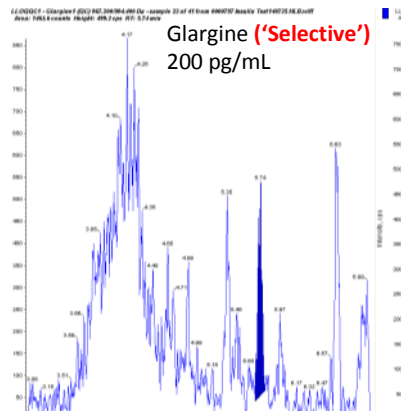
1. Buffer  
2. Water  
3. Elution

Dispense Eluent  
into a Microtiter Plate

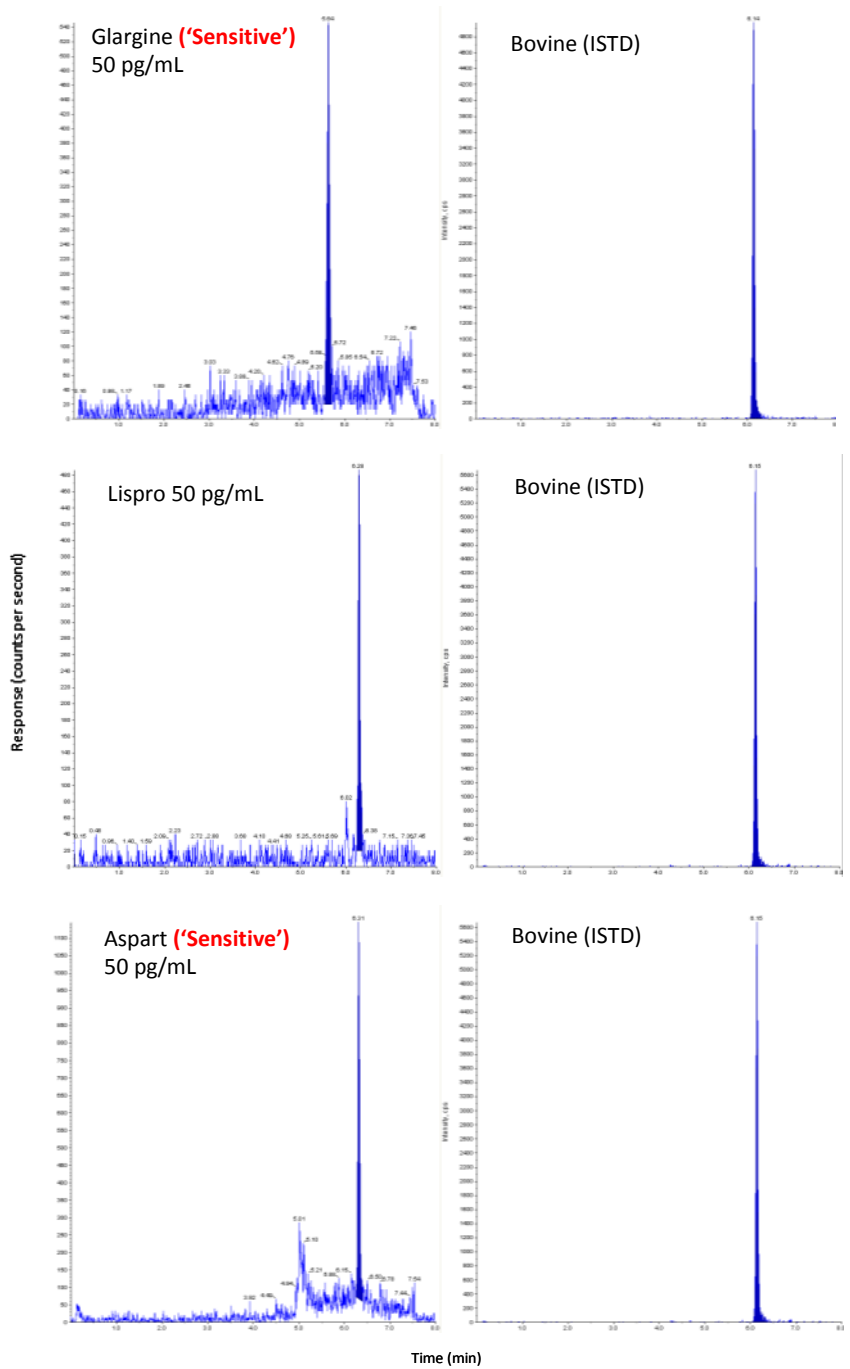








Time (min)



# Triple Quadrupole – accelerating in sensitivity

## Microsampling

## Selectivity solutions

- Selective extraction
- SelexION

# Conclusion

## High resolution

- Data advantage
- Needs to be more sensitive

## Triple Quadrupole

- Unbeaten for regulated bioanalysis
- Technological developments to overcome shortfalls