TMS – The Magnificent Separator (or Trouble, Magic, Stress)

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Why is TMS the tool of choice for IEM?
Brief history lesson
How does it work? (Magic)
What could possibly go wrong?
Troubleshooting and preventative measures

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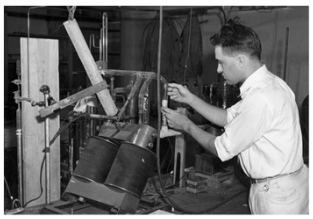
TMS timeline

- 1922 - 'Invention'
- 1940s –Commercially available
- Dominated by Physicists until Alfred Neir



Alfred Neir

JJ Thompson

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Men of the Masses

- 1950s - McLafferty, Biemann and Djerassi

Fred Mclafferty

Klaus Biemann

Carl Djerassi

- 1960s Further advances –
- Marshall and Comisarow

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How we got here

- 1980s - small organic molecules were routinely being analyzed by MS
- 1990s/2000s – Commercial analysers were available and being used within NHS laboratories with further advances in electron spray ionisation
- 2002-2004 – MS/MS analysers exponentially were implemented in NHS newborn screening laboratories

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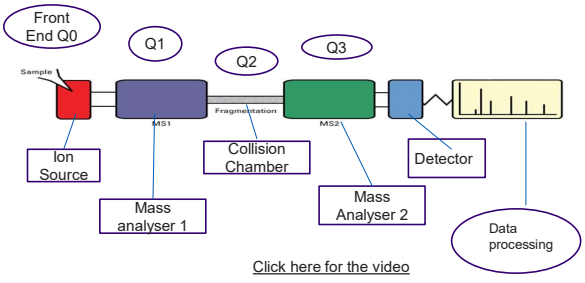
Molecule Smasher



Click here for the video

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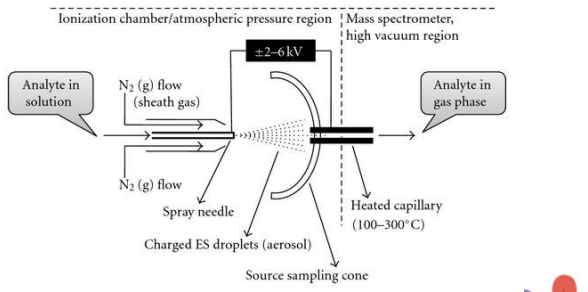
Ionisation



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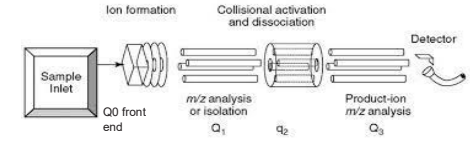
Quadrapole Magic



Click here for video

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Troubleshooting

Enhance your troubleshooting capability – know your engineer!
Most common issues : ION SUPRESSION and 'DIRTY'

HOUSEKEEPING – Good Lab Practice

- Good sample preparation and maintenance protocols
- Detailed maintenance charts with practical language
- Clear and understandable SOP
- Clean specific glassware
- Have spare clean MS/MS parts ready to install
- Track column and lot changes for as many chemicals, reagents, solvents as possible and avoid plastic!

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Troubleshooting

Is it the mass spectrometer or the LC?

More likely to be LC

- Poor peak shapes
- Change in retention time of peaks
- High pressure

More likely to be mass spectrometer

- Low intensities

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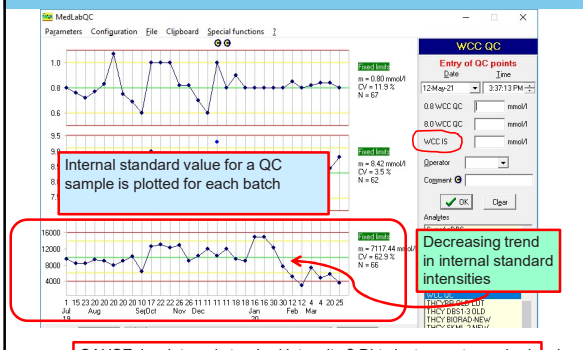
Plot internal standard values for each batch



CAUSE: low internal standard intensity ? Dirty instrument, needs cleaning

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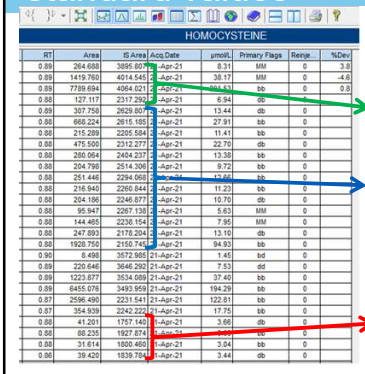
Expected internal standard values



Aqueous standards: less ion suppression, internal standard values will be higher than plasma samples

Plasma samples

Dried blood spot samples: slightly lower internal standard values due to increased ion suppression

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Decreasing internal standard intensities

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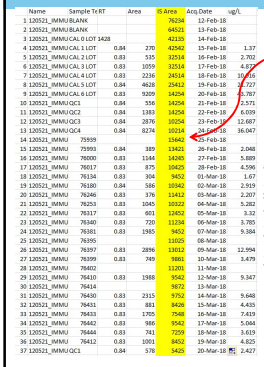
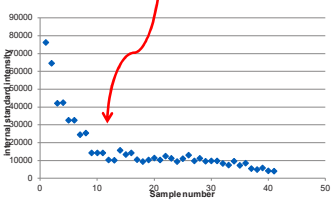


Decreasing internal standard intensities through the batch



CAUSE: 'Charging' – Mass spectrometer is dirty
Ion block and/or quadrupoles need cleaning

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Low intensities, unknown cause, check the instrument parameters

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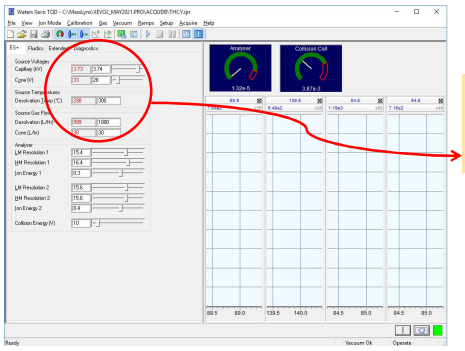

Check the instrument read back values are as expected

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Record pump pressure for each assay

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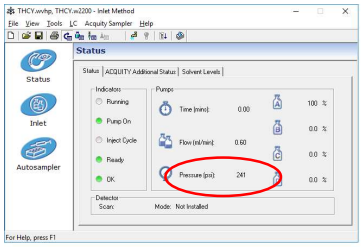

Record the pressure for each assay, it should be consistent from batch to batch

High pressure or Erratic pressure

? blockage

Low pressure
? leak
? Wrong column
? Wrong mobile phase

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Investigating high pressure

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Poor chromatography?

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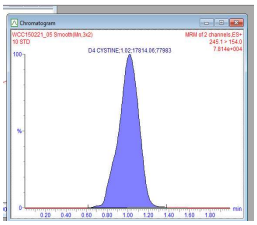
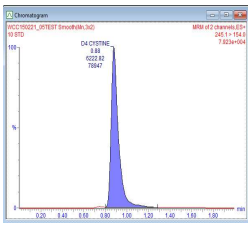
Check the column…



Old column ☹



New column ☺

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Further reading and thanks

NHS Birmingham Women's and Children's NHS Foundation Trust

https://pubs.acs.org/doi/10.1021/ac8013065#

- Many thanks to colleagues at Birmingham Children's
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