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

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By your side

1

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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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2

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TMS timeline

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

Alfred Neir

JJ Thompson

3

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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

4

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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

5

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Molecule Smasher

Click here for the video

6

Ionisation

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7

Quadrapole Magic

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[Click here for video](#)

8

Troubleshooting

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Enhance your troubleshooting capability – know your engineer!
Most common issues : **ION SUPPRESSION** 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!

9

Troubleshooting

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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

10

Plot internal standard values for each batch

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Internal standard value for a QC sample is plotted for each batch

Decreasing trend in internal standard intensities

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

11

Expected internal standard values

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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

12

Decreasing internal standard intensities

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Name	Sample Text	Area	% Area	Acq Date	ug/L
1	120521_MW_MU_BURKIN	76234	0.84	12-Feb-18	
2	120521_MW_MU_CAL 1 LOT 1438	40230	0.83	14-Feb-18	
3	120521_MW_MU_CAL 2 LOT 1438	40230	0.84	14-Feb-18	
4	120521_MW_MU_CAL 3 LOT 1438	40230	0.83	14-Feb-18	
5	120521_MW_MU_CAL 4 LOT 1438	40230	0.83	14-Feb-18	
6	120521_MW_MU_CAL 5 LOT 1438	40230	0.83	14-Feb-18	
7	120521_MW_MU_CAL 6 LOT 1438	40230	0.83	14-Feb-18	
8	120521_MW_MU_CAL 7 LOT 1438	40230	0.83	14-Feb-18	
9	120521_MW_MU_CAL 8 LOT 1438	40230	0.83	14-Feb-18	
10	120521_MW_MU_CAL 9 LOT 1438	40230	0.83	14-Feb-18	
11	120521_MW_MU_CAL 10 LOT 1438	40230	0.83	14-Feb-18	
12	120521_MW_MU_CAL 11 LOT 1438	40230	0.83	14-Feb-18	
13	120521_MW_MU_CAL 12 LOT 1438	40230	0.83	14-Feb-18	
14	120521_MW_MU_CAL 13 LOT 1438	40230	0.83	14-Feb-18	
15	120521_MW_MU_CAL 14 LOT 1438	40230	0.83	14-Feb-18	
16	120521_MW_MU_CAL 15 LOT 1438	40230	0.83	14-Feb-18	
17	120521_MW_MU_CAL 16 LOT 1438	40230	0.83	14-Feb-18	
18	120521_MW_MU_CAL 17 LOT 1438	40230	0.83	14-Feb-18	
19	120521_MW_MU_CAL 18 LOT 1438	40230	0.83	14-Feb-18	
20	120521_MW_MU_CAL 19 LOT 1438	40230	0.83	14-Feb-18	
21	120521_MW_MU_CAL 20 LOT 1438	40230	0.83	14-Feb-18	
22	120521_MW_MU_CAL 21 LOT 1438	40230	0.83	14-Feb-18	
23	120521_MW_MU_CAL 22 LOT 1438	40230	0.83	14-Feb-18	
24	120521_MW_MU_CAL 23 LOT 1438	40230	0.83	14-Feb-18	
25	120521_MW_MU_CAL 24 LOT 1438	40230	0.83	14-Feb-18	
26	120521_MW_MU_CAL 25 LOT 1438	40230	0.83	14-Feb-18	
27	120521_MW_MU_CAL 26 LOT 1438	40230	0.83	14-Feb-18	
28	120521_MW_MU_CAL 27 LOT 1438	40230	0.83	14-Feb-18	
29	120521_MW_MU_CAL 28 LOT 1438	40230	0.83	14-Feb-18	
30	120521_MW_MU_CAL 29 LOT 1438	40230	0.83	14-Feb-18	
31	120521_MW_MU_CAL 30 LOT 1438	40230	0.83	14-Feb-18	
32	120521_MW_MU_CAL 31 LOT 1438	40230	0.83	14-Feb-18	
33	120521_MW_MU_CAL 32 LOT 1438	40230	0.83	14-Feb-18	
34	120521_MW_MU_CAL 33 LOT 1438	40230	0.83	14-Feb-18	
35	120521_MW_MU_CAL 34 LOT 1438	40230	0.83	14-Feb-18	
36	120521_MW_MU_CAL 35 LOT 1438	40230	0.83	14-Feb-18	
37	120521_MW_MU_CAL 36 LOT 1438	40230	0.83	14-Feb-18	
38	120521_MW_MU_CAL 37 LOT 1438	40230	0.83	14-Feb-18	
39	120521_MW_MU_CAL 38 LOT 1438	40230	0.83	14-Feb-18	
40	120521_MW_MU_CAL 39 LOT 1438	40230	0.83	14-Feb-18	
41	120521_MW_MU_CAL 40 LOT 1438	40230	0.83	14-Feb-18	
42	120521_MW_MU_CAL 41 LOT 1438	40230	0.83	14-Feb-18	
43	120521_MW_MU_CAL 42 LOT 1438	40230	0.83	14-Feb-18	
44	120521_MW_MU_CAL 43 LOT 1438	40230	0.83	14-Feb-18	
45	120521_MW_MU_CAL 44 LOT 1438	40230	0.83	14-Feb-18	
46	120521_MW_MU_CAL 45 LOT 1438	40230	0.83	14-Feb-18	
47	120521_MW_MU_CAL 46 LOT 1438	40230	0.83	14-Feb-18	
48	120521_MW_MU_CAL 47 LOT 1438	40230	0.83	14-Feb-18	
49	120521_MW_MU_CAL 48 LOT 1438	40230	0.83	14-Feb-18	
50	120521_MW_MU_CAL 49 LOT 1438	40230	0.83	14-Feb-18	
51	120521_MW_MU_CAL 50 LOT 1438	40230	0.83	14-Feb-18	

Decreasing internal standard intensities through the batch

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

13

Low intensities, unknown cause, check the instrument parameters

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Check the instrument read back values are as expected

14

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

15

Investigating high pressure

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Poor chromatography?

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Check the column...

Old column ☹️

New column 😊

17

Further reading and thanks

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

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18