BIOANALYSIS ZONE | Spotlight

Large molecule analysis by LC-MS

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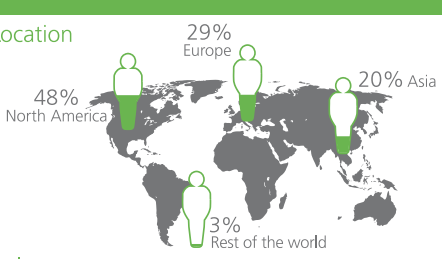
As part of our Spotlight on large molecule analysis by LC-MS, we carried out a community survey on various aspects of your large molecule assays and your opinion on key issues. The results of the survey can be seen in this infographic.

About the respondents

Location



Employer

- 15.7% Academic
- 9.6% Biotech
- 34.9% Pharma
  - 21.7% large
  - 7.2% small–mid
  - 6.0% generic
- 3.6% Other
- 27.7% CRO/CMO
- 8.4% Equipment vendor

Role

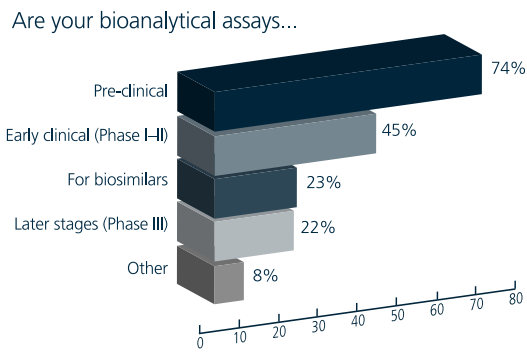
- Director/CEO/VP
- Manager/Group leader
- Chemist/Scientist
- Technician
- Student
- Other

Large molecule LC-MS assays in your laboratory

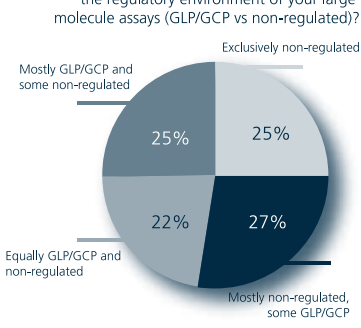
What large molecules do you quantify in biological matrices?

Large peptides	Monoclonal antibodies	Therapeutic proteins	Antibody–drug conjugates
64%	51%	54%	37%
Fusion proteins	**Bi-/multi-domain biologics**	**Oligonucleotides**	**Other**
28%	13%	19%	13%

Are your bioanalytical assays...



Which of the following best describes the regulatory environment of your large molecule assays (GLP/GCP vs non-regulated)?

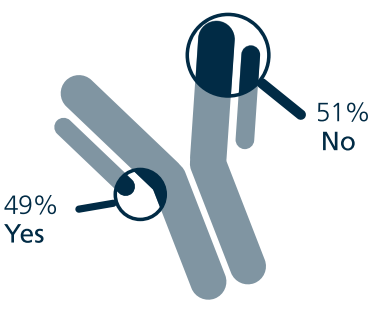


What acceptance criteria do you use for standards and QCs?

We use a tiered approach ranging from no-acceptance criteria (just empirical description of QC performance in terms of accuracy and precision for exploratory, non-regulated studies) to acceptance criteria for small molecule LC-MS/MS assays.

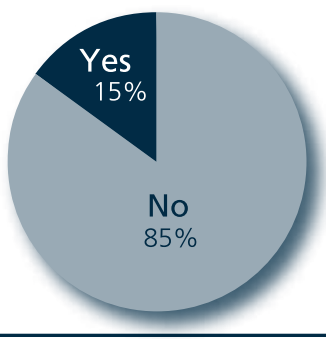
- 52% — Those employed for LC-MS/MS assays of small new chemical entities (four out of six QC samples should be within 15% of the nominal value, 20% at the LLOQ)
- 37% — Same as that for ligand-binding assays (LBAs; four out of six QC samples should be within 20% of the nominal value, 25% at the LLOQ)
- 11% — Other

Do you also use LBAs?



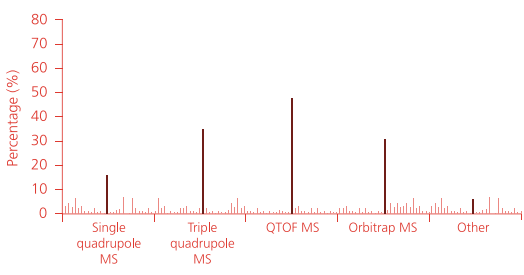
> Choice of platform depends upon target, antibodies available, question being asked of the data (to be generated).

Do you characterize your LC-MS or hybrid LBA/LC-MS method with regard to influences of soluble binding partners, e.g., soluble target, anti-drug antibodies (ADAs)?

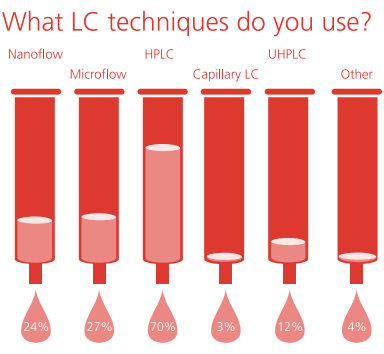


LC & MS platforms used

What MS quantification techniques do you use?

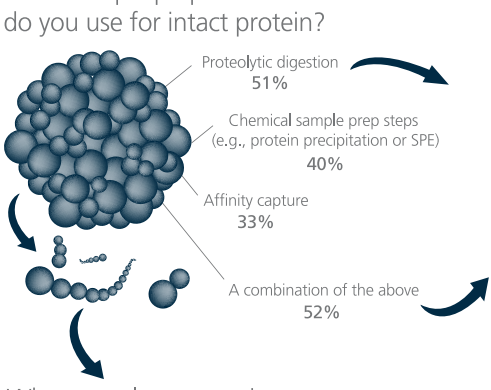


What LC techniques do you use?

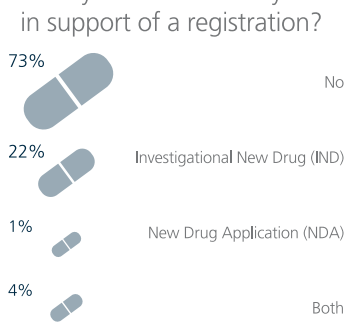


Sample preperation steps

What sample preparation do you use for intact protein?



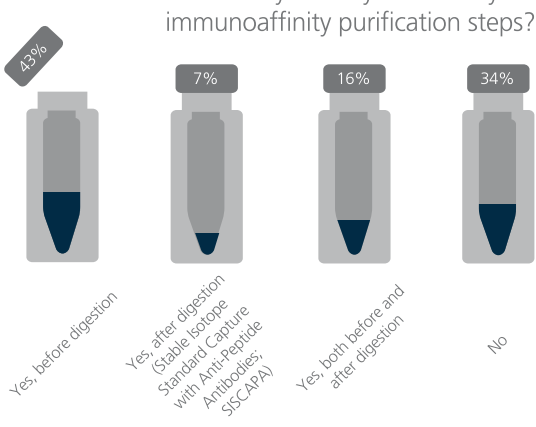
Have you submitted any of this data in support of a registration?



What sample preparation steps do you use for surrogate peptides?

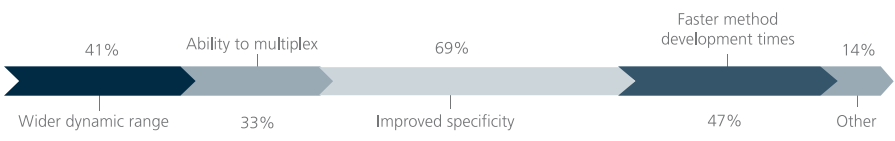
Chemical (e.g., PPT)	28%
Affinity capture	33%
Proteolytic digestion	57%
SPE clean up	60%
Peptide AC clean up	13%

Do you carry out affinity or immunoaffinity purification steps?

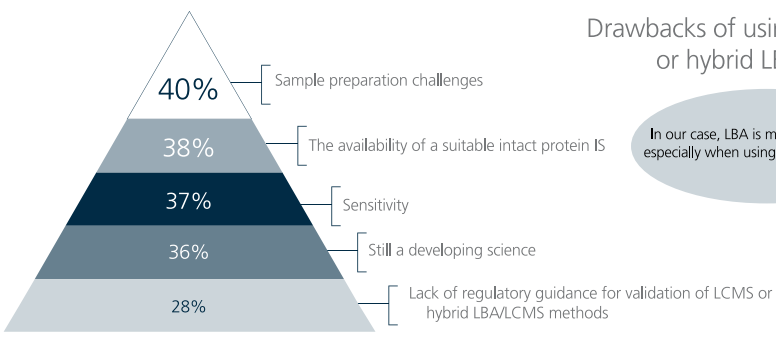


Advantages, disadvantages & future outlook

Why do you employ LC-MS or hybrid LBA/LCMS with/rather than traditional LBA techniques?

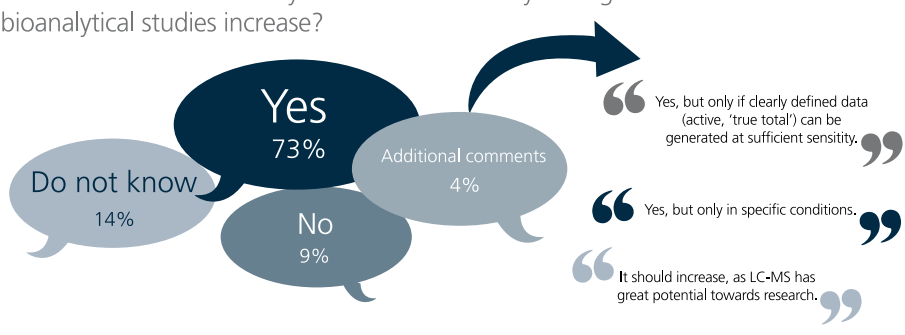


Drawbacks of using LC-MS or hybrid LBA/LCMS?



> In our case, LBA is more cost efficient, especially when using in-house reagents.

Will the use of LC-MS or hybrid LBA/LC-MS assays in regulated bioanalytical studies increase?

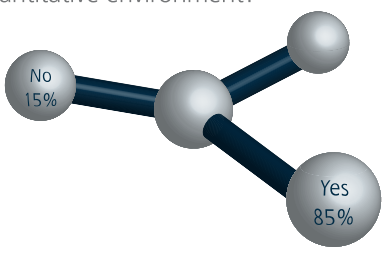


> Yes, but only if clearly defined data (active, 'true total') can be generated at sufficient sensitity.

> Yes, but only in specific conditions.

> It should increase, as LC-MS has great potential towards research.

Do we need a harmonized descriptive nomenclature for the large molecule quantitative environment?



> Harmonized descriptive nomenclature is an abolute prerequisite to provide clear BA data and to enable a scientific rational when the most approriate technology is selected.

Read more articles and analysis on LC-MS at www.bioanalysis-zone.com

Find out what our experts think about the results — Register for the panel discussion

Make sure you don't miss our next Spotlight — Hybrid LBA/LC–MS starting this October