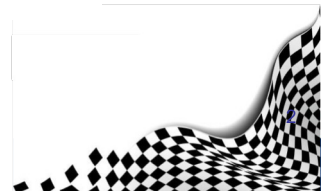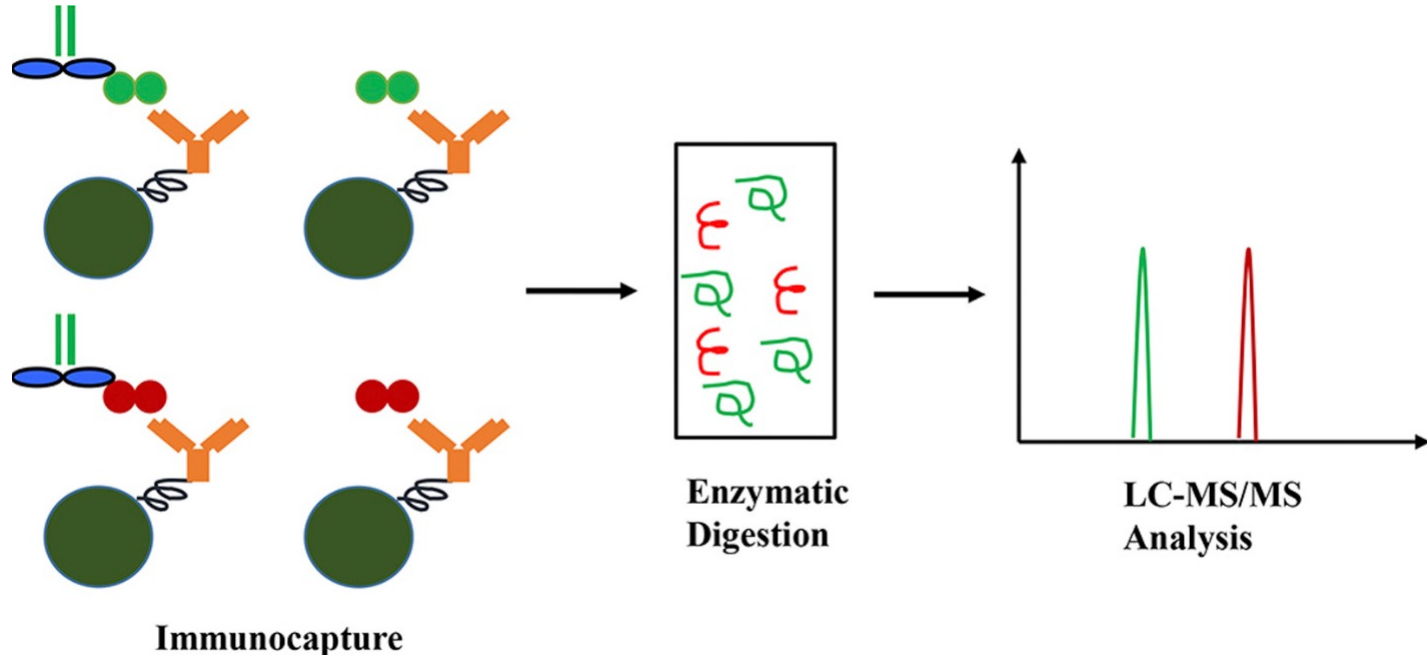**EBF**

16th Open Symposium

Science Winning the Race

Hybrid assays, the scientific and regulatory Journey continues

Matt Barfield, on behalf of the EBF

15-17 November 2023, Barcelona

Immunocapture LC–MS(/MS)

Immunocapture → Enzymatic Digestion → LC-MS/MS Analysis

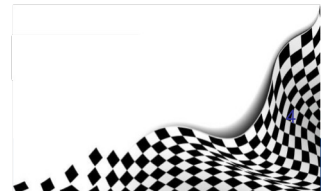# A powerful partnership

➢ Is Hybrid MS?

- – A LBA assay with a different detector?
- – A mass spec assay with a different sample prep?
- – A combination of LBA & MS with the pros and cons of each technique?
- – Going forward, it may be even less straightforward → into new territory

How extensive are Hybrid assays
A finger on the pulse survey outcome

- ➢ 2/3 companies that responded are using LC-MS for protein analysis

- ➢ Protein analysis by LC-MS is used across all phases of R&D
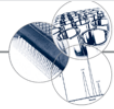
- ➢ The most used application is for PK assays

EBF leadership over the years
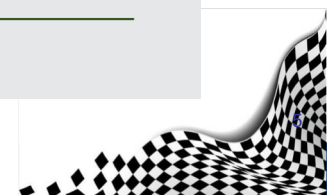
2020 – A new dawn

- Continue the journey and keep the discussion ongoing. The discussion's don't just impact Protein LC/MS/MS but all new future technologies that support PK/safety

- We need to have a simple solution, fit for the future

Name	Company
Amanda Wilson	Astra Zeneca
Mark Jean Gnoth	Bayer
Benno Ingelse	Byondis
Iain Love	CRL
Nico van de Merbel	ICON
Peter Blattmann	Idorsia
Fabrizia Fusetti	Genmab
Gregor Jordan	Roche
Rob Wheller	Resolian
Sune Hove Sporring	Novo Nordisk
Mike Blackburn	Quotient Sciences
Matt Barfield	Roche

Method validation: acceptance criteria

- Is 'Size of molecule' or 'Technology' the driver to define acceptance criteria?
- Why is 4-6-20 acceptable for LBA assays and not Chromatography?

➢ Should the acceptance criteria be based on the end point

➢ **Should we as an industry move to decision-based acceptance criteria e.g. PK acceptance criteria?**
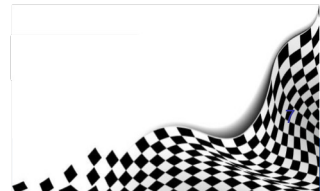
Immunocapture LC–MS(/MS) assays for biotherapeutic and biomarker proteins: the European Bioanalysis Forum continuing discussions on scientific and regulatory challenges

Matthew Barfield, Michael Blackburn, Peter Blattmann, Benno Ingelse, Gregor Jordan, Fabrizia Fusetti, Mark J Gnoth, Sune H Sporring, Iain Love, Stephane Muccio, Nico van de Merbel, Rob Wheller, Amanda Wilson & Philip Timmerman ✉

Sections 📄 PDF/EPUB   🔧 Tools   � Share

Abstract

The use of LC–MS(/MS) assays to quantify (biotherapeutic or biomarker) proteins is commonplace and well accepted across industry. There is a good understanding on the added value over conventional analytical technologies (i.e., ligand-binding assays). In fact, the impact of combining small- and large-molecule technologies for large-molecule analysis has played a significant part in bringing the bioanalytical communities closer together and building a mutual respect and understanding between scientists. This paper from the European Bioanalysis Forum presents a history of the journey and future perspectives for hybrid assays, with focus on the unanswered scientific questions, including regulatory discussions to be had. Hybrid assays are essentially a combination of ligand-binding assays and MS, and the ICH M10 guideline does not address this approach directly. Decision-based acceptance criteria are still being discussed, and the industry should continue to do so.
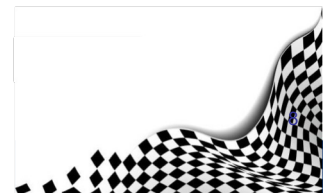
In conclusion, over the last decade, the EBF's message has been consistent and clear. In a world where companies' portfolios become ever more complex and new modalities continue to test and challenge the bioanalyst, let us concentrate on sound science and pave the way to harmonized, science-driven acceptance criteria in support of the fast delivery of safe and effective medicines for patients.

The next installment

➤ The EBF team has a wealth of experience
➤ Lets share those experiences
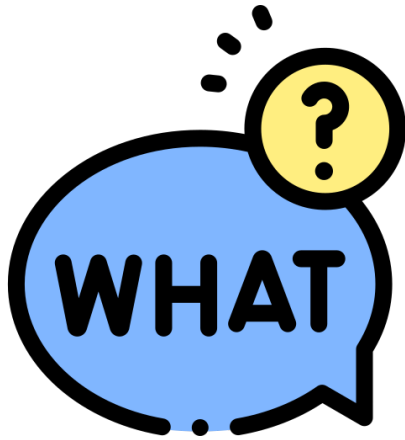
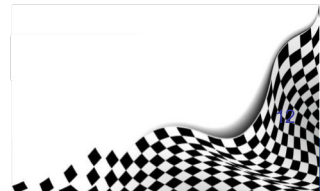## Paper 1

➢ "What" to measure (intact or partial protein)

➢ "What" signature peptide to select

➢ "What" reference materials to use

➢ "What" internal standards to select

THE WHAT.

Paper 2

➢ "How" to pre-treat samples

➢ "How" to select the correct instrumentation

➢ "How" to process data

➢ "How" to automate

➢ "How" to perform pre-validation

➢ "How" to validate

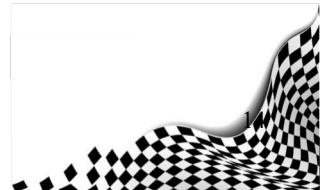THE
HOW

The Race Continues

Science-driven acceptance, to support the fast delivery of safe and effective medicines for patients

Acknowledgements

To the many who have contributed over the years and those that continue to learn and challenge

Contact Information

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