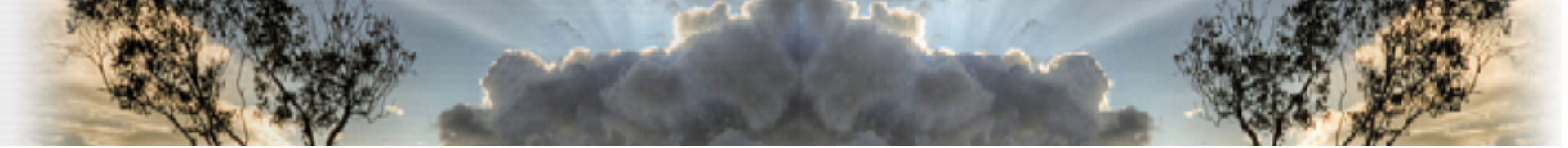


EBF Cyberconnect Events

Focus Workshop: Spotlight on (LBA/CBA and Automation) TECHNOLOGY

20-21 May 2021

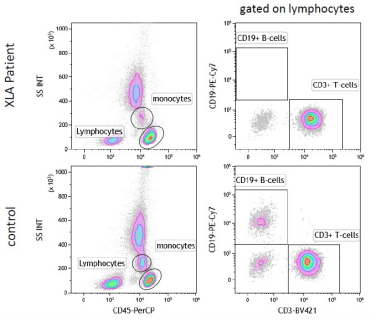
Intro to Session 2 and Round Tables

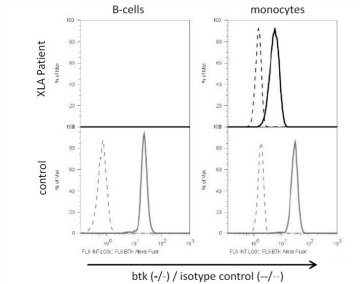
Anna Laurén, on behalf of the EBF

15:00	**16:50**	**Session 2: Functional assays becoming ready for the toolbox of the regulated BA lab**
15:00	15:10	SHORT recap of introduction into the session 2 & round tables by session chair (Anna Laurén, Novo Nordisk)
15:10	15:30	Henko Tadema, PRA-HS *Flow cytometry: The pivotal use of flow cytometry in cell therapy development*
15:30	15:50	Sion Lewis, UCB Pharma *Flow cytometry: Evolution of the flow lab into the Bioanalytical world*
15:50	16:10	Julian J. Freen-van Heeren, Sanquin *Proof of principle for the use of the T cell ELIspot in clinical trial settings*
16:10	16:30	Chiara Cazzin, on behalf of EBF *Considerations for the context of use of qPCR application and validation in the BA*
16:30	16:50	Jessica Zheng Wang, AstraZenca *Development of a mechanism of action reflective and robust potency assay for a therapeutic antibody against alpha toxin using rabbit erythrocytes*

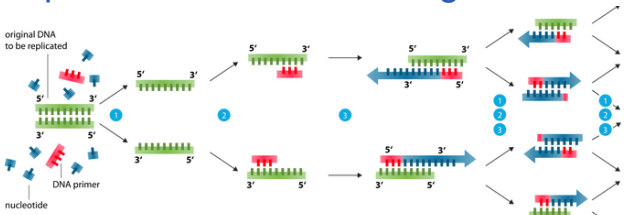
Session Chair: Anna Laurén, NovoNordisk
Question moderator: Robert Nelson, Covance

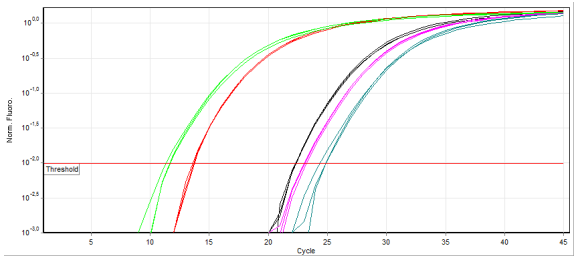
Are these technologies really new?





- The technologies have been used in research and diagnostic for a few decades
  - Flow cytometry was invented in the 60´s
  - PCR developed in the 80´s, qPCR in the 90´s
  - Cell based assays for test of *in vitro* functionality has been used for ages
- However: The regulated BA labs have only used these technologies the recent years, often with focus on new drug modalities, often in a Discovery/Early development space, away from the ‘hard’ regulatory question
- And slowly, the technologies enter the toolbox of the lab also in later stages of development, prompting possible regulatory questions
- The expected outcome from this session is a continued discussion on what can be expected for new technologies on those regulatory questions





Regulated guidelines and ”new technologies”

- The Bioanalytical Method Validation (BMV) guidelines focus on chromatographic assays (CCs) and ligand binding assays (LBAs) for quantification of drug in biological matrices
- Other recommendations and guidelines can apply for “new technologies”
- Examples is to use inspiration from ICH Topic Q2 (focus on GMP/CMC), Immunogenicity validation guidelines, white papers and recommendation papers.
- Both qPCR and Flow Cytometry are used as diagnostic tests and can give inspiration to validation and QC acceptance criteria

Note: Quantitative biomarker assays are included in the FDA guideline but also wordings such as fit-for-purpose validation – Biomarkers are out of the scope in EMA and draft ICH M10

Neither GLP nor GCP guidelines details how assays shall be validated - examples

From OECD GLP FAQ	Reflection paper for laboratories that perform the analysis or evaluation of clinical trial samples
Unless stipulated in national regulations, there is no requirement to perform method validation in compliance with GLP. Since parameters of the validated method are used in the GLP study (for example threshold, linearity, accuracy, precision, stabilities, equipment settings, etc.), data should be accurately recorded and stored in a manner that protects its integrity. Validation data may be required for study reconstruction and, consequently, it should be retained for an appropriate period of time. (Posted on 21 January 2016)	In all but exceptional circumstances, analysis should be performed using appropriately validated methods with defined acceptance criteria where appropriate. The validation of methods should be documented and, on completion, this documentation should be archived Relevant storage stability data must be available if samples are to be stored prior to analysis. Routine system suitability tests, such as the analysis of quality control (QC) samples, should be considered and included in the analytical methodology as required. It is important that analytical factors that may potentially affect clinical trial results are considered. (Effective 2012)

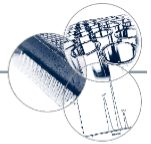
Examples on EBF publications on Context of Use for assay validation

WHITE PAPER

For reprint orders, please contact reprints@future-science.com

European Bioanalysis Forum recommendation on method establishment and bioanalysis of biomarkers in support of drug development

Bioanalysis (2012) 4(15), 1883–1894



White Paper

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Bioanalysis

Toward decision-based acceptance criteria for Bioanalytical Method Validation: a proposal for discussion from the European Bioanalysis Forum

Philip Timmerman*[,1], Michaela Golob[2], Joanne Goodman[3], Magnus Knutsson[4], Robert Nelson[5], Marianne Scheel Fjording[6] & Steve White[7]

Bioanalysis (2018) 10(16), 1255–1259

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White Paper

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Bioanalysis

Best practices in performing flow cytometry in a regulated environment: feedback from experience within the European Bioanalysis Forum

Bioanalysis (2017) 9(16), 1253–1264

White Paper

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A strategic approach to nonclinical immunogenicity assessment: a recommendation from the European Bioanalysis Forum

Anna Laurén[1,1], Joanne Goodman[2], Jonas Blaes[3], John Cook[4], Kyra J Cowan[5], Madeleine Dahlbäck[1], Joanna Grudzinska-Goebel[6], Deborah McManus[7], Robert Nelson[8], Susanne Pihl[9] & Philip Timmerman*[,10]

Bioanalysis (2021) 13(7), 537–549

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Bioanalysis

Update to the European Bioanalysis Forum recommendation on biomarkers assays; bringing context of use into practice

Joanne Goodman[1], Kyra J Cowan[2], Michaela Golob[3], Lars Karlsson[4], Ulrich Kunz[5], Robert Nelson[6], Hans Ulrichts[7], Lauren Stevenson[8], Linda Terry[9] & Philip Timmerman*[,10]

Bioanalysis (2020) 12(20), 1427–1437

Plus several EBF project discussion groups ongoing with aim for upcoming publications

Take home message: Use a scientific approach for the context of use for the assay!

Focus on Round tables

- Pre-survey on considerations on validation for Flow Cytometry and qPCR in the BA lab resulted in limited responders
- Round Table will continue on the discussion with 4 main streams:
  - qPCR
  - Flow Cytometry
  - Other emerging technologies in the BA lab
  - Automation
- You will be split into 4 break-out rooms each chaired by Anna, Matt, Joe or Rob
- Approximately 10-15 minutes on each topic

- Feedback from the round table discussions will be summarised during Day 2 at 1700-1800 and includes a Panel Discussion on remaining questions

On each topic (qPCR, Flow Cytometry, emerging techs in the BA lab, Automation)

- Discussions on the hurdles and how to remove the hurdles
- Agree on three items on each topic
- Allow 10-15 minutes for discussion on each topic

- Ideas to stimulate the discussions can include:
  - Stakeholder communication
  - How to understand the Context of Use for the given assay
  - Not knowing from early discovery projects which assays and platforms may need to end up in a regulated BA lab
  - Change management
  - Communication to QA
  - What makes sense in automation

Feedback form: qPCR

Q1: Why would we want to use BMV for qPCR?

- ..
- ..
- ..

Q2: Why wouldn't we want to use BMV qPCR?

- ..
- ..
- ..

For each, consider

- Who is requesting this and why?
- Who has seen regulatory impact of one or the other approach
- What are the advantages
- What are the disadvantages
- For Q2: What are the hurdles
- For Q2: How can we mitigate/overcome the hurdles

Feedback form: flow cytometry

Q1: Why would we want to use BMV for flow cytometry?

- ..
- ..
- ..

Q2: Why wouldn't we want to use BMV flow cytometry?

- ..
- ..
- ..

For each, consider

- Who is requesting this and why?
- Who has seen regulatory impact of one or the other approach
- What are the advantages
- What are the disadvantages
- For Q2: What are the hurdles
- For Q2: How can we mitigate/overcome the hurdles

Feedback form: other emerging technologies

Q1: Which are other emerging technologies on the horizon at risk of ending up in a similar discussion on CoU/regulation as qPCR and Flow?

Free text here: (please limit to 4 bullet max)

- ..
- ..
- ..
- ..

Feedback form: automation

Q1: What and who were/are the drivers of successful automation in your lab?

- ..
- ..
- ..

Q2: What and who were/are the forces of slowing down automation in your lab?

- ..
- ..
- ..

Q2: Can you define your role related to automation in your lab?

- ..
- ..
- ..

Contact Information

Questions: info@e-b-f.eu

European Bioanalysis Forum vzw

www.e-b-f.eu