UTOPIA: THE SCIENCE OF A MODERN GUIDELINE

Feedback from the EBF

Philip Timmerman,
presented at the 8th JBF Meeting on behalf of the EBF

08-09 February 2017

タワーホール船堀
TOWER HALL FUNABORI

Background

EBF has been actively promoting and supporting international harmonization since 2006

Harmonization amongst EBF member companies and, in extension industry was and remains the primary mission of EBF

From the EBF Mission and Vision

Our mission is to share, discuss, optimize and seek alignment on a broad array of bioanalytical topics including science, procedures, business tools and technology, and regulatory issues.

Internal discussions within EBF aim to recommend or influence opinions/procedures towards our members, business partners, regulatory bodies and any other stakeholders.

Background

EBF has been actively promoting and supporting international harmonization since 2006

EBF is founding member of GBC

Original drivers of GBC

= harmonized reading of what was the only Guidance at that time → the 2001 FDA CDER Guidance

- *Because of ambiguity, many chapters were interpreted in different ways by individual scientist and inspectors*

= worry that emerging guidelines would create an even more complex landscape

- *more ambiguity, slight differences in expectations and wordings*

A lot of the *GBC Open Letter to the Authorities* became reality

Note: Japanese membership into GBC gave rise to formation of the JBF

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CVG

OPEN LETTER

Request for Global Harmonization of the Guidance for Bioanalytical Method Validation and Sample Analysis

Open letter to the bioanalytical community. Sent to the US FDA/European Medicines Agency in February 2010

ICH….

- The idea to involve ICH in regulated BA harmonization sparked at the 2012 EBF meeting, as part of a GBC Round table (http://bcn201211.europeanbioanalysisforum.eu/wp-content/uploads/2016/03/Program-of-EBF-5th-Open-Meeting.pdf)
- At first, it was parked as “a long shot”.
- The idea slowly developed into a desire and finally it was identified as an excellent way forward in harmonizing the regulated BA landscape.
- Coinciding proposals were made in spring 2016…
  - JBF/AAPS/EBF proposal to EFPIA.
  - NIHS final proposal to ICH MC, accepted June 2016
- Challenge: ICH ≠ the world

So…

- The interest of the broader BA community in harmonization was and remains high
  - many relevant publications from EBF, JBF, GBC and others provide recommendations of ‘best practices’ - ‘clarifications of ambiguities’ …
  - Discussions on Harmonization and best practices, providing expert opinions and insights, continue in many meetings across the globe.
  - EBF hosted a panel discussion at their recent 9th open Symposium (OS)

So…

In the continuation of this presentation, feedback is provided from a recent discussion at the 9th EBF OS, building on a recent survey amongst EBF member companies:

"THE SCIENCE OF A MODERN GUIDELINE

Disclaimer: The view and suggestions provided in this feedback reflects the discussions at the meeting and is not an official opinion of the EBF

EBF 9th Open Symposium.
Day 3 – Friday 18 Nov 2016)

11:25	**12:55**	**UTOPIA: THE SCIENCE OF A MODERN GUIDELINE**
11:25	11:30	***General Introduction – aim of the session***
11:30	12:55	***The science of a modern guidance in 5 questions***

The 5 questions are inspired by a recent EBF survey – September 2016

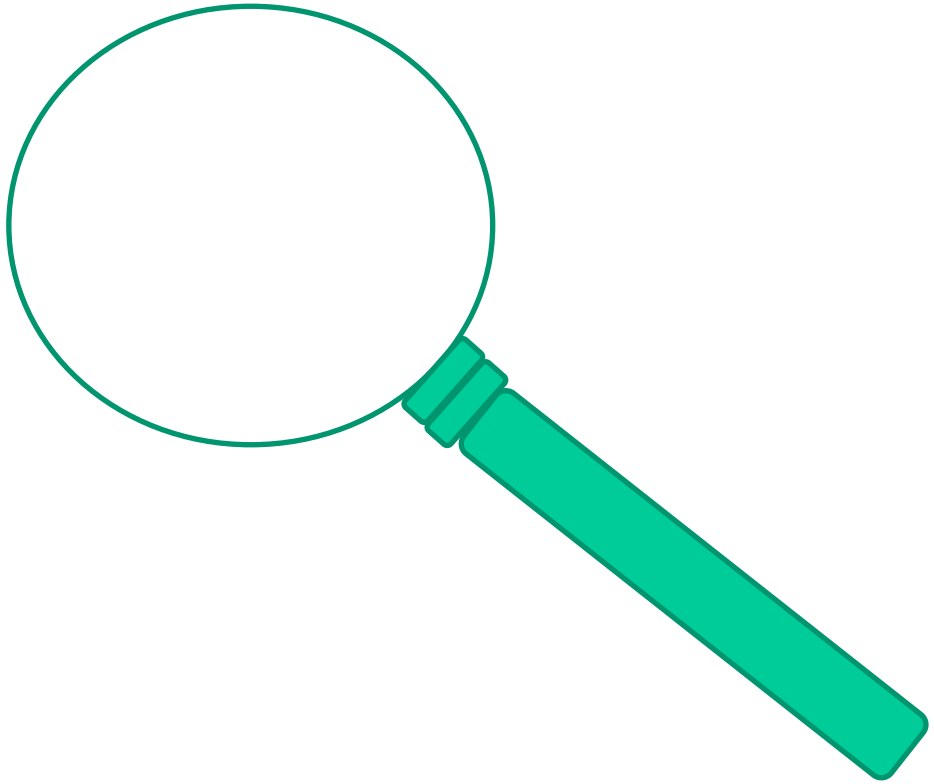
The 5 questions → Do we feel that:

1. a modern guideline should give more details on experimental execution or not?
2. some of the current requirements for method validation should be refined or even removed from the guideline, and if so, which?
3. some requirements for method validation should be added to the guideline and if so, which?
4. alternative validation approaches (e.g. tiered approach, scientific validation) should be included in a modern guideline?
5. assay requirements for new technologies should be included in a modern guideline and if so, which? And why? Or why not?

View from the expert panel

John Smeraglia, UCB Biopharma
Timothy Sangster, Charles River
Yoshiaki Ohtsu, for JBF
Michaela Golob, Nuvisan
Barry van der Strate, PRA Health Sciences
Amanda Wilson, AstraZeneca

View from the auditorium in a panel discussion with 300 people in the auditorium



1. **Do we feel that a modern guideline should give more details on experimental execution or not?**

Two main thoughts from the audience

1. YES - If the scope of a modern guideline could be clarified, it adds value to provide more clear executional details to prevent current practices in industry of over- or under interpretation.
2. NO - a too prescriptive guideline may prevent industry to do the correct experiment for a certain study. Certainly if guideline encompasses a too broad range of study templates

Number 1 seemed to have won in the end….

2. Do we feel that some of the current requirements for method validation should be refined or even removed from the guideline, and if so, which?

A few suggestions were given on requirements that could be removed or refined

1. Refine:
   - interference testing
   - matrix effects
   - internal standard evaluation
   - call for clearer terminology
   - the title of the document
2. Remove
   - extraction recovery
   - parallelism
   - partial validation,
   - assay development,
   - selectivity testing
   - inclusion of 20% of chromatograms in submissions with flat files

3. **Do we feel that some requirements for method validation should be added to the guideline and if so, which?**

The audience couldn’t identify 1 item that should be added

4. Do we feel that alternative validation approaches (e.g. tiered approach, scientific validation) should be included in a modern guideline?

Some thoughts from the audience

1. Unisonic:
   A. Yes, principles and added value of alternative approaches to validation should be recognized by a modern guideline. Today's ambiguity of where and when this approach is (or isn't) acceptable remains the single most important worry from industry as expressed in the EBF survey, at other meetings and confirmed in the discussions at the 9th OS in Barcelona
   B. Strong scientific thinking from the audience: build regulations on science *vs.* follow a 1-size-for-all template

4. Do we feel that alternative validation approaches (e.g. tiered approach, scientific validation) should be included in a modern guideline?

Some thoughts from the audience - cntd

2. A modern guideline should recognize the fact that current guidelines stimulates over-engineered validations in many (mostly early development) studies
3. A few different ideas on how to include these principles were proposed
   A. a modern guideline should indicate the studies in scope & out of scope
   B. a modern guideline should indicate the studies in scope (but not the studies out of scope, since not part of 'in scope' equals 'out of scope')
   C. work in table format (e.g. like in the GBC paper)

   ('B' got most traction)

5. Do we feel that assay requirements for new technologies should be included in a modern guideline and if so, which? And why? Or why not?

Some thoughts from the audience

1. New technologies deserve a special and continued discussion between industry and regulators.

But also, the audience reflected on the hurdles…

- What is the definition of “new technology”?
- How do you regulate what you don’t know yet?
- There were mixed visions on “how” to include new technologies…..
- A modern Guideline should consider new technologies but cannot define fixed requirements.
- DBS, hybrid technologies, immunogenicity and biomarkers came up as current examples – see next slide.

5. Do we feel that assay requirements for new technologies should be included in a modern guideline and if so, which? And why? Or why not?

Some thoughts from the audience

DBS, hybrid technologies, immunogenicity and biomarkers came up as current examples

- DBS → makes sense to mention clear specifics related to DBS in a modern guideline. Is being used, and scientific challenges and specific requirements are know, → **YES, we see value of inclusion in a new Guideline**
- hybrid technologies → industry struggles to understand if this falls into LBA or Chromatography requirements. Does it make sense to continue having two sets of acceptance criteria? → **YES, we see value of inclusion in a new Guideline**
- Immunogenicity: although technology-wise it fits many aspects of a modern LBA guideline, including it as part of a PK guideline is seen as not appropriate. A separate guideline is suggested (even within ICH if possible) → **NO, we don't see value of inclusion in a new Guideline**
- Biomarkers → difficult to capture the full biomarker question in 1 guideline, let alone in a PK guideline → **NO, we don't see value of inclusion in a new Guideline**

In conclusion

- Many valid suggestions were made on "**THE SCIENCE OF A MODERN GUIDELINE**"
- The EBF reflects on the added value of writing a publication on the outcome of the panel discussion in view the panel discussion echoed current thinking
- The EBF plans to continue connecting scientist and stimulate discussions on harmonization
- A modern guideline should build a new bioanalytical future promoting a handshake of science and process

Acknowledgment

EBF community

Our partnerships

- JBF
- AAPS

Our audiences

- At the 9th EBF Open Symposium
- All of you

ありがとうございます