09:00 – 10:10  The current landscape and future challenges on immunogenicity
   09:00 - 09:30  The current regulatory landscape on immunogenicity
      Michaela Golob, on behalf of the EBF
   09:30 - 09:50  EMA view on immunogenicity regulations
      Venke Skibeli, Avd. for legemiddelutredning, Norway
   09:50 - 10:10  FDA Regulatory perspectives on therapeutic protein immunogenicity - an update
      João A. Pedras-Vasconcelos, FDA/CDER/OBP/DRR3, US

10:10 – 10:40  Coffee break & networking

10:40– 12:30  A rapidly changing regulatory environment
   10:40 - 11:00  EBF’s feedback to the EMA and FDA draft guidance
      Jo Goodman, on behalf of the EBF
   11:00 - 12:30  Panel discussion

12:30 – 13:30  Lunch
The current regulatory landscape on immunogenicity

Presenter: Michaela Golob
on behalf of EBF

Immunogenicity Focus Workshop
27th September 2016
Lisbon

http://www.europeanbioanalysisforum.eu
Guidance for Industry

Immunogenicity Assessment for Therapeutic Protein Products

Additional copies are available from:
Office of Communication
Division of Drug Information
WHO, Room 2311
Centre for Drug Evaluation and Research
Food and Drug Administration
1801 Jefferson Drive, N, Suite 710
Alexandria, VA 22302
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communications@cdrf.hhs.gov

Guideline on Immunogenicity Assessment of Biotechnology-Derived Therapeutic Proteins

DRAFT GUIDANCE

Guideline on Immunogenicity assessment of biotechnology-derived therapeutic proteins
Draft

http://www.europeanbioanalysisforum.eu
Regulations on Immunogenicity in EU (EMA)


- Guideline on similar biological medicinal products (2015 CHMP/437/04 Rev 1)

New Guideline draft
August 2015

Incl. New Chapter (10):
Summary of the Immunogenicity Program

=> More about this by Venke Skibeli, Norway
Regulations on Immunogenicity in US (FDA)

- “Immunogenicity Assessment for Therapeutic Protein Products” (2014, clinical / medical)
- “Scientific Considerations in Demonstrating Biosimilarity to a Reference product” (2015)
- “Assay Development for Immunogenicity Testing” (2009 – draft)
  currently in revision =>
  Assay Development and Validation for Immunogenicity Testing of Therapeutic Protein Products (2016)
More about this by Joao Pedra – Vasconcelos, FDA
Japan

Currently there is no regulation or guidelines on Immunogenicity published by Japanese Health Authorities (PMDA).

**JAPANESE REGULATORY PERSPECTIVE ON IMMUNOGENICITY**

Takao Hayakawa and Akiko Ishii-Watabe

Detection and Quantification of Antibodies to Biopharmaceuticals, First Edition. Edited by Michael G. Tovey.
…This book chapter describes (1) the impact of immunogenicity on safety and efficacy of therapeutic protein products, (2) the quality attributes and other factors that affect antibody formation against the products, and (3) approaches to assessing immunogenicity in nonclinical and clinical studies during drug development and in postmarketing surveillance.

Based on these considerations …… practical approaches to minimizing the risks associated with immunogenicity are discussed
Current plans in Japan

- **In preparation:**
  Manuscript about “points to consider for ADA assay” is in preparation by a research group founded by AMED (Japan Agency for Medical Research and Development)
  - members are from NIHS, PMDA, pharmaceutical companies and CROs

However, the manuscript is a research paper not a regulatory guidance.
Current plans in Japan

- The contents will be typical method for ADA assay, strategies for ADA assay, validation of ADA assay, study sample analysis, and other issues.

- The publication will be in Japanese.

- This would be the first regulatory research paper about technical issues of ADA assay in Japan.
Current landscape on Immunogenicity outside of ICH?

i.e.:

- Brasil?
- China?
Brazil (ANVISA)

- Currently there is no regulation or guidelines on Immunogenicity published by Brazilian Health Authorities (ANVISA).

- When Biologics regulation were published back in 2010, it mentions that immunogenicity clinical data needs to be presented as part of the marketing license application, however it does not instruct on how to do it.

- ANVISA uses international guidelines (FDA or EMA)
China (CFDA)

- CFDA plans to form consensus among industry and research instates by publishing a series of “white papers”, each for one biosimilar product, which includes immunogenicity portion.

- After industry consensus is formed, guidance will be planned.
EBF – „Finger on the Pulse“
(23 companies answered)

- What guidance for immunogenicity do you currently follow (most) for your immunogenicity strategy and assay/validation decisions
  - EMA (new version, but draft 2015)
    EMA (actual final version from 2012) => 13%
  - FDA (new version, but draft 2016)
  - Try to cover both EMA & FDA => 87%
  - Any other guideline from other regions to your knowledge? => No

- Any experiences in other countries than EU or US with immunogenicity discussions/data submissions?
Experiences with other regulatory agencies than EMA or FDA?

➢ “Not aware of any specific immunogenicity guidance for many other regions, but there are biosimilar guidance from many regions that cover immunogenicity assessment.”

Example:
Korean FDA requesting Nab assays in pre-clinical work for a low risk compound.
Experiences with other regulatory agencies than EMA or FDA?

- China and Japan request immunogenicity data in their own population, in general they accept to follow the EMA guideline. Data can be included in a general/PK Bioanalysis report.

- Brazil => follow EMA, but ask for a separate Immunogenicity report

- Swiss Medic => follows EMA
Acknowledgements

- EBF-IGM members
- EBF contacts in Japan, Brazil and China
Two new draft regulatory documents for Immunogenicity

Guideline on Immunogenicity assessment of biotechnology-derived therapeutic proteins

Draft

Draft agreed by Biosimilar Medicinal Products Working Party (BWP) August 2015
Adopted by CHMP for release for consultation 24 September 2015
Start of public consultation 01 October 2015
End of consultation (deadline for comments) 31 January 2016

This guideline replaces "Guideline on Immunogenicity assessment of biotechnology-derived therapeutic proteins" (EMA/CHMP/BWP/14327/2006).

Comments should be provided using this template. The completed comments form should be sent to BWP.secretariat@ema.europa.eu

Keywords Immunogenicity, therapeutic proteins, anti-drug antibodies (ADA), assays, assay strategy, binding antibodies, neutralising antibodies, risk factors, safety, efficacy, pharmacokinetics, risk management, integrated summary of immunogenicity

Assay Development and Validation for Immunogenicity Testing of Therapeutic Protein Products

Guidance for Industry

DRAFT GUIDANCE

This guidance document is being distributed for comment purposes only.

Comments and suggestions regarding this draft document should be submitted within 60 days of publication in the Federal Register of the notice announcing the availability of the draft guidance. Submit electronic comments to http://www.regulations.gov. Submit written comments to the Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm.1061, Rockville, MD 20852. All comments should be identified with the docket number listed in the notice of availability that publishes in the Federal Register.

For questions regarding this draft document, contact (CDER) Susan Kavaler at 301-827-1731; (CBER) Office of Communication, Outreach and Development, 800-835-4709 or 240-402-8010; or (CDRH) Office of Communication and Education, 800-638-2041 or 301-796-7100.

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)
Center for Devices and Radiological Health (CDRH)

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