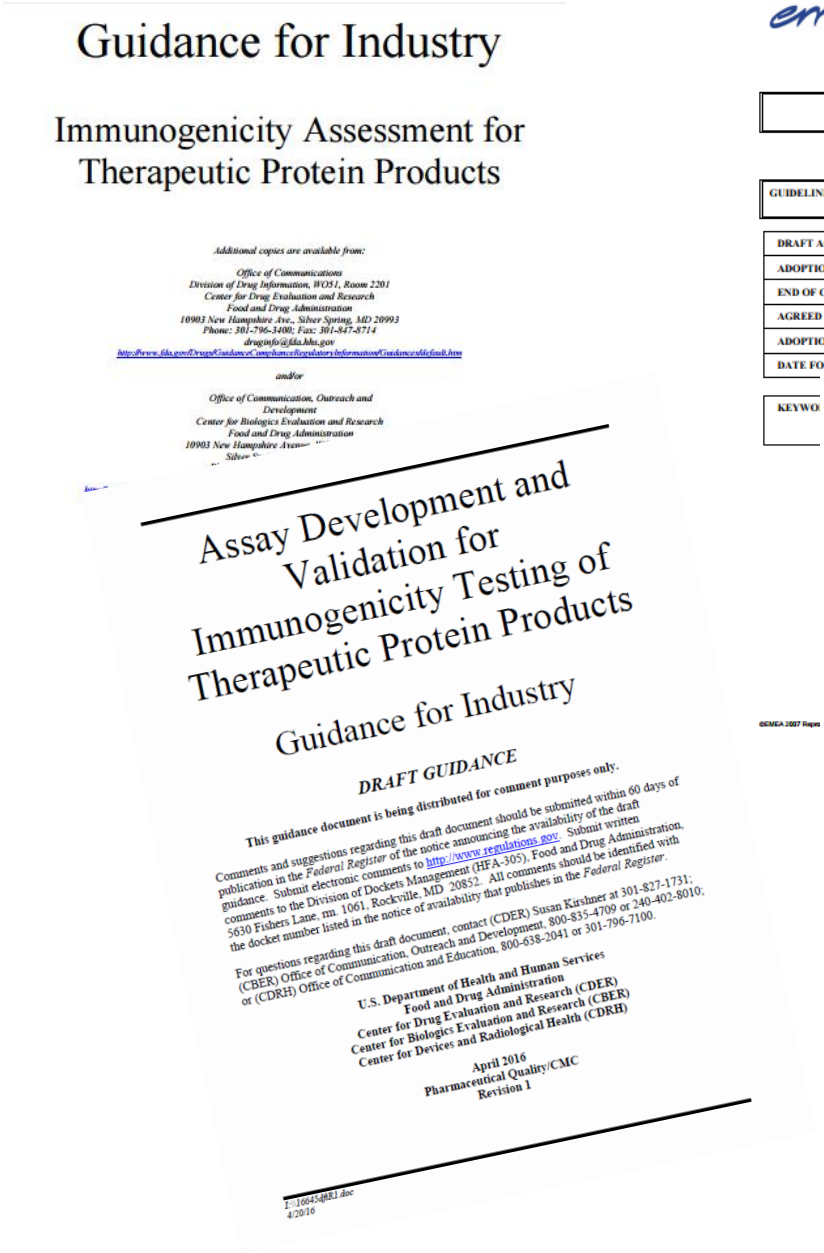
09:00 – 10.10	**The current landscape and future challenges on immunogenicity**
09:00 - 09:30	The current regulatory landscape on immunogenicity *Michaela Golob, on behalf of the EBF*
09:30 - 09:50	EMA view on immunogenicity regulations *Venke Skibeli, Avd. for legemiddelutredning, Norway*
09:50 - 10:10	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10:40 - 11:00	EBF's feedback to the EMA and FDA draft guidance *Jo Goodman,* on behalf of the EBF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



Guidance for Industry

Immunogenicity Assessment for Therapeutic Protein Products

Additional copies are available from:

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druginfo@fda.hhs.gov
http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/default.htm

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Office of Communication, Outreach and Development
Center for Biologics Evaluation and Research
Food and Drug Administration
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Assay Development and Validation for Immunogenicity Testing of Therapeutic Protein Products

Guidance for Industry

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For questions regarding this draft document, contact (CDER) Susan Kirshner 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.

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Center for Devices and Radiological Health (CDRH)

April 2016
Pharmaceutical Quality/CMC
Revision 1

1 10645dftRI.doc
4/20/16

European Medicines Agency

London, 13 December 2007
Doc. Ref. EMEA/CHMP/BMWP/14327/2006

COMMITTEE FOR MEDICINAL PRODUCTS FOR HUMAN USE (CHMP)

GUIDELINE ON IMMUNOGENICITY ASSESSMENT OF BIOTECHNOLOGY-DERIVED THERAPEUTIC PROTEINS

DRAFT AGREED BY BMWP	**July 2006**
ADOPTION BY CHMP FOR RELEASE FOR CONSULTATION	**January 2007**
END OF CONSULTATION (DEADLINE FOR COMMENTS)	**July 2007**
AGREED BY BMWP	**October 2007**
ADOPTION BY CHMP	**December 2007**
DATE FOR COMING INTO EFFECT	**April 2008**

KEYWO

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EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

1 24 September 2015
2 EMEA/CHMP/BMWP/14327/2006 Rev. 1
3 Committee for Medicinal Products for Human Use (CHMP)
4
5

6 Guideline on Immunogenicity assessment of
7 biotechnology-derived therapeutic proteins
8 Draft

Draft agreed by Biosimilar Medicinal Products Working Party (BMWP)	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

9
10 This guideline replaces 'Guideline on Immunogenicity assessment of biotechnology-derived therapeutic
11 proteins' (EMEA/CHMP/BMWP/14327/2006).

12 Comments should be provided using this template. The completed comments form should be sent to
13 BMWP.secretariat@ema.europa.eu
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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***

15
16

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EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

24 May 2012
EMA/CHMP/BMWP/86289/2010
Committee for Medicinal Products for Human Use (CHMP)

Guideline on immunogenicity assessment of monoclonal antibodies intended for in vivo clinical use.

ft agreed by Similar Biological Medicinal Products Working Party	October 2010
tion by CHMP for release for consultation	November 2010
f consultation (deadline for comments)	May 2011
	March 2012
	24 May 2012
	1 December 2012

f as an addendum to Guideline on Immunogenicity assessment of roteins EMEA/CHMP/BMWP/14327/2006 and should be read in

ity, monoclonal antibodies, similar biological medicinal cal use, assay strategy.

Regulations on Immunogenicity in EU (EMA)

- Immunogenicity assessment of monoclonal antibodies intended for in vivo clinical use (**2012**- EMA/CHMP/BMWP/86289/2010)

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

- "Immunogenicity Assessment of Biotechnology-Derived Therapeutic Proteins" (**2008** – EMEA/CHMP/BMWP/14327/2006)

  currently in revision =>

  Guideline on Immunogenicity assessment of biotechnology-derived therapeutic proteins (**2015** - EMEA/CHMP/BMWP/14327/2006 Rev. 1)

EU

New Guideline draft August 2015

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

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

24 September 2015
EMEA/CHMP/BMWP/14327/2006 Rev. 1
Committee for Medicinal Products for Human Use (CHMP)

Guideline on Immunogenicity assessment of biotechnology-derived therapeutic proteins

Draft

Draft agreed by Biosimilar Medicinal Products Working Party (BMWP)	August 2015
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=> 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)

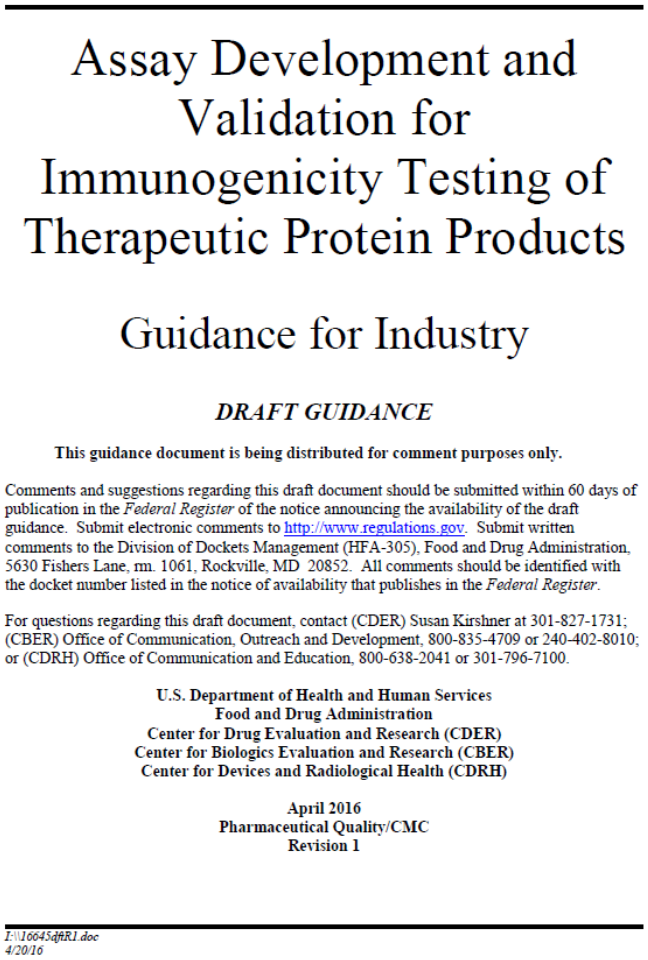
- "Assay Development for Immunogenicity Testing" (2009 – draft)

  currently in revision =>

  Assay Development and Validation for Immunogenicity Testing of Therapeutic Protein Products (2016)

US:

New Guideline draft
April 2016



Assay Development and Validation for Immunogenicity Testing of Therapeutic Protein Products

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Revision 1

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4/20/16

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 lincense 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 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

24 September 2015
EMEA/CHMP/BMWP/14327/2006 Rev. 1
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