

## Workshop on immunogenicity assessment of biotechnology-derived therapeutic proteins

### **Session 3**

## Summary of immunogenicity program and risk assessment

### **General introduction**

European Medicines Agency

9.3.2016

Pekka Kurki

Finnish Medicines Agency

## Immunogenicity assessment of biotechnology-derived therapeutic proteins, EMA/CHMP/BMWP/14327/2006 Rev. 1

### Concept paper:

- Requirements of data on antibody assays
- Role of non-clinical studies
- Clinical data to study the correlations of anti-drug antibodies to clinical symptoms and signs
- *Risk-based approach to immunogenicity*
- Comparative immunogenicity studies
- *Post-licensing immunological studies*
- *Specific guidance for the presentation of immunogenicity data*

# Immunogenicity assessment of biotechnology-derived therapeutic proteins, EMA/CHMP/BWP/14327/2006/rev1

## **Chapter 8: Immunogenicity and Clinical Development**

Rationale for sampling schedule and kinetics of the antibody response

Consequences on pharmacokinetics of the product

Impact of immunogenicity on safety and efficacy

Methodological aspects to assess comparability of immunogenicity

Management of immunogenicity

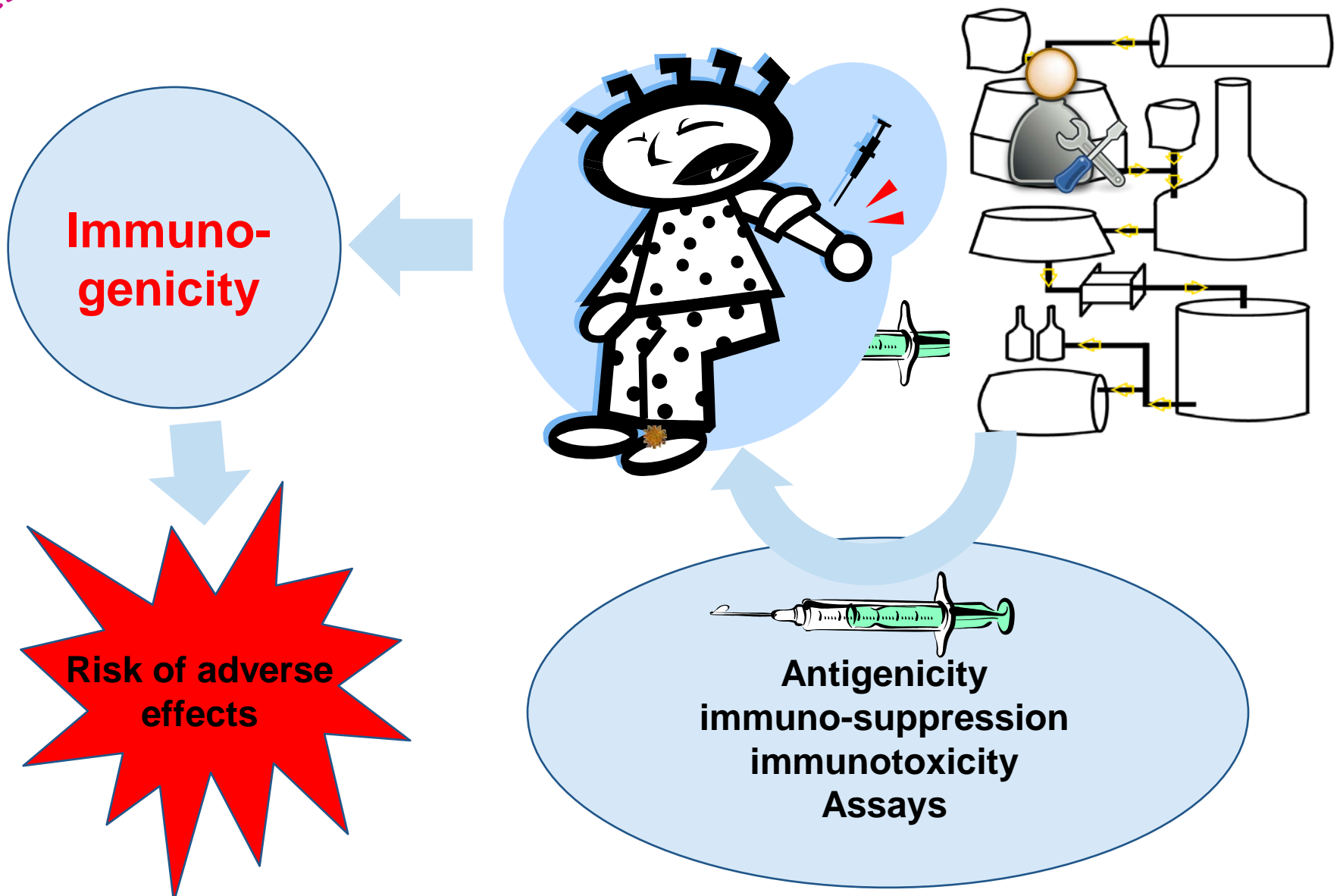
## **Chapter 9: Pharmacovigilance**

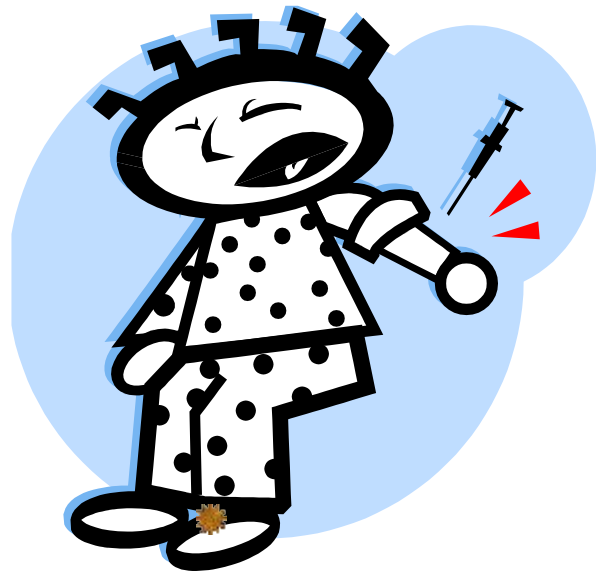
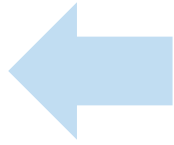
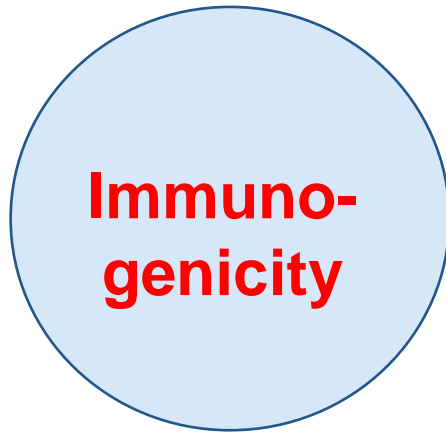
## **Chapter 10: Summary of the immunogenicity program**

# Are we taking immunogenicity too seriously?

## Comments from the written consultation

- Should immunogenicity be always studied, e.g. in phase 1 studies and oral administration?
- Double standard:  
Switching between products, difference between manufacturing changes and biosimilar development
- Should neutralizing Abs be always measured?
- More emphasis on **risks** of immunogenicity
- PK+ADA samples during phase III: analysed and reported routinely or just “in case”?
- Relative immunogenicity: Search for increased immunogenicity or clinically significant immunogenicity, i.e. risk of immunogenicity or risk of immunogenic risks?
- Typing of ADAs and epitope mapping: a waste of time?





# Immunogenicity assessment of biotechnology-derived therapeutic proteins

EMA/CHMP/BMWP/14327/2006/rev1

## Chapter 8: Immunogenicity and Clinical Development

- Rationale for sampling schedule and kinetics of the antibody response
- Consequences on pharmacokinetics of the product
- Impact of immunogenicity on safety and efficacy
- Methodological aspects to assess comparability of immunogenicity
- Management of immunogenicity

## Chapter 9: Pharmacovigilance

## Chapter 10: Summary of the immunogenicity program

squeezing  
of  
information

# Summary of the immunogenicity program

## Why???

- Currently, it is difficult to find the relevant data and understand the rationale of the immunogenicity studies



### Unnecessary questions by the assessors

- Promotion of multidisciplinary collaboration before the conduct of clinical studies
- Comments from the public consultation
  - Interpretation of the results require some understanding of the assay methodology
  - Pitfalls of various assay formats: more guidance for the clinical assessor?

## Summary of the immunogenicity program

- Analysis of risk factors
- **The risk-based immunogenicity program**
- Immunogenicity results
- **Conclusions on the risk(s) of immunogenicity**
  - Impact of the immunogenicity on the benefit/risk
  - Tools to manage the risk
  - How to link adverse events to immunogenicity post-marketing

# The risk-based immunogenicity program

- **Assay strategy**
- **Approach to immunogenicity in clinical trials**
  - a. Sampling for immunogenicity testing
  - b. Justification for the length of the follow up
  - c. Pharmacokinetics
  - d. Pharmacodynamics, efficacy and safety trials
- **Impact on the risk assessment on the immunogenicity program**