

**C B G**  

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*M E B*

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## Non-clinical assessment of immunogenicity

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## General considerations

- Conventional animal tests are not predictive for immunogenicity in humans
- Immunogenicity studies in animals are normally not required
- Material should be representative
- Impurities should be controlled at acceptable levels instead of setting up a non-clinical development plan for their qualification
- *Contentious issue*
  - Animal studies should be omitted altogether

## Novel technologies

- In silico assessment
- In vitro approaches
- Novel in vivo approaches (transgenic models)
  
- Consider their use where appropriate
- *Comments*
  - Clinical validation needed
  - Only relevant for very early development
  - Should not be mandatory
  - Relevance of novel *in vivo* models considered low
  - More detail on *in silico* and *in vitro* models should be provided

## ADA assessment in animal studies

- Collect samples and assay when needed in accordance with ICH S6
- *Contentious issues*
  - Is the use of a single assay to detect binding antibodies sufficient?
  - No requirement for titer assessment?
  - Not needed for a single-dose study?
  - Should ADA assays for toxicology studies be GLP-conform?
  - Are ADA samples required to be collected for biosimilar studies?

## Biosimilars

- Comparative studies in animals to evaluate immunogenicity are not recommended

## Therapeutic protein representing a counterpart to an endogenous protein

- ADA can be neutralising and cross-reactive
- ADA formation in animals is not predictive for humans
- Effects are predictable based on biology
- Rarely if ever need for animal studies