Immunogenicity Assays Working Group Update

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on behalf of the

EIP Immunogenicity Assays Working Group

EIP Open Symposium

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EIP
European Immunogenicity Platform

Disclaimer

This presentation represents the view of the EIP working group and is not necessarily reflective of the specific views of any member company.

Mission Statement

- The **Immunogenicity Assays Working Group** is part of the Strategy Working Group and was founded in 2021.
- The goal of the Working Group is for the members to exchange their company's practices on immunogenicity assay related topics and work to publish industry best practices as recommended by EIP.
- The Working Group currently meets every 3 weeks for 1h.
- Currently, discussion topics include: all stages of humoral immunogenicity (or anti-drug antibody (ADA)) assays, including assay cross validation
- Thanks to EIP, we now have our own Teams site: *https://teams.microsoft.com/_#/FileBrowserTabApp/General?threadId=19:8c92SJNmbtPFAXVGusob2Jc5brdKAlvq5BsFp7hBtdc1@thread.tacv2&ctx=channel*

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Discussion Topics of the Working Group

- Assay development:
  - Strategies to develop drug- and target-tolerant ADA, Domain Characterization & NAb (neutralizing antibody) assays
  - Assay optimization strategies (Titer, MRD, new technologies)
  - Strategies for sample preparation, handling and storage
- Assay validation:
  - Best practices (Preclinical vs. Clinical)
  - Qualification vs. Validation
  - Determination of Sensitivity and, Low positive control
  - Cut point calculations
- Post-validation:
  - Bridging of critical reagents, negative control matrix change
  - In-study cut points evaluation
  - Cross-validation strategies for ADA and NAb assays

Immunogenicity Assays Working Group Members

- Active members from 11 companies
  - Benstein, Karin /DE <Karin.Benstein@**sanofi**.com>
  - Deiser, Katrin <katrin.deiser@**sandoz**.com>
  - Elm, Stefanie <selm@**amgen**.com>
  - Goodman, Jo <jo.goodman@**astrazeneca**.com>
  - Grudzinska, Joanna <joanna.grudzinska@**bayer**.com>
  - Ichetovkin, Marina <marina_ichetovkin@**merck**.com>
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  - Luo, Linlin <linlin.luo@merck.com> - Colead
  - McManus, Deborah <DMcManus@**alliancepharmaco**.com>
  - Potthoff, Bernd <bernd.potthoff@**ucb**.com> - Colead
  - Schaefer, Martin <martin.schaefer@**roche**.com>
  - Sickert, Denise <denise.sickert@roche.com>
  - Ullmann, Martin <martin.ullmann@**fresenius-kabi**.com>

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Progress of the Working Group *(1 of 2)*

- Decide on “hot”/critical topics to be covered:
  - Assay development –
    - ❑Drug tolerance (e.g., When is it needed to detect ADA in the presence of high levels of drug?)
    - ❑Target tolerance
    - ❑MRD determination
    - ❑My own question: technologies? Platforms?
  - Assay validation –
    - ❑Is STS needed, such as F/T, bench top, and 2-8 C?
    - ❑My own question: CP too low? Sensitivity too low?
    - ❑Assay acceptance criteria (how to harmonize? E.g. among different CROs)
  - Post-validation (LCM) –
    - ❑In-study CP evaluation (When to trigger; What to consider)
    - ❑ADA/NAb assay x-validation (Best practice)
    - ❑Critical reagents (How to bridge)

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Progress of the Working Group *(2 of 2)*

- In-depth discussion topics:
  - Nonclinical immunogenicity assessment
    - ❑ADA assay qualification vs. validation
    - ❑What's the minimum to do in a qualification?
    - ❑How to report ADA magnitude? (S/N vs. titer)
  - Clinical in-study cut point evaluation
    - ❑When to trigger
    - ❑What to consider
  - Cross validation
    - ❑ Practices from different companies
    - ❑ Literature review
    - ❑ What's next

Validation Strategies on ADA Assays *(ongoing/next steps)*

- A survey on x-val practices at different companies – to be sent out
- A manuscript (*Perspective*) on x-validation
  - Lack of regulatory guidance different approaches
  - An overview of different practices from each companies or published
    - ❑ The case can be method transfer
    - ❑ The case can also be reagent change
      - ✓ Methodology, including validation parameters done from two labs
      - ✓ How comparability was done
        - *Samples used*
        - *What tiers were compared*
        - *Criteria used*
        - *Outcome*
  - Description and discussion/comparison of different approaches, highlighting requirements, key differences and similarities, tools and reporting strategies for the statistical comparison
  - Provide recommendations if possible
  - Targeting to send to Bioanalysis

14th Open Scientific EIP Symposium on Immunogenicity of Biopharmaceuticals

26th — 28th April 2023

Lisbon, Portugal

Thank you !

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