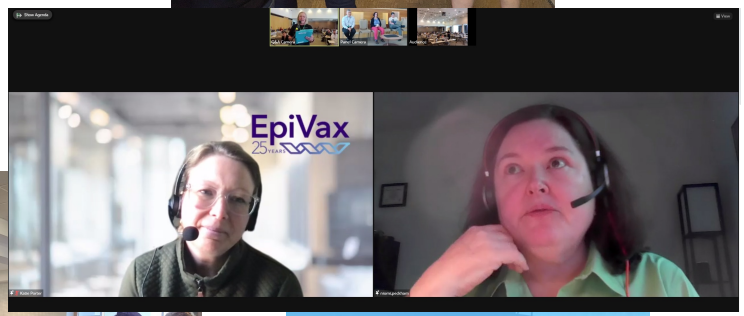
Welcome to BEBPA's 11th ~~6th~~ Annual HCP Conference!

1st Hybrid HCP Conference!



11th Annual Host Cell Protein Conference

HCP Profiling During Process Development

- Impact of upstream and downstream process on HCPs
- LC-MS/MS is a valuable tool to understand how cell age, cell culture process and Protein A parameters influence HCP population and understand process robustness (little change with upstream changes)
- Is native digest significant difference given improvements in MS?

Implementation of HCP ELISAs

- Different global health authorities may have a very different view on suitability of HCP assay
- It takes a long time to build an HCP ELISA! Coverage numbers are estimates!
- Sometimes product cross reactivity is real (moss expression system)

Alternatives to ELISA for HTP and Routine HCP Testing

- Several promising technologies are being used for high throughput analysis
- May not be needed in GMP (low throughput); but there may be possible path forward to put in QC labs based on methods in GLP labs.

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Low Abundance HCPs

- Potential mechanisms for HCP co-purification with product (HMWS association)
- There are likely 10s-100s of HCPs at very low levels in most biopharmaceutical

Guidance

- Approvability of an assay is dependent on data presented and clarity of data
- Review of new 1132.1 Draft chapter on using MS for HCP quantitation; ARMs in the pipeline at USP
- In silico immunogenicity assessment and in vitro cell based assays can be used to bolster risk assessment

HCP Critical Reagent Characterization Methods

- Coverage result is method dependent
- Case studies from 2 companies showed enrichment of HCPs with immunoaffinity column/AAE yields similar coverage numbers as 2D gel/blot methods.
- Enrichment methods for determining coverage may generate results less relevant for ELISA (ie; protein can be “covered” but still missed in the ELISA).
- Coverage analysis using ELISA capture with MS can give information on coverage in assay-relevant format and potentially provide data on highly immunoreactive proteins (jackpot proteins)

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Advanced MS Topics – critical look at MS

- What is MS supposed to deliver, how do we deliver, how do we ensure produce meaningful high-quality results
- Analytical Instrumentation and Software Qualification, System Suitability, and Control Checks
- Suitability of Analytical Methods – this closely followed the USP 1132.1 chapter draft

Critical Reagent Generation and Qualification

- Best practices for generating HCP ELISA standards, controls, and antibodies

Phase-Specific HCP Strategy

- 3 case studies were presented and worked through by small groups

Intro to MS

- How MS is used to demonstrate product purity and for qualification of HCP critical reagents
- How to look critically at MS data and talk to MS colleagues to improve collaboration

Risk Assessment

- There is no “safe” level of HCP(s); suitability of HCP profile in a product is determined in a context-dependent way

12th Annual Host Cell Protein Conference

Location tbd (USA)

CALL FOR TOPICS

Topic Requests Based on Last 3 Days

- Risk Assessment Workshop →
  - In vitro immunogenicity assays, activity (e.g. histamine release) (Ingrid Nasman Bjork)
  - Risk assessment case-studies

- Phase-Specific HCP Strategy →
  - Cell line engineering for reduction of HCPs
  - Gene and cell therapy, vaccines (Carl Co?)

Topic Requests Based on Last 3 Days

- Advanced MS Workshop →
  - Improvements in data analysis – case studies

- Detection of Low Abundance HCPs →
  - Activity assays (e.g. lipase or protease activity)

- Chat GBT

See You Next Year!