Table 4: HCP Testing Strategies

Scope:
Host cell proteins (HCPs) are process-related impurities, expressed by the host cell used for production of biopharmaceutical proteins. National regulatory authorizations require that biopharmaceuticals must be analysed and purified to reduce HCPs to an acceptable level. Analysis of HCPs is not simple, since the HCP mixture consists of a large number of protein species, which are unique to the specific host and not related to the intended recombinant protein. Current trends related to analytical technologies and testing strategy will be discussed during roundtable discussion.

Questions of Discussion:
1. What is your current HCP Testing strategy? To which level do you perform HCP identification, quantitation? What types of analytical techniques do you use for HCP analysis? What is your target sensitivity for testing? Is there a specific focus on some portion of the HCPs?
2. How do you assess criticality of HCPs and their control levels? How do you acquire information of the criticality? What is considered the most critical attribute of HCPs?
3. What are the most urgent needs to address with respect to HCP testing? What drives change in HCP testing – regulatory challenges, cost, sample turnaround time, sensitivity, selectivity?
4. Is your organization building up HCP data bases (if yes, decentralized or centralized)?
5. What level of information is requested by authorities ? Protein specific information or general HCP amounts?

Discussion Notes:
A reasonable and often used approach to control HCPs could be for example: First goal: set the list of HCPs, for that, proposal is to do both, DDA (Data Dependent Acquisition mode) and DIA (Data Independent Acquisition mode) mass spec to asses both protein identity and quantity. Second goal: Define what to monitor (or monitor all) and to what levelIf a method could systematically and constantly monitor an abundance of HCPs, e.g. high-resolution mass spec, in QC, would we apply this? High resolution mass spec may replace ELISA development (if needed), e.g. if a new cell line is used, since the advantage of MS is clearly flexibility. However in case a HCP ELISA is available this would be better for high throughput analysis. To implement MS for HCP batch release it needs to become applicable for high throughput testing (including sample preparation). Also, mass spec robustness and QC compatibility must be given, e.g. by use of triple quad mass spec systems.

Change in testing strategy for HCP is both driven by needs (stable product, safety), regulatory requests and evolving technologies. Key might be sound risk assessment. Assess risks based on prior knowledge from clinical studies (humans), route of application, dose frequency.
For product consistency over time MS might be required to monitor critical HCPs for e.g. product stability. However, risk assessment of specific HCPs is extremely hard especially for HCP originating form novel (none CHO) cell lines. This is another driver for applying mass spec already early in development and the whole development process to learn about your product and potential impact of specific HCPs on product stability and safety.

Generically accepted levels of HCPs have been discussed controversially. Low levels as achievable for mAbs might not be achievable for e.g. vaccines. Further, these generically accepted levels are only of use when it is sure all HCPs are covered by the HCP ELISA.

Starting with public databases own databases/libraries are built-up for CHO, ecoli and others are built-up for faster identification and easier quantification. Public databases maintained and improved by all academia and pharma would be helpful to manage HCP accordingly.