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Host Cell Protein Assays

Charles River is able to offer clients generic host cell protein (HCP) assays as well as assist with the development of customized assays for the detection of host cell proteins. The type of assay required to determine HCP concentration is dependent upon the phase of product development. In the early process development phase, as well as in the early clinical phases, generic assays are normally acceptable. However, once the biopharmaceutical is used in Phase III clinical studies, a validated, product-specific HCP assay is usually required. Charles River can help you with assay development and validation regardless of whether you are in preclinical development or embarking on Phase III studies.

What are Host Cell Proteins?

Host cell proteins (HCP) are an inevitable impurity of biopharmaceuticals, regardless of whether they are produced by recombinant fermentation or extracted from natural sources. Even after multiple sophisticated purification steps, HCPs may remain or co-purify. They represent a heterogeneous variety of different proteins that need to be quantified in the drug substance and in intermediates from the downstream purification process. The risk for adverse effects, such as immunogenic reaction, does not necessarily correlate with the amount of certain host cell proteins, and even small traces of certain HCPs can be highly immunogenic.

Traditional protein detection methods such as HPLC and total proteins stains are not suitable for HCP detection due to their insufficient sensitivity and specificity. Consequently, optimized immunoassays (ELISA) have established themselves as the method of choice for the measurement of HCPs.

Service Areas

- ELISA-based assay
- Multispecies capabilities, including:
  - Mammalian cells (e.g., MRC-5, Vero, A549, BHK, CHO, 293)
  - Insect cells (e.g., Sf9)
  - Bacteria (e.g., *E. coli*, *S. aureus*)
  - Yeast (e.g., *P. pastoris*, *S. cerevisiae*)
- Rapid assay qualification
- In-house production of antisera available to support late-phase product development

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Development of a Customized Quantitative HCP Assay

Arriving at a product-specific, quantitative HCP assay involves several steps:

- Preparation of host cell antigens
- Production of antisera
- Purification of antibodies from crude serum
- Quality control of the antibodies with respect to specificity and sensitivity
- Host cell protein assay setup and optimization
- Validation for the assay in compliance with ICHQ2(R1) guidance

Charles River can support you in all of the above processes to ensure that your biopharmaceutical product remains uncontaminated and is ready for use in each stage of the drug development pipeline.

Antisera Production for Customized HCP Assays

In contrast to single contaminants or leachables such as trypsin or protein A, which can be approached by a monoclonal antibody, the heterogeneity of the HCPs always requires a polyclonal antiserum for the assay development. Within Charles River, polyclonal antisera production is available in a variety of species, including rodents, companion animals and farm animals (most commonly used are sheep and goats). Many immunizations are performed in SPF (specific pathogen-free) animals. Projects are set up on request to client-specific requirements and to cGMP standards.

Advantages/Disadvantages of Kit-Based vs. Customized HCP Assays

	Generic Kit-Based Assays	Customized HCP Assays
Availability	Able to be ordered as needed	Require antigen preparation, including cloning of a mock cell line
Development	Not necessary	Antigen characterization, immunization and qualification takes a minimum of four months
Diversity	Availability is limited to the most common expression systems	Feasible for all recombinant expression systems
Specificity	Low specificity; high risk of undetected HCP species	Typically enhanced specificity; antibody coverage more customized to the specific HCP pattern
Cost	Initially fairly cheap, but for an entire DSP, development costs add up fast	Initially costly, but typically the break-even point is at a value of 100 kits
Dependence	Rely on one vendor and black box for reagents and controls	Full control of all reagents and buffers; optimization/ adaptation is always possible
Regulatory Needs	Not suitable for supporting marketing authorization applications	Suitable from early development to final product release of authorized product

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