charles river

BIOLOGICS TESTING SOLUTIONS

In Vivo Biosafety Testing

Services

- Antibody production assays
- Inapparent virus/Adventitious agent assay
- Safety tests
- Tumorigenicity

Charles River has laboratories in both the US and Europe, accredited against the relevant regulatory standards and programs (e.g., GLP, GMP, AAALAC) to perform *in vivo* broad range screening assays to detect potential contamination by unspecified agents. We partner with clients to understand the unique requirements of each study, and customize our existing standard operating procedures where necessary to meet these needs. Charles River also can facilitate the handover from *in vivo* testing of clinical material to GMP release testing at one of our US or EU sites.

Testing Requirements

Viral vaccines and cell lines used to produce biologics must be tested to ensure they are free of adventitious agents (e.g., viruses). While methods such as PCR can detect specific viruses, a broad range *in vivo* screening assay can detect potential contamination caused by unspecified agents. Each lot of biologic product intended for human use requires safety testing for extraneous toxins. Additionally, some products require determination of the tumorigenic properties of the cell substrate. Charles River's *In Vivo* Biosafety groups routinely perform these tests.

Antibody Production Assays

Mouse, rat and hamster antibody production (MAP, RAP and HAP) testing are immunologically-based procedures for the detection and identification of murine viral contaminants in biological specimens. Using highly susceptible natural hosts (i.e., mice, rats, or hamsters) and sensitive and specific serologic assays, Charles River offers a comprehensive screening method for biological contaminants.

Virus antibody-free (VAF) mice, rats or hamsters are inoculated by multiple routes with a test article and held in isolation for four weeks. Serum samples are collected and tested for virus-specific antibodies using the enzyme-linked immunosorbent assay (ELISA) or immunofluorescence (IFA). Detection of specific antibodies is tantamount to identifying a virus in the test article. Antibody production testing can be supplemented with an intracranial challenge to test for the presence or absence of lymphocytic choriomeningitis virus (LCMV) in the test article. This method of LCMV detection is more sensitive than the serologically-based assay.

EVERY STEP OF THE WAY

Inapparent Virus/Adventitious Agent Assay

Whether clients are producing a biologic or viral vaccine, we can perform adventitious agent testing to meet various regulatory requirements. Guinea pigs, young adult mice, suckling mice and embryonated eggs can all be utilized to determine the viral status of a cell line or substrate. While this test does not serve to identify a specific virus, it is a critical component in the viral safety testing profile.

Safety Tests

Charles River also offers a variety of *in vivo* safety tests, which are required by federal regulatory agencies in support of investigational and new drug filings. The General Safety and Abnormal Toxicity Tests are industry standards that we routinely perform under GMP compliance.

Tumorigenicity

Human epithelial cells and all cells used for live viral vaccine production must undergo tumorigenicity testing. To meet multiple regulatory requirements, we offer 84-day and 120-day tumorigenicity tests in athymic nude mice.

Regulatory References:

- Guidance for Industry, Characterization and Qualification of Cell Substrates and Other Biological Materials Used in the Production of Viral Vaccines for Infectious Disease Indication (February 2010) – Antibody Production Test, Adventitious Agent Assay, Tumorigenicity
- European Pharmacopoeia 2.6.16 – Adventitious Agent Assay
- European Pharmacopoeia 2.5.3 – Tumorigenicity
- European Pharmacopoeia 2.6.9 – Abnormal Toxicity
- 21CFR610.11 – General Safety Test
- Points to Consider (PTC) in the Characterization of Cell Lines Used to Produce Biologicals as Recommended by the US FDA Center for Biologics Evaluation and Research (1993) – Antibody Production Test, Adventitious Agent Assay, Tumorigenicity
- International Conference on Harmonisation (ICH), Guidance for Industry Q5A (R1): Viral Safety of Biotechnology Products Derived from Cell Lines of Human or Animal Origin (1999) – Adventitious Agent Assay, Antibody Production Test