



In Vivo Biosafety Testing

Viral vaccines and cell lines used to produce biologicals must be tested to ensure they are free of adventitious agents (e.g. viruses). While specific viruses can be tested for by tests such as PCR, there remains a requirement for an *in vivo* broad screening assay to detect potential contamination by unspecified agents. Charles River has laboratories in both the USA and Europe, accredited against the relevant regulatory standards (e.g. GLP, GMP, AAALAC) to perform such tests. We partner with you to understand your study and will customize our existing standard operating procedures where necessary to fulfill your needs. Safety testing for extraneous toxins is required on each lot of biological product intended for human use and requirements may exist for the tumorigenic properties of a cell substrate to be determined. Charles River's *In Vivo* Biosafety groups have the capabilities to conduct these tests as well.

Services

- Antibody Production
- Inapparent Virus/Adventitious Agent Assay
- Safety Tests
- Tumorigenicity

Antibody Production

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 multiplexed fluorometric immunoassay[®] MFIA[®]. 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.

Inapparent Virus/Adventitious Agent Assay

Whether producing a biologic or viral vaccine, Charles River 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 your 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 GLP compliance.



Tumorigenicity

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



Compliances

In vivo Biosafety testing can be performed under GLP, GMP or non-GLP study conditions. GLP and GMP studies include Quality Assurance (QA) oversight and document review upon test conclusion. Testing protocols have been designed to meet the requirements of:

- 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