

BioOutsource – *in vitro* Virus Safety Testing

The potential for virus contamination in biologic products and vaccines produced using mammalian systems is one of the major concerns of any production process. Accidental (adventitious) contamination can be introduced at any step through a variety of means including operator error, GMP breakdown or through the use of contaminated reagents such as starting raw materials of animal origin.

BioOutsource has developed and validated a comprehensive range of *in vitro* virus detection assays that can be used to test for the presence of viruses in a variety of different product types. Currently, BioOutsource provides GMP testing services for batch release in the USA and Europe.

Expertise, Quality, Communication

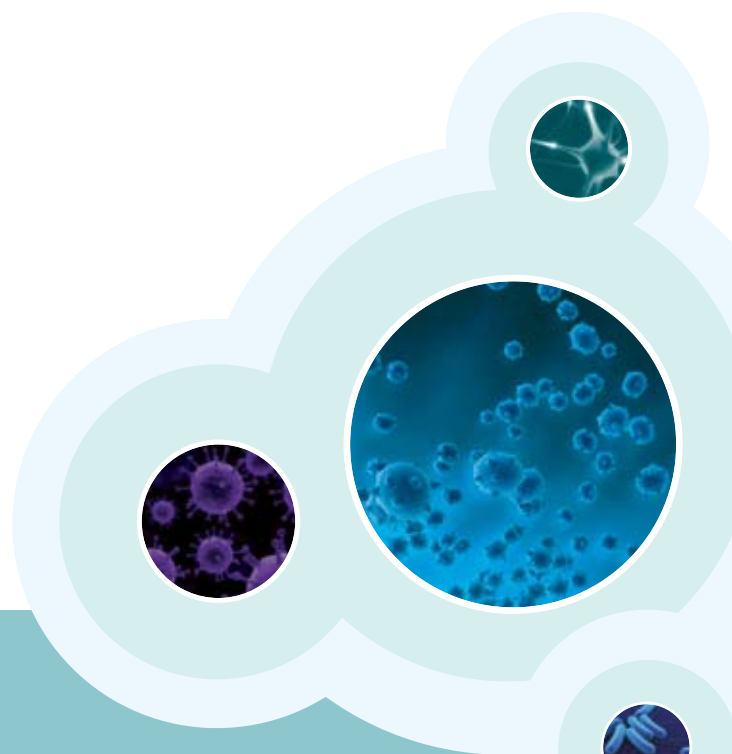
BioOutsource's service in adventitious virus testing is based upon a strong understanding of virology and many years of experience in virus safety testing for a wide range of products from monoclonal antibodies to live virus vaccines and gene therapies.

BioOutsource's facilities and services have been inspected by the UK MHRA and are GMP compliant. Virus safety testing is carried out in compliance with GMP and with the following regulatory guidance:

- European Pharmacopeia Guidelines 2.6.16: Tests for Extrinsic Agents in Viral Vaccines for Human Use
- Q5A (Viral Safety Evaluation of Biotechnology Products Derived from Cell Lines of Human or Animal Origin – 1997)
- "Points to Consider in the characterization of cell lines used to produce biologicals" (FDA, CBER, 1993)

BioOutsource extensive validation package provides a detailed report on the validation of the assays to ICH guidelines and is available to all clients to use as part of their regulatory submission; facilitating regulatory approval for the GMP compliant batch release of their product.

All BioOutsource's clients benefit from the industry-leading BioWeb technology which has been developed to allow our clients unprecedented access to study documentation and data. Through the BioWeb our clients have 24/7, on-line access to their studies which allows early access to results, informed decision-making and effective project management.

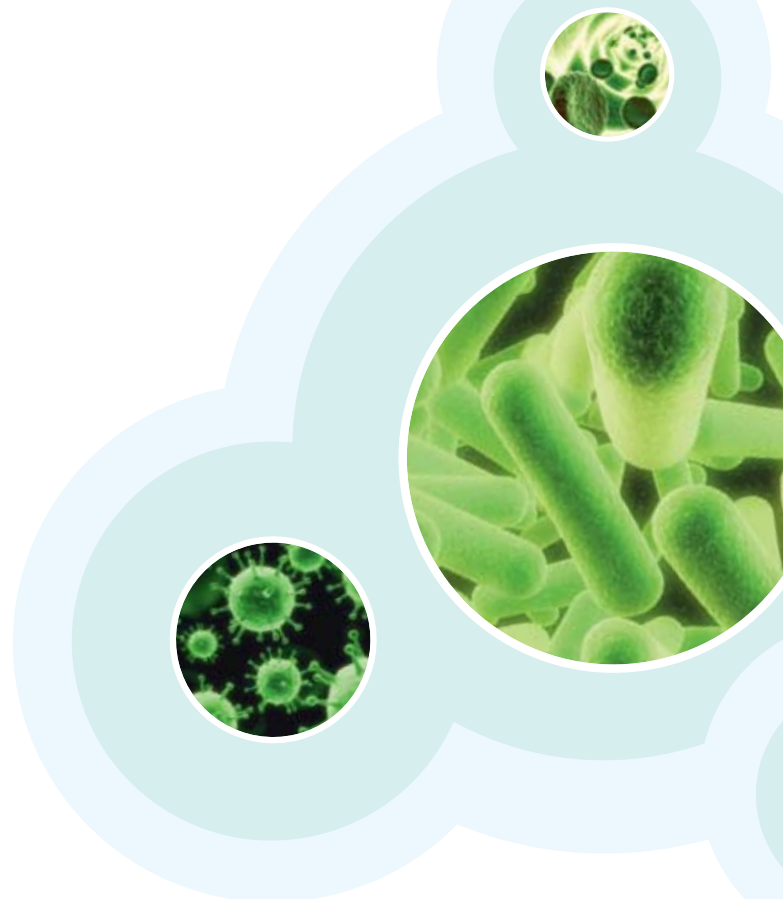


Service Offering

In vitro testing for adventitious virus is used/required at a number of different points in the production of products derived from growth in mammalian cell culture. Typically, Master and Working cell banks, End of Production cell banks, and bulk harvests are tested and tests are designed to detect a broad spectrum of potential contaminants as well as species specific and retroviruses which may require more specific tests.

Benefits of BioOutsource *in vitro* testing service include:

- Fully GMP compliant facility and services (inspected by the MHRA in March 2008).
- Compliance with the following regulatory guidance:
 - European Pharmacopeia Guidelines 2.6.16: Tests for Extraneous Agents in Viral Vaccines for Human Use
 - Q5A (Viral Safety Evaluation of Biotechnology Products Derived from Cell Lines of Human or Animal Origin – 1997)
 - Points to Consider in the characterization of cell lines used to produce biologicals” (FDA, CBER, 1993)
- Validated and characterised detection cell banks including – the human diploid cell line MRC-5, the Human cells line HeLa, the primate cell bank Vero, Chinese Hamster Ovary cells, Bovine cell line [Madin Darby Bovine Kidney], Porcine cell line [Primary Porcine Kidney cell line], Mouse cells [SC-1], the canine cell line [Madin Darby Canine Kidney]
- Validated Haemagglutination and Haemadsorption end points
- Validated and characterised control virus banks including – *Adenovirus*, *Herpes Simplex type 1 virus*, *parainfluenza virus*, *Influenza virus* and, *Reovirus Type*
- Extensive experience of handling a variety of Test Materials requiring appropriate sample preparation
- Production, assessment and qualification of neutralising antiserum available for live virus vaccine testing



- Primary cell lines also available on request for specialist requirements
- Qualification of Limit of Detection of specific viruses dependant on sample type; typical sample detection already achieved is between 10-1000 TCID50

Sample Requirements

The client will provide sufficient sample for analysis.

Using the BioWeb, online sample submission eliminates the potential for errors with sample receipt.

Product samples: Raw materials of animal origin, bulk harvest and in-process samples.

Control samples: Qualification samples typical of the testing matrix.

Reporting of Results

All reports and laboratory data are available on line using our BioWeb web based interactive tool following completion of the assay. The Final Report can be custom designed to the sponsor's requirement using any format.

High Speed turnaround of studies – Sample receipt to final certificate of analysis within one week of study completion.