VIRUSURE
VIRUS & PRION TESTING

Cell Bank Characterisation

In Vitro Tests for Adventitious Viruses

Identifying unknown viruses still represents a significant challenge for virologists, and is the main reason only a fraction of viruses circulating have been identified. Virus growth in tissue culture is not always possible, with viruses often displaying distinct tissue tropisms. Certain viruses may also fail to demonstrate any visible cytopathic effect even when growing to high titres, and thus virus growth may not be immediately apparent. Despite these challenges however, certain cell lines have proven useful in the detection of a wide range of potential virus contaminants, including Vero, MRC-5 and HeLa cells.

The *in vitro* assay for detection of viruses uses a selection of cell lines with a proven history in the detection of a wide range of potential virus contaminants. It is used both in the testing and characterisation of recombinant cell banks, as well as in the testing of raw materials (e.g. bovine serum). No single cell culture based assay can provide guarantees for the detection of all potential contaminants, but rather the aim is to cover a broad spectrum. Thus testing is routinely performed on a minimum of 3 cell lines, almost always including Vero and MRC-5 cells, and the third cell line being selected based on the species of origin of the production cell line or raw material. The table below provides an overview of commonly used cell lines for the *in vitro* assay along with a selection of potential viral contaminants likely to be detected.

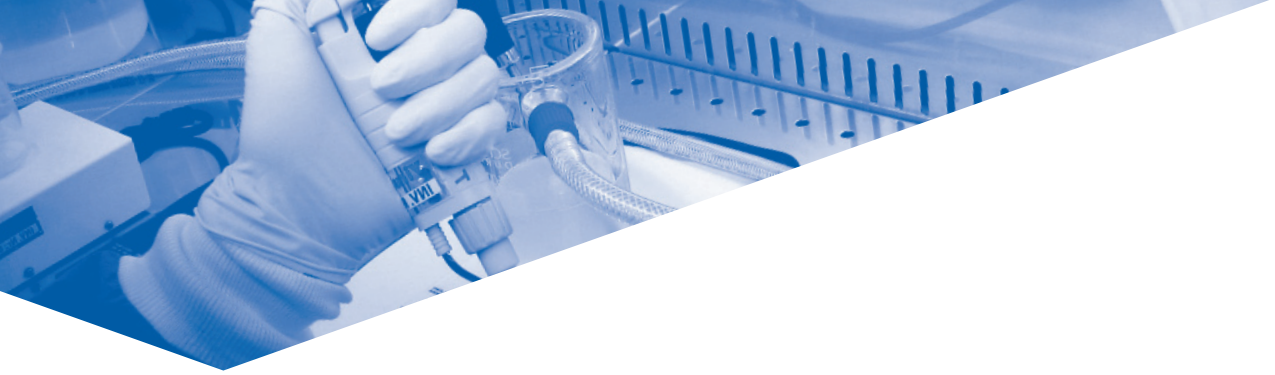
Virus Permissivity for Cell Lines Commonly Used in the *In Vitro* Adventitious Agent Test

Cell Line	Example viruses detected
MRC-5	Ortho- and Paramyxovirues, selected Picornaviruses, Herpesviruses
Vero	SV40, Vesicular stomatitis virus, Adenoviruses, Herpesviruses, Reoviruses
HeLa	Adenoviruses, Coxsackieviruses, Poliovirus
A9	Mice minute virus, Adenoviruses
BT	Bovine Adenoviruses, Herpesviruses, Polyomaviruses and Arboviruses

In vivo Tests for Adventitious Viruses

In vivo adventitious agent tests remain one of the critical cell bank characterisation tests despite ethical concerns around the use of animals for testing. The main advantage of the *in vivo* test is the broad range of viruses detected. The use of this test is restricted primarily to the characterisation of master cell banks, and ethical concerns normally preclude the use of this test as a general QC release test for biopharmaceutical products. For products of higher risk, however, lot release testing using the *in vivo* test may be requested.

ViruSure GmbH
Tech Gate Science and Technology Park,
Donau City Strasse 1, A-1220 Vienna, Austria
Telephone: +43-1-2699-120
Telefax: +43-1-2699-12022
E-Mail: andy_bailey@virusure.com
virusure.com



Other QC Virus Safety Tests

Testing of Animal Derived Products and Recombinant Products for Virus Contamination

The term *in vitro* testing is applicable both to tests performed on the production material as well as to the testing of raw materials. For example, guidelines have been established in both Europe and the US FDA for the testing of bovine serum prior to use in manufacture. This includes tests on permissive bovine cell lines with specific end point detection for Bovine adenovirus, Bovine parvovirus, BRSV, Reovirus, Bovineparamyxovirus, IBRV and Bluetongue virus.

I*n vitro* adventitious agent testing also plays an important role the lot release of of recombinant biopharmaceutical products and is required at the following stages of biopharmaceutical product development and production:

- **Master cell bank or virus seed bank testing**
- **Working cell bank testing**
- **Production lot release testing**

Retrovirus Testing

Retroviruses are a known and accepted viral contaminant of e.g. recombinant cell lines. Despite their acceptance, guidelines still require the characterisation of any retrovirus contamination in terms of:

- **Type of retrovirus particles observed (e.g. A-Type, C-Type, R-Type)**
- **Quantification of retrovirus particle count**
- **infectivity (and if infectious the tropism)**
- **Levels of virus associated reverse transcriptase (e.g. FPERT determination)**

ViruSure can offer a range of retrovirus testing services to service the above regulatory requirements, including:

- **Retrovirus infectivity tests**
- **FPERT Retrovirus testing**
- **Electron microscopy for characterisation and quantification of retrovirus particles**
- **Co-cultivation assays**

Contact ViruSure today to find out more about our cell bank characterisation services, or to see how we can support your your adventitious agent testing requirements.