

Mammalian Cell Line Characterization

**Comprehensive testing programs for
regulatory acceptance worldwide**

*ILLUSTRATION:
Retrovirus infection of cell*

 **WuXi AppTec**

**THE
VIROLOGY
EXPERTS**



WuXi AppTec – Trusted Leader in Cell Line Characterization (CLC)

Characterization of mammalian cell lines used in the production of biopharmaceuticals requires technical expertise across a wide range of biological disciplines. In addition, understanding the requirements and subsequent development of the testing regimens to ensure acceptance by worldwide regulatory agencies takes experience only gained through the performance of hundreds of these studies. WuXi AppTec has this experience – in both the technical and regulatory aspects – and has established all the necessary laboratories, assays and quality oversight to conduct these critical testing programs.

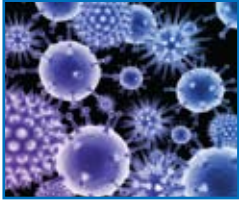
As cell line characterization is a case-by-case program, WuXi AppTec’s team of experts can consult with you to determine the testing regimen that will stand-up to regulatory scrutiny while providing you a program that is also cost effective.

	MASTER CELL BANK	MANUFACTURERS WORKING CELL BANK	END OF PRODUCTION CELLS <small>Cells at the limit of in vitro cell age</small>
Authenticity & Characteristics			
Identity	Yes	Optional	Yes
Growth / Morphology	Yes	Yes	Yes
Genetic Stability	Program Dependent	Program Dependent	Program Dependent
Tumorigenicity	Cell Line Dependent	No	No
Adventitious Agents			
Sterility	Yes	Yes	Yes
Mycoplasma	Yes	Yes	Yes
General Virus Screens	Yes	No	Yes
Species-Specific Virus Tests	Yes	No	No
Retrovirus Tests	Yes	No	Yes
Adventitious Agents from Raw Material	Yes	Program Dependent	Program Dependent

The table above provides an overview of the tests typically required to characterize mammalian cell lines as outlined in the worldwide regulatory guidance documents. Which tests to conduct and at which stage – and the quality oversight required – is where WuXi AppTec’s extensive, 20-year experience can make the critical difference.

The following WuXi AppTec laboratories support cell line characterizations, with each lab offering world-class expertise.

VIROLOGY

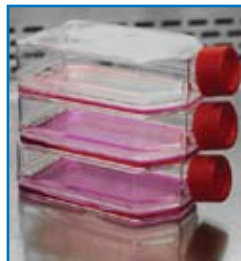


WuXi AppTec's professional staff has a broad and detailed understanding of human and animal virology. For virology testing, we employ over 50 well-characterized cell stocks for use as indicator cells to propagate and detect adventitious virus, and over 60 different virus positive controls..

A variety of in-vitro and cell-based virology tests, including the general virus screens to detect adventitious and infectious virus, are available. These assays enable our highly trained personnel (including many Ph.D. level virologists) to detect the various forms of virus cytopathic effect (CPE) and the hemadsorption, hemagglutination and IFA endpoints. Specific assays designed to detect infectious retroviruses using a variety of end point analysis, including XC plaque and PG4 S+L-, are utilized. Co-cultivation assays used to amplify and detect infectious retroviruses are also employed if and when necessary. Routinely conducted as well are the 9 CFR protocols for the detection of adventitious virus from the use of animal-derived raw materials or cell culture components. Customized assays can be developed and validated for novel cell substrates.

CELL BIOLOGY

All CLC programs require that cell line growth characteristics and morphology be well-documented. WuXi AppTec's expertly trained cell biologists can conduct the cell growth and provide the necessary written assessment as a GLP report. A wide variety of cell line identity assays are also performed, including isoenzyme analysis or, if necessary, cell-marker identification assays using flow cytometry or ELISA.



The cell biology laboratory has experience with over 50 different cell types and acts as the support lab for growing WuXi AppTec's own extensive cell stock, such as the cell lines used as indicator cells in virology assays. This group can also expand your cells after cell banking activities to provide the necessary test articles for each individual assay used in a CLC program.

IN-LIFE / IN-VIVO



WuXi AppTec provides fully accredited AAALAC facilities for GLP animal assays, including testing in a wide variety of rodents, guinea pigs and eggs. Staff veterinarians and experienced in-life study directors test cell lines using the required routes of administration as dictated in guidance document protocols.

Methods for detecting adventitious virus that follow both US and EU requirements are available. If required, tumorigenicity and oncogenicity protocols can be conducted for novel and diploid cell substrates. General Safety assays are also available

MICROBIOLOGY



Individual sterility and mycoplasma laboratories perform the necessary detection of adventitious microorganisms testing required for all CLC programs. These labs conduct with exacting standards the bacteriostasis/fungistasis, sterility, mycoplasma and mycoplasma detection assays. All microbial assays used in cell line characterization programs follow the harmonized USP/EP/JP protocols. If required, specific assays that follow CFR or Points-to-Consider protocols and guidelines are available. In addition, alternative methodologies such as BacT[®] Alert are available if applicable for your cell line characterization program. Highly trained and skilled personnel process over 30,000 samples per month in these laboratories while maintaining industry-leading turnaround times.

MOLECULAR BIOLOGY

WuXi AppTec's extensive molecular biology program offers state-of-the-art nucleic acid-based molecular detection technologies (e.g., qPCR methodologies) for the identification and quantification of species-specific virus. An EP compliant and validated TD-PCR method for detection of mycoplasma is also available if applicable for your CLC study.

Understanding the genetic stability of your production cell line from Master Cell Bank to the End of Production Cells is an eventual and critical component of a regulatory filing. Genetic stability analysis encompasses a wide variety of molecular biology techniques including:

- Southern & Northern Blotting
- qPCR for Copy Number Determination
- DNA & RT-PCR cDNA Sequencing

WuXi AppTec's experienced staff and state-of-the-art labs employ the latest techniques and instrumentation to efficiently assess the genetic stability of your cell line.



Additional Related Services Offered by WuXi AppTec:

- Construct/Vector Cloning and DNA Sequence Confirmation
- Cell Line Engineering and Development
- GMP Cell Banking
- Long-Term Cryopreservation of Master and Working Cell Banks



Mammalian Cell Line Characterization

A successful characterization program has many essential elements, including identity and detection of microorganisms and mycoplasma. The most highly customized element is the detection of adventitious virus.

EXPERIENCE

WuXi AppTec is the clear leader in this field with exceptional expertise and over 20 years of experience.

- Complete assay panels performed for hundreds of cell lines and allogeneic/autologous cell therapy products.
- Strong track record for supporting IND, BLA, and market approvals by regulatory agencies worldwide.
- Senior staff members serve on industry task forces to remain current on regulatory policies.

PROGRAM FEATURES

- Over 50 cell lines of human and animal origin and over 60 human and animal viruses.
- Over 40 viral PCR probes and over 100 PCR assays developed and implemented to assess potential virus contamination.
- Expert advice/consulting on worldwide regulatory requirements.
- Custom assays developed for unique cell lines as needed.
- Dedicated virology, molecular biology, cell biology, and analytical labs of over 21,000 square feet.



Contact WuXi AppTec for your cell line characterization studies:

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