Viral Clearance Studies

Capabilities, capacity and expertise that create a clear difference

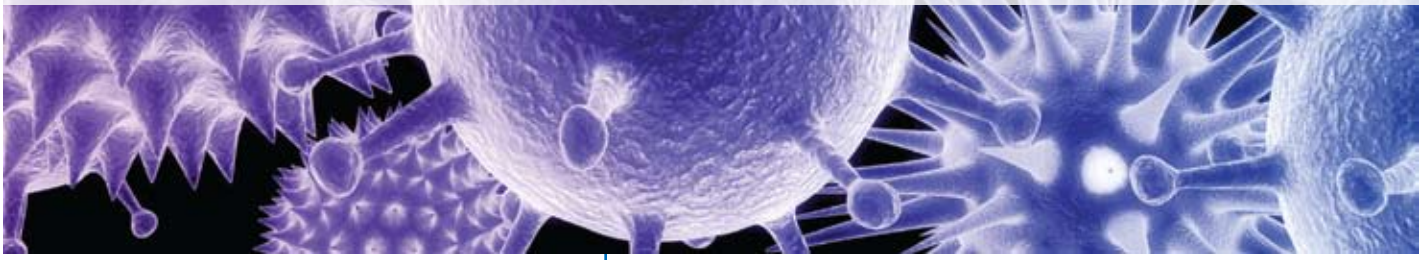
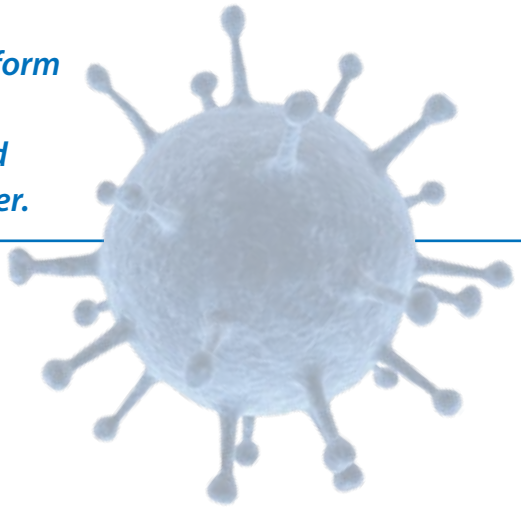


ILLUSTRATION:
Variety of potential virus contaminants

药明康德
WuXi AppTec

Viral Clearance Studies

WuXi AppTec has the capability to design and independently perform all levels of your viral clearance studies. Our extensive expertise, unparalleled suite capacity, comprehensive database mining and ultra-pure, high-titer virus stocks make us the clear industry leader.



WuXi AppTec offers custom studies to validate removal, inactivation, or cleaning processes for viruses. Our scientific and quality teams, with over 20 years of experience, offer comprehensive expertise in infectivity and quantitative PCR assays, process development, and international regulatory considerations for early- and late-stage products.

STUDY DESIGN

Our experienced staff can help design and then perform your entire study for you, including scale-down and resin cycling, or can work side-by-side with you during execution of the study.

Study Experience

Products for which we have conducted studies for R&D, Phase 1-3, BLA, and 510K submissions include:

- Monoclonal antibodies
- Recombinant proteins
- Blood-derived products
- Gene therapy vectors
- Viral vaccines
- Tissues
- Virus removal/inactivation instruments, resins, matrices, and devices

Processes Experience

Our experience spans a broad range of different processes, including:

INACTIVATION

- Heat / Pasteurization
- Low and high pH
- Solvent / Detergent
- Irradiation
- Sterilization
- High-energy light
- Ethanol

REMOVAL

- Column chromatography
- Filtration

CLEANING

- Kinetics of inactivation
- Coupon studies

Process Development Support Through Database Mining

Utilizing over 20 years' experience and over 2,200 studies conducted at WuXi AppTec generating over 20,000 data points, we have assembled a powerful database mining tool to help our clients in their process development efforts. WuXi AppTec can consult on which process steps or process parameters may be ideal or problematic in achieving the desired clearance levels before performing the actual clearance studies. This information could be critical to avoid costly delays, or the inclusion or evaluation of unnecessary process steps.

Search parameters include:

CLEANING SOLUTIONS

- Virus type and percent spike
- Type of cleaning solution/reagent
- Concentration
- Time
- Mechanism of action

CHROMATOGRAPHY STEPS

- Virus type and percent spike
- Matrix
- Conductivity
- pH
- Protein load
- Mechanism of action

NANOFILTRATION STEPS

- Virus type and percent spike
- Nanofilter type
- Flux
- Load volume
- Protein load concentration

Preparation of High-Titer, Highly Purified Virus Stocks

The preparation, purification and use of high-titer viral stocks is one of the most critical aspects in the performance and eventual success of a viral clearance study. WuXi AppTec has conducted extensive research to produce highly purified, high-titer virus stocks for use in viral clearance studies. We have set the standard for how these stocks should be made and the results from our clients' studies demonstrate the success of our research efforts.

We believe our "five-tiered" system of virus stock generation is the best available in the industry for production of highly qualified virus stocks. The five tiers – production of clones, master viral seed bank preparation, purification of virus stock, testing and comprehensive qualification of lots, and issuance of certificate of analysis – are employed in conjunction with three different levels of virus purity and our proprietary purification system.

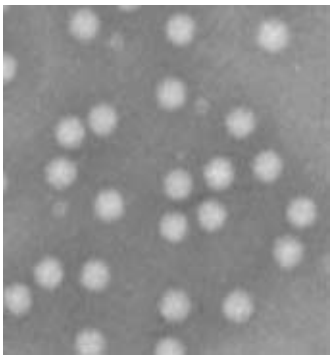
These ultra-purified stocks help ensure the data generated is the most accurate assessment of your processes' ability to clear or inactivate virus. They can also dramatically increase total log reduction values (LRV) for nanofiltration and other steps. The LRV results from utilizing these stocks can often provide the necessary clearance to potentially eliminate low LRV steps, greatly reducing the cost of your viral clearance program and process development efforts.

Other Features	Ultra 1 Purification Grade	Ultra 2 Purification Grade	Ultra 3 Purification Grade
Stock Generation (triple-plaque purification, MVB, WVB, Production Lot)	✓	✓	✓
Certificate of Analysis	✓	✓	✓
Release Criteria	Identity, purity, titer	Identity, purity, titer, residual DNA, total protein	Identity, purity, titer, residual DNA, total protein
Recommended Steps for Evaluation	Removal And Inactivation Steps	Polishing Chromatography, Nanofiltration, and Inactivation Steps	Polishing Chromatography and Nanofiltration Steps
Viruses Available	30 Virus Types	X MuLV, REO *	MVM, PPV *

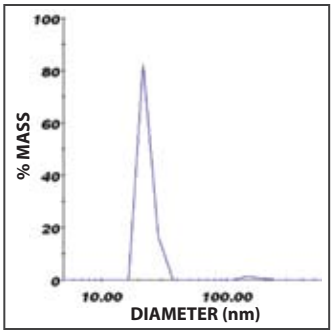
**Other viruses will be available as purification processes are optimized*

Purification Methodology	Ultra 1 Purification Grade	Ultra 2 Purification Grade	Ultra 3 Purification Grade
Serum Free or Reduced Serum	✓	✓	✓
Low & Mid Speed Centrifuged	✓	✓	✓
Ultra-centrifuged (Glycerol Shelf)	✓		✓
Chromatography		✓	✓

ULTRA 3



Ultra 3 (MVM):
Highly purified intact viral particles (TEM)



Ultra 3 purified parvoviruses have primarily monomeric virus particles (dynamic light scattering analyses)

Capacity

To help ensure clients meet critical timelines, we offer the highest capacity in the industry, as demonstrated by:

- 10 BSL-2 and 2 BSL-3 client labs/suites
- 12 AKTA Explorer and AVANT systems
- Suites for Real Time qPCR analyses
- Analytical labs for analysis of process intermediates/parameters
- Project managers dedicated to viral clearance/inactivation studies
- A team of study directors, each with extensive experience in more than 100 clearance studies
- Over 100 lots of virus made and purified per year

Real-Time Quantitative PCR

For processes in which both clearance/removal and inactivation occur, qPCR has become a leading technology in determining clearance and removal, or to complement standard viral titration assays if required. WuXi AppTec has developed over 15 qPCRs assays to common model viruses used in viral clearance studies.

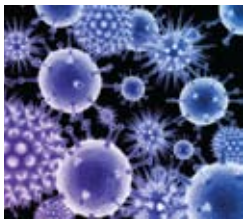
Additional Services

Cleaning validations

Resin cycling studies

Process scale-down validations

Proof of concept (R&D) studies



Viral Clearance Studies

WuXi AppTec is the clear leader in this field with exceptional expertise and more than two decades of experience, offering program features that can dramatically affect your process development efforts and significantly reduce your costs.

EXPERIENCE

- Over 2200 custom viral clearance studies performed for IND, BLA, 501K, Marketing-Approval, and other filings for the US, EU, Japan, Korea, China and more.
- Over 30 human and animal viruses available as high-titer stocks.
- Experience with recombinant proteins, monoclonal antibodies, tissue and plasma products, vaccines, gene therapy vectors, and other product types.
- Testing services conducted based on global regulatory requirements – including FDA, ICH, ISO, CEN, AAMI, HIMA, USP, JMHLW, ANSI, WHO and ASTM – and applicable GLP and GMP guidelines.

PROGRAM FEATURES

- A core team of virology experts and process development scientists – with over 20 years' experience and 2200 studies conducted – to provide assurance that your study will meet technical and regulatory expectations.
- Industry-leading capacity – with 12 viral clearance suites and 12 AKTA Explorer and AVANT systems – to allow unsurpassed scheduling flexibility.
- Large-volume testing to improve log-reduction claims.
- Experienced staff who can perform entire study for you, including scale-down and resin cycling, freeing you of personnel time out of office, travel accommodations, and support your critical scheduling and timing needs.
- Viral clearance database mining to assist you *before* studies begin in determining what process parameters and steps are optimal for viral clearance, potentially mitigating the use of ineffective steps.
- Use of highly purified, high titer stocks that can help reduce overall viral clearance and process development costs by achieving greater viral clearance for steps that demonstrate complete removal or inactivation, such as low PH, solvent/detergent, and other chemical inactivation.
- Regulatory advice and consulting – from executing risk analysis to mining WuXi AppTec's database of previous study results.
- Senior staff study directors and dedicated project managers with experience on hundreds of custom studies yearly.

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Contact WuXi AppTec for your viral clearance studies:

(1) 651-675-2000 / 888-794-0077 • www.wuxiapptec.com • www.virologyexperts.com