YOUR RELIABLE BIOSAFETY PARTNER, WE BRING NEAR-BY SERVICE CLOSER TO YOU

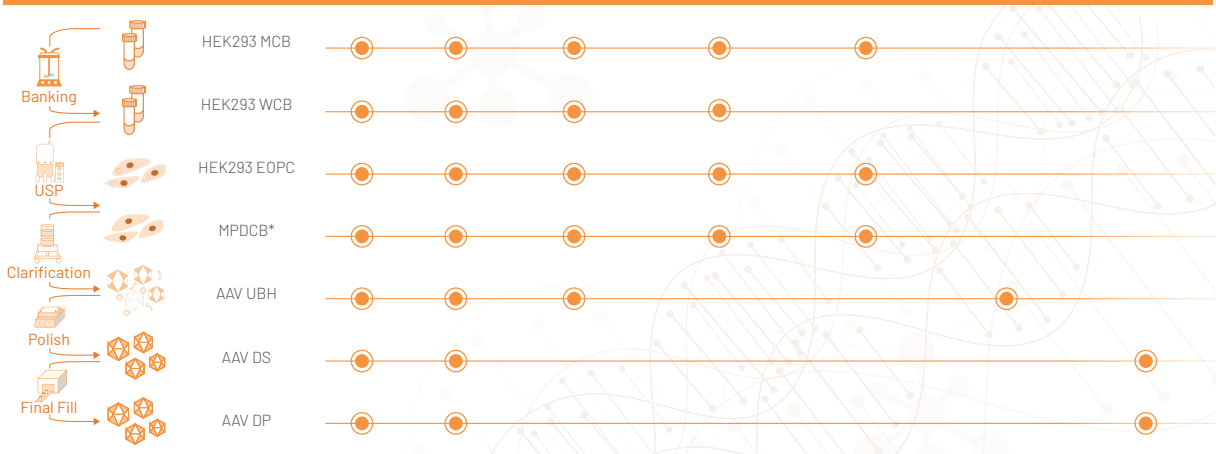
Biosafety Testing for HEK293 Produced rAAV Gene Therapy Products

Gene Therapy involves the introduction of exogenous genes into target cells through viral or non-viral methods to correct, replace, or compensate for diseases caused by abnormal genes, including genetic diseases, malignant tumors, cardiovascular diseases, infectious diseases, etc. To date, dozens of gene therapy products have been approved and marketed worldwide.

Adeno-associated virus (AAV) vectors are considered the most suitable gene delivery tools due to their extremely low immunogenicity, high safety, and long-term expression. As a commonly used rAAV producer cell line, the HEK293 co-transfection system with three plasmid has supported the successful approval of Luxturna and Zolgensma. Analysis of host cells and viral bulk harvest in AAV processing are focusing on gene therapy products biological safety.

BRC Biotechnology (Shanghai) Co., Ltd. is committed to providing professional compliance biosafety testing service, assay development services and testing products for cell & gene therapy, antibodies, vaccines, nucleic acid drugs and other biological products. As your reliable biotech-service partner on the way to success, we are committed to providing world-class the biosafety services for you.

- Safety - Comprehensive Solutions for biosafety testing
- Efficiency – Automatic process empowering testing capabilities
- Compliance - Meet the requirements of different regulatory systems
- Scientific - Rigorous customization solution capability



* Using the same upstream process as that for producing recombinant viruses, but without plasmid transfection.

※ Human-specific high-risk pathogens, as well as potential wild type adenoviruses and/or adeno-associated viruses in HEK293 cells.

§ The residual rcAAV standard is < 1 rcAAV per 1E8 vg.

Reference

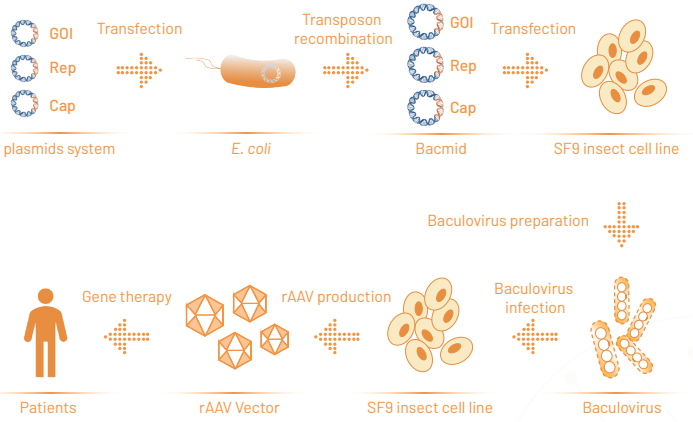
ChP	• 2020 Part Three: Preparation and Quality Control of Animal Cell Substrates for the Production and Testing of Biopharmaceuticals. • 2020 Part Three: General Principles of Gene Therapy for Human Use.
USP	• 2023 〈1046〉 Cell-Based Advanced Therapies and Tissue-Based Products • 2023 〈1047〉 Gene Therapy Products
EP	• 2011 EP 5.2.3 Cell substrates for the production of vaccines for human use • 2011 EP 2.6.16. Tests for extraneous agents in viral vaccines for human use
FDA	• 2010 Guidance for Industry: Characterisation and qualification of cell substrates and other biological materials used in the production of viral vaccines for infectious disease indications.
WHO	• 2010 WHO Recommendations for the evaluation of animal cell cultures as substrates for the manufacture of biological medicinal products and for the characterization of cell banks. TRS 978, Annex 3
ICH	• ICH Q5A, Viral safety evaluation of biotechnology products derived from cell lines of human or animal origin. Insect cells included in ICH's definition of animals. • ICH Q5B, Analysis of expression construct in cell lines for the production of biotechnology / biological products • ICH Q5D, Derivation & characterisation of cell substrates used for the production of biotechnology / biological products. This document covers all cells of metazoan origin.

YOUR RELIABLE BIOSAFETY PARTNER, WE BRING NEAR-BY SERVICE CLOSER TO YOU

Biosafety Testing for Insect Cell Produced rAAV Gene Therapy Products

The baculovirus infected SF9 insect cell packaging system for rAAV production integrates the advantages of efficient gene delivery by baculovirus and high-density suspension culture of insect cells, meeting the commercial demand for large-scale clinical-grade preparation of rAAV. As of November 2022, out of the six AAV gene therapy drugs currently on the market, Glybera, Roctavian, and Hemgenix all use the SF9/Bac baculovirus packaging system.

The SF9/Bac baculovirus packaging system uses the Tn7 transposon system to prepare baculoviruses that individually contain AAV Rep, AAV Cap, and ITR-GOI-ITR genes to infect SF9 cells. This enables efficient assembly of rAAV within SF9 cells, ultimately achieving the goal of large-scale production of AAV.



Technology Roadmap	Test Article	Identity	Microbiology Examination	Adventitious Virus Screen	Retroviruses Detection	Specific Species Viruses Detection※	Replication Competent AAV§	Impurities
Banking	SF9 MCB	●	●	●	●	●		
	SF9 WCB	●	●	●				
USP Trans	Master Viral Seed	●	●	●*	●	●		
	SF9 EOPC	●	●	●	●	●		
Clarification	SF9 CAL	●	●	●	●	●		
Polish	AAV UBH	●	●	●			●	
	AAV DS	●	●					●
Final Fill	AAV DP	●	●					●

* Screening for adventitious virus can be performed using NGS sequencing analysis.

※ Arthropod-specific virus detection.

§ The residual standard for rcAAV is < 1 rcAAV per 1E8 vg.

NGS sequencing analysis

BRC BIOTECHNOLOGY

www.brcbiotech.com

info@brcbiotech.com

Boston · America
625 Mt Auburn Street, Suite 105 Cambridge, MA 02138

Shanghai · China
Building 3, Simbay Park, No.160 Basheng Road, Free-trade Zone

LinkedIn Facebook Youtube