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Best practices in viral vector analytical characterization

Viral vectors are a critical part of the advanced therapies supply chain as they are used to introduce the gene of interest, whether that's into a cell intended for therapeutic gene transfer or for direct viral-mediated gene transfer into the patient. Thus, viral vectors intended for use in advanced therapeutics must meet stringent safety guidelines and require robust and validated characterization analytics.

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Tips for ensuring robust viral vector analytical characterization

- Establish a potency assay early to aid in optimization of the manufacturing process
- Develop fit for purpose methods for product and process characterization
- Ascertain strong reference material (standards and controls)
- Ensure data integrity from the start
- Follow International Council for Harmonization (ICH) guidelines for assay validation

ICH guidelines help define when to validate and what parameters to take into consideration

Types of validations as defined by ICH M10, Bioanalytical Method Validation guidance[1]:

Full validation	Performed when implementing new analytical methods or when major changes occur to an existing method that impact its intended use
Partial validation	Performed when modifying an existing fully validated method
Cross validation	Performed when a comparison of validation parameters is needed. Could be when two or more methods are used within or across studies, or when two or more labs are utilizing the same method.

The objective of bioanalytical method validation is to demonstrate the method is fit for purpose

The following parameters are recommended by ICH M10 when demonstrating a method is fit for purpose:

Selectivity	**Matrix effects**	**Upper and lower limits of quantitation**	**Carry-over**	**Linearity of dilution and parallelism**
Specificity	**Calibration curve**	**Accuracy**	**Precision**	**Stability**

Methods must be established to assess critical quality attributes (CQAs) that impact safety and/or efficacy

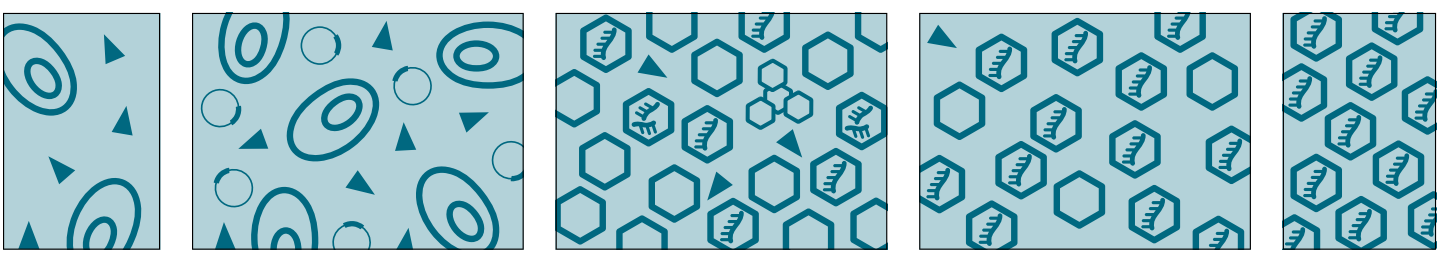
Standard CQAs include identity, strength, potency, purity, and stability. For viral vector manufacturing, there are also specific process, host cell, and viral vector product related impurity considerations.

Viral vector process related impurity considerations	Viral vector host cell related impurity considerations	Viral vector product related impurity considerations			
Cell culture media and additives	Host cell proteins and DNA				
		AAV	**Full capsids (intended product)**	Partially filled capsids	Empty capsids	Aggregates
		LV	**Full vector (intended product)**	Non-functional vectors	Free vector envelopes and components	Vector aggregates

Challenges in viral vector analytical characterization

- **Low throughput and long turnaround time**
- **Sample diversity throughout the manufacturing process**
- **Lack of qualified reference materials**

Cell culture → Transfection → Harvest → Purification → Formulation → Fill/Finish



AAV	Add rep/cap, helper, and transfer plasmids	Separate full capsids from impurities (empty, partially filled, and aggregate capsids)	Change viral particle concentration and buffer	Final vial
LV	Add envelope, packaging, and transfer plasmids	Separate proper envelope vector from impurities (non-functional and vector aggregates, and free envelopes and components)		

Utilizing methods that can distinguish between components in complex samples can help properly characterize your viral vector product and optimize the manufacturing processes.

Robust characterization is critical to ensuring safety and efficacy of viral vector therapies.

Learn how Thermo Fisher Scientific can help you assess CQAs to bring you closer to defining a robust manufacturing and characterization process.

[1] ICH M10 Bioanalytical Method Validation Guidelines

About us

Thermo Fisher Scientific provides industry-leading pharma services solutions for drug development, clinical trial logistics and commercial manufacturing to customers through our Patheon brand. With more than 65 locations around the world, we provide integrated, end-to-end capabilities across all phases of development, including API, biologics, viral vectors, cGMP plasmids, formulation, clinical trials solutions, logistics services and commercial manufacturing and packaging. Built on a reputation for scientific and technical excellence, we provide pharma and biotech companies of all sizes instant access to a global network of facilities and experts across the Americas, Europe, Asia and Australia. We offer integrated drug development and clinical services tailored to fit your drug development journey through our Quick to Care™ program. Our Quick to Clinic™ programs for large and small molecules help you balance speed and risk during early development so you can file your IND quickly and successfully. Digital innovations such as our mysupply Platform and Pharma 4.0 enablement offer real-time data and a streamlined experience. Together with our customers, we're rapidly turning pharmaceutical possibilities into realities.

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