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The National Institute for Innovation in Manufacturing Biopharmaceuticals

Capsid Titer Interlab Study

RFA 2025.03

RFA Release Date: October 21, 2025

Submission Due Date: November 18, 2025

Target Decision Date: December 19, 2025

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1. Executive Summary

The mission of the National Institute for Innovation in Manufacturing Biopharmaceuticals (NIIMBL) is to accelerate biopharmaceutical manufacturing innovation, support the development of standards that enable more efficient and rapid manufacturing capabilities, and educate and train a world-leading biopharmaceutical manufacturing workforce. NIIMBL is pleased to announce this Request for Application (RFA) to participate in an interlab study to evaluate whether utilizing the new USP AAV9 Reference material as a calibrant can improve the accuracy and precision of AAV9 capsid titer measurements from commercial ELISA kits.

For questions, please contact projectcalls@niimbl.org.

Funding Opportunity Title: RFA: Capsid Title Interlab Study VV 2025.03

Responses must be submitted via the NIIMBL Proposal Submission Hub. Submissions received after the deadline (see Table 1), or are otherwise non-compliant with the submission requirements, will not be considered.

The RFA concludes with a decision to fund or not fund applications by the NIIMBL Viral Vector Program Leadership Team. No feedback will be provided to applicants. Awarded projects will be expected to complete contracting within 90 days after formal notification of NIIMBLs intent to fund. NIIMBL reserves the right to rescind offers of funding to awardees.

Table 1. Timeline

EVENT	DATE
Submission Due by 5:00 pm ET	Tuesday, November 18, 2025
Application Review Period:	November 21 – December 19, 2025
Award Decisions Announced	Mid-January 2026
Estimated Project Start Date	April 1, 2026

Total Amount to be Awarded

NIIMBL intends to fund up to (10) ten different study participants under this RFA, with each study participant eligible to receive funding up to $25,000. Cost share requirements are described in the Submission Requirements section.

2. Project Requirements

Background

The National Institute for Innovation in Manufacturing Biopharmaceuticals (NIIMBL) is announcing a funding opportunity to evaluate whether utilizing the new USP AAV9 for Capsid Titer Analytical Reference material as a calibrant can improve the accuracy and precision of AAV9 capsid titer measurements when using different commercial ELISA kits.

Purpose

Recombinant adeno-associated virus (AAV) gene therapies commonly use capsid titer methods to determine dosage and infer purity of a sample when comparing to other methods, such as genome titer. Enzyme-linked immunosorbent assay (ELISA) is the most common technique to measure capsid titer. However, the variability between commercial ELISA kits and calibrants introduces uncertainty in the accuracy and precision of reported capsid titers. This subsequently impacts the ability to compare AAV9 capsid titer values across projects, products, and regulatory submissions.

Specific Area of Interest and Expected Outcomes

This study aims to address this critical gap in the field by evaluating a new AAV9 analytical reference material developed by the United States Pharmacopeia (USP, catalog #1800241), which can be used as an ELISA calibrant. By quantifying test articles relative to this new USP standard, it may be possible to improve the accuracy and precision of AAV9 capsid titer measurements across commercial ELISA kits. If found to be the case, this study has the potential to advance analytical harmonization and support regulatory confidence in gene therapy manufacturing and testing.

Study Goals

- Compare the accuracy and precision of AAV9 capsid titer measurements across multiple commercial ELISA kits when the standard curve is comprised of (1) the USP calibrant vs. (2) the kit-included standard
- Compare intra- and inter-laboratory variability using the USP calibrant vs. existing ELISA kit standards
- Support regulatory alignment and qualification of the USP calibrant for broader industry use

Study Design Overview

For the purpose of this study, “assay run” is defined as the standards and samples analyzed on a single ELISA plate. “Replicate” refers to sample or standard replicates.

Element	Description
Analyte	AAV9 capsids
Assay	AAV9 capsid sandwich ELISA
Calibrants (Standards)	For each assay run (plate), two full standard curves will be prepared following the kit-included instructions and analyzed in triplicate using the following calibrants: • Kit-included ELISA calibrant • AAV9 for Capsid Titer (USP Cat# 1800241)

Test articles (Samples)	For each assay run (plate), two samples will be evaluated as follows: • AAV9 testing material with known approximate titer (note: titer will be assigned via an orthogonal method, e.g. SEC-MALS) AAV9 test articles with known approximate titer Two or three dilutions will be evaluated for each sample, with each dilution evaluated in triplicate on the ELISA plate.
Replicates	For each vendor (ELISA kit): three independent assay runs (plates). Each assay run will include: (1) kit-provided standard curve (in duplicate), (2) standard curve comprised of USP calibrant (in duplicate), (3) two samples with each sample dilution performed in triplicate.
Data Collected	Standard curve parameters, sample OD values, calculated titers, intra- and inter-assay CVs
Participating Labs	Targeting 6–10 labs across industry, academia, and CROs
# ELISA kits	Targeting four commercial kits to be tested by each laboratory, depending on the total number of participants

Study Format and Participant Roles

Participating laboratories will procure the following materials:

- AAV9 ELISA kits from four commercial vendors, including the standard curve material in the kit (see table below)
- Additional calibrant to prepare an extra standard curve:
    1. AAV9 for Capsid Titer (USP Cat# 1800241)
- Two blinded samples:
    1. An AAV9 test article with known approximate titer
    2. AAV9 for Capsid Titer (USP Cat #1800241)

Each laboratory will evaluate <u>each of the commercial ELISA kits</u> as follows:

- Assign 1–2 operators (based on staffing and internal workflow).
- Perform three full assay runs (total of three plates, ideally spread over two or more days per kit), using manufacturer's instructions provided in the kit.
- For each assay run (plate), include the following:

- Kit-provided standard curve in triplicate (prepared following kit instructions)
- Standard curve comprised of USP calibrant in triplicate (prepared following kit instructions)
- Two test articles (samples) with 2-3 dilutions each and triplicate wells for each dilution. (Note: Dilutions should be prepared such that at least one dilution falls within the middle of the standard curve range.)

- For each assay run (plate), quantify the two AAV9 test articles against each of the two standard curves.

Following method completion, participants will submit all data to NIIMBL for analysis:

- Participants will submit the following to the central coordinating team: raw OD values, anonymized operator ID (e.g. A vs. B), date tested, R^2, curve formula, slope, max OD, min OD, and calculated titers.
- Data will be anonymized and blinded before aggregation.
- Statistical analyses will assess:
  - Relative accuracy (comparison to nominal sample titer)
  - Precision of each commercial ELISA kit and across the different kits (%CV)
  - Inter-laboratory agreement (Bland-Altman, ANOVA)

Note: Each laboratory will be given up to 6 months from signing of contact to complete testing and data submission

Data Sharing and Community Benefit

- The overall goal of this study is to improve transparency, comparability, and confidence in AAV analytical methods. While data will be anonymized and blinded before analysis, participating laboratories will be included as co-authors on any results made publicly available. This may be in the form of any of the following:
  - A white paper or peer-reviewed publication
  - Presentations at scientific and regulatory forums (e.g., ASGCT, NIIMBL, USP workshops)
- By participating, labs contribute to the generation of pre-competitive data that will be broadly shared with the gene therapy field and regulators to promote harmonization.

Study Materials

Material	Manufacturer	Catalogue #	Quantity
ELISA kit – A	Progen	PRAAV9	3
ELISA kit – B	ACROBiosystems	AAV-A009H	3
ELISA kit – C	Creative Diagnostics	DEIAAV9	3
ELISA kit – D	Syd Labs (or similar)	EK0400	3
AAV9 for capsid titer	USP	1800241	12-15*
AAV test article #2	(TBD)		

*Suggested for single time use. Could use less vials if doing multiple plates per day.

2. Eligibility Criteria

Membership

Proposers need to be a federal employee or NIIMBL member. Non-NIIMBL organizations should submit a partially executed NIIMBL Membership Agreement by 5:00pm EST two weeks prior to the submission due date. Information on how to join NIIMBL is available at: https://www.niimbl.org/membership/

Cost Share

Proposers must offer and document their cost share commitment consistent with their Membership tier requirements. Project teams should be aware that the institutional cost share requirements for NIIMBL member organizations vary based on institution type (e.g., industry, academic/non-profit organization) and tier level. This RFA does not have a minimum cost share required.

Federal Agency Participation

NIIMBL solicitations are open to federal proposers. NIIMBL welcomes and encourages the participation of Federal employees. Federal employees may suggest a project that NIIMBL should undertake as a community, participate on a project team, or lead a project, as appropriate, within the mission and constraints of their agency. Participation in a NIIMBL project must be compatible with agency missions and any constraints related to accepting resources from NIIMBL. In general, NIIMBL will try to accommodate the unique needs of federal proposers in this process to reduce barriers to participation. Federal employees should review the Guide for Information for Federal Stakeholders.

Human Subjects Activities are not expected and will require prior written approval before work can begin.

Vertebrate Animal Activities are not expected and will require prior written approval before work can begin.

3. Application Instructions

3.1 General Instructions

Submissions

Applications must be submitted via the NIIMBL Proposal Submission Hub and must be received no later than the submission deadline in Table 1. Submissions received after the deadline, or otherwise not compliant with the requirements of this solicitation, will not be considered.

Confidentiality

Teams are expected to mark their submissions as "NIIMBL Confidential," in accordance with the NIIMBL Bylaws, limiting access to NIIMBL members or Federal representatives. The exception is the Proposal Abstract, which will be released to the public if an award is made.

3.2 Application

The proposal narrative must be no more than 4 pages.

Applications will be evaluated by the NLP/Viral Vector Program Leadership Team, composed of subject matter experts from member organizations and federal stakeholders.

The application must address and include the following:

1. Application Narrative must be no more than 4 pages.
2. Abstract (200 words max; not counted towards narrative page count)
3. Executive Summary (up to 1 page; not counted towards narrative page)
4. Required Appendices (not counted towards narrative page count)

Appendix A	Biosketches 2-pages
Appendix C	Project Plan – **see template**
Appendix D	Budget & Justification (.xlsx & .docx – **see templates**)
Appendix F	NA
Appendix G	NA
Appendix H	Project Partner Organization Identification Form – **see template**

Table 2. Summary of Application submission documents.

	Constraints
Abstract	200 words
Application Narrative	Maximum of 4 pages File Type: .pdf only
Required Appendices	No page limits. Adhering to templates provided at: https://www.niimbl.org/projects-programs/viral-vector-capsid-titer-study-rfa2025-03/ File Type: consistent with templates

Abstract

The abstract must include the PI name and organization, and a brief description of the proposal. The abstract will be released to the public if an award is made; therefore, proposers are expected to ensure that it does not contain any confidential or proprietary information.

NOTE: The Abstract should be included in the .pdf file of your proposal documents. You will also be required to copy and paste the Abstract into a text field in the Submission Hub. The names and organizations are not included in the 200-word count.

Executive Summary

Application Narrative: All documents listed above should be included in one .pdf file with the exception of Appendices A, C, and D, which should be uploaded separately in their appropriate file format.

- **Technical Approach**

  A confirming statement that the study procedure as described above is understood and can be followed and completed within the proposed timeframe.

- **Description of Capabilities**

  This RFA seeks to fund single-organization(s). This section should be used to describe the capabilities at your organization that enable the work to be carried out, including personnel, instrumentation, and facilities. Identify the Principal Investigator and any other senior/key personnel that will play a leadership role on the project. Each of these individuals should have a Biosketch (Appendix A). Include considerations for how the team will communicate, maintain timelines, stay within budget, and how decisions will be made.

- **Description of Outputs**

  A confirming statement that the data submission and sharing for community benefit is acceptable. A formalized data sharing agreement will be included in the terms of a funding contract.

Required Submission Appendices

Appendix A: Biosketches

Provide biosketches for the PI and all named senior/key personnel. Biosketches are limited to two pages each.

Appendix C: Project Plan

The project plan should include a Gantt Chart detailing the major tasks, and deliverables for the proposed project. It will visually show how the work will be completed over time, with a minimum of 1-month increments. **The Period of performance is not to exceed 6 months**. The Gantt chart should be submitted as a .pdf, or .xlsx file.

Appendix D: Budget & Justification

The Budget should be broken into requested funding segments that align with the Gnatt Chart in the Project Plan. The budget should include the NIIMBL funding request and cost share commitment and be submitted as an .xls File. The budget justification should be a written narrative explaining in detail the need for the identified cost categories and submitted in a .docx file.

Appendix F: References

Provide a complete list of references cited in the project proposal. If references are not used, indicate N/A.

Appendix G: List of Acronyms

Provide a complete list of acronyms used in the project proposal. If acronyms are not used, indicate N/A.

Appendix H: Subrecipient Commitment Form

The proposing organization must submit either a Subrecipient Commitment Form or a Letter of Intent.

If your organization is a federal agency or is a participant in the Federal Demonstration Partnership (FDP) Clearinghouse, your organization should submit a Letter of Intent.

All other organizations requesting NIIMBL funding and committing cost share are required to complete and submit the Subrecipient Commitment Form.

Large Industry partners who are only providing a leveraged cost share commitment, volunteer participating organizations essential to complete the project or from an end user of the developed technology, and state cost share commitments should complete a Letter of Commitment.

Templates can be found on the NIIMBL website https://www.niimbl.org/projects-programs/viral-vector-capsid-titer-study-rfa2025-03/

4. Application Review and Evaluation

4.1 NIIMBL Review Process

Applications must comply with the requirements outlined in this RFA. All formatting requirements, administrative requirements, terms and conditions, and other requirements will be assessed for completeness.

Automatic rejection will occur if the submission is received after the published deadline or if the proposer did not meet the deadline to submit a membership request.

NIIMBL will review applications to ensure suitability of the work within the project description (see Section 2 of this RFA). Applications will be provided to the NLP/Viral Vector Program Leadership Team for review.

4.2 NIIMBL Acceptance Criteria

NIIMBL Subject Matter Expert Review Panel

Proposals will undergo a merit review by a panel of subject-matter experts, and will be assessed using the following criteria:

1. The proposal's ability to address the defined need outlined in the project description
2. Budget and cost share commitment

Awarded project teams will be expected to complete contracting within 60 days after formal notification of the award. NIIMBL reserves the right to rescind offers of funding to awarded project teams that have not completed contracting within that time frame.

5. Reporting

Project reporting requirements will be outlined in the Subaward contract.

6. Abbreviated List of Acronyms

AAV	Adeno-Associated Virus
Co-PI	Co-Principal Investigator
CQA	Critical Quality Attribute
ELISA	Enzyme-Linked Immunosorbent Assay
FDP	Federal Demonstration Partnership
FFRDC	Federally Funded Research and Development Centers
IP	Intellectual Property
NIIMBL	National Institute for Innovation in Manufacturing Biopharmaceuticals
PI	Principal Investigator
RFA	Request for Application
SEC-MALS	Size-Exclusion Chromatography with Multi-Angle Static Light Scattering
ST	Steering Team
USP	US Pharmacopeia
VVP	Viral Vector Program