



The National Institute for Innovation in Manufacturing Biopharmaceuticals

Project Call 8.1T

Request for Proposals

Concept Papers due: September 30, 2024

Full Proposals due: January 31, 2025

VERSION August 2024

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1. Executive Summary

The mission of NIIMBL (the National Institute for Innovation in Manufacturing Biopharmaceuticals) 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 Proposals (RFP) for Project Call 8.1, with member- driven and industry-led priority topic areas for technical development proposals.

Funding Opportunity Title: Project Call 8.1

Stage 1: The Concept Phase includes the submission of a Concept Paper and a short slide deck. Principal investigator (PI) with accepted concepts will be notified about participating in a virtual summit and will be requested to upload a Showcase Video at that time. No teaming, budget, or cost share information is required at this stage but if information is available for a given Concept, it may be included at the Concept stage. Concepts may only be submitted by NIIMBL members or a Federal employee although non-members may be contemplated as part of the proposed team. Concept submissions must be submitted via the NIIMBL Proposal Submission Hub. Submissions received after the deadline (Table 1), or that are not compliant with this RFP, will not be considered and will be declined without review.

Following submission of Concepts, each submission will be reviewed by NIIMBL, Industry and federal stakeholder subject matter experts to prioritize those Concepts that have the potential for the highest industry impact and likelihood of success. To help facilitate the review and potential teaming at the Full Proposal stage, NIIMBL is requesting Showcase Videos (a short, 90 second maximum, video that summarizes the main points of the proposed project and desired teaming opportunities). For Technical Concepts, the starting Biomanufacturing Readiness Level (BRL) of a given Concept will also be a factor. The Concept Phase (Stage 1) concludes with invitations issued for submission of a Full Proposal (Stage 2). Declination notices will be sent to unsuccessful proposers. Deadlines and key dates are summarized in Table 1.

Stage 2: The Full Proposal Phase includes submission of a 14-page proposal with teaming, detailed budget, cost share, and other requirements listed in this announcement. Full Proposal submissions must be submitted via the NIIMBL Proposal Submission Hub. Submissions received after the deadline (see Table 1), or otherwise non-compliant with the submission requirements, will not be considered.

The Full Proposal Phase concludes with a decision to fund or not fund the proposal by the NIIMBL Governing Committee (GC). Awarded project teams will be expected to complete contracting within 90 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.

Table 1. Summary of Key Dates and Deadlines

EVENT	DATE
Concept Paper Due by 5:00 pm ET	September 30 th , 2024
Virtual Summit	Mid-October, 2024
Invite for Full Proposal	Early-November, 2024
Full Proposal Due by 5:00 pm ET	January 31 st , 2025
Proposal Review	February 2025
Award Decisions Announced	Expected by March 2025

Priority Topic Areas

The priority topic areas are summarized in Section 6.

Total Amount to be Awarded

NIIMBL will make available up to \$4,000,000 to fund both Technology and Workforce Development proposals submitted in response to this Open Project Call. An additional \$1,700,000 is being made available to fund Global Health Fund projects.

2. Project Requirements and Eligibility Criteria

Proposer Eligibility

Stage 1: Concept Phase, only the lead Concept proposer must be an individual from a NIIMBL member organization or a Federal employee.

Stage 2: Full Proposal Phase, the lead project proposer AND all members of the proposed project team must be a NIIMBL member or a Federal employee. To participate on a project proposal team, an organization must be a member or have submitted a partially executed NIIMBL Membership Agreement by **5:00 p.m. Eastern Time at least one week prior to the due date for the Full Proposal (see Table 1)**

Information on how to join NIIMBL is available at: <https://www.niimbl.org/membership/>

Project Constraints

Concepts and Full Proposals must be consistent with NIIMBL Membership Agreements, the NIIMBL Bylaws, and should be labeled as NIIMBL Confidential.

Technology development Concepts and Full Proposals shall be within NIIMBL Biomanufacturing Readiness Level (BRL) 4-7. More information on BRL can be found at: <https://www.niimbl.org/industry-solutions/brls/>



Invited Full Proposals will be accepted with the following constraints:

- A maximum \$500,000 of NIIMBL funding for Technology development proposals
- A minimum of 2 project partners (see *Teaming* section below)
- All project partners must be NIIMBL members before the submission deadline
- A minimum 1:1 (partners: NIIMBL) cost share requirement
 - All committed cost share must be from non-Federal funding sources.
 - Projects with higher cost share ratio (partners: NIIMBL) will be more competitive.
- A maximum of 18-month period of performance
- Technology development proposals will be required to complete a NIIMBL BRL assessment.

This project call solicits proposals for Institute-Wide Projects; however, projects may request to be treated as Partner-Specific Projects¹. License rights to intellectual property developed in Institute-Wide Projects and Partner-Specific Projects are treated differently; therefore, project teams should carefully review Article IV of the NIIMBL Bylaws before requesting that a project be authorized as Partner-Specific. NIIMBL envisions occasions where Partner-Specific projects are applicable to the technology being advanced will be rare. If Project teams plan to request permission to be treated as Partner-Specific, they must make this request in the Proposal Narrative and provide a justification for the request. Such a designation will be reviewed prior to project authorization to ensure it is appropriate for the type of project being proposed. Approval for a project to be designated as Partner-Specific is subject to the special approval of the Governing Committee, which will review the justification closely to determine if a Partner-Specific designation is in line with the intent of the distinction.

Cost Share

There is no requirement to have cost share documented or described at the Concept Phase.

Full Proposals must offer and document the required minimum cash or in-kind cost share commitment in the budget that is submitted as part of the Full Proposal. Cost share must be consistent with requirements in the NIIMBL Membership Agreement. 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.

¹ Institute-wide Projects address broad challenges faced by the biomanufacturing industry at large, with the goal of developing solutions that will benefit the overwhelming majority of manufacturers. Partner-specific Projects address the needs of more narrow sectors of the biopharmaceutical industry and are more limited in participation and IP than Institute-Wide Projects, performed pursuant to a Project Award Agreement. See Article IV of the NIIMBL Bylaws for more information related to intellectual property rights.

Due to these different cost share obligations, project teams may allocate cost share



commitments amongst team members however necessary to meet the minimum overall project cost share. For example, not every team member is required to commit cost share, and some team members may exceed the ratio required by their Membership Agreement. However, the project team collectively must still meet the requirement, and each project team member must individually meet their requirements per their Membership Agreement, as applicable.

For Delaware based organizations requesting state of Delaware cost share support, additional review and approval is required. Project proposal teams should include confirmation of the support (Appendix I).

Delaware: Contact Marta Rosario, (martar@udel.edu) **by 5:00 p.m. Eastern Time two weeks before the full proposal due date (see Table 1)** to request a State of Delaware cost share commitment. The request should include a 1-paragraph description of the project, title, partners, and budget narrative.

Teaming

There is no requirement to have all partners identified during the Concept Phase. If partners have been identified, they should be noted in the Concept Paper and slide deck.

Full Proposals must have at least two distinct member organizations participating on the project. Each project proposal team shall have a designated lead partner that coordinates the activities of all partners on the project team. Teams that are led by industry members are strongly encouraged.

NIIMBL expects inclusion of Tier 3 industry members for Technology development projects. Project teams without one or more Tier 3 industry members must complete a justification form (Appendix H).

Note: When appropriate, project proposal teams may seek collaboration with Federal Organizations, National Laboratories, or Federally Funded Research and Development Centers (FFRDCs) within the limits of their mission, rules, and Federal approvals. In accordance with regulations, Federal entities are not permitted to commit cost share towards NIIMBL projects to meet the team obligation.

Federal Agency Participation

NIIMBL Project Calls are open to Federal proposers. NIIMBL welcomes and encourages the participation of Federal employees in the project call process, both during the Concept Phase and the Full Proposal Phase. 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. Federal employees may determine if participation in specific NIIMBL projects would be beneficial. Participation in this Project Call process and any resulting projects 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

If proposing activities with human subjects, all activities involving human subjects must satisfy the requirements of the Common Rule for the Protection of Human Subjects, as provided for by the Department of Health and Human Services in 45 C.F.R. Part 46 and codified by the Department of Commerce in 15 C.F.R. Part 27. The Common Rule, and the institutional policies that enforce its requirements in activities involving human subjects, exist to ensure adequate protection of human subjects. Additional guidance related to activities involving human subjects can be found in the [Human Subjects Research Guidance Document](#).

Vertebrate Animal Activities

If proposing activities with vertebrate animals, all activities must comply with the Laboratory Animal Welfare Act of 1966 (as implemented in 9 C.F.R. Parts 1, 2 and 3), and all other applicable statutes pertaining to the care, handling, and treatment of warm-blooded animals held for research, teaching, or other activities. Additional guidance related to activities involving vertebrate animals is available in [Activities Involving Vertebrate Animals Guidance Document](#).

3. Proposal Instructions

3.1 General Instructions

Submissions

Stage 1: Concept submissions must be submitted via the NIIMBL Proposal Submission Hub. All submissions must be received no later than the deadline in Table 1. Submissions received after the deadline, or otherwise not compliant with the requirements of the Concept phase, will not be considered (see below for full requirements). PI's with accepted concepts will be notified about participating in a virtual summit and will be requested to upload a Showcase Video at that time.

Stage 2: Full Proposal submissions must be submitted via the NIIMBL Proposal Submission Hub. Proposals must be received no later than the deadline in Table 1. Submissions received after the deadline, or otherwise not compliant with the requirements of the full proposal phase, will not be considered (see below for full requirements).

Confidentiality

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

3.2 Stage 1: Concept Phase

NIIMBL will facilitate the review and prioritization of the Concept Papers, Slide Deck, and Showcase Videos by subject matter experts from industry members and federal stakeholders, as noted in Table 1. The feedback will identify the Concepts that are best aligned with industry needs and priorities and will inform the selection of invitations to submit a Full Proposal in Stage 2 of the process.

Applicants are strongly encouraged to submit a 90sec video that will be shared with SME reviewers to complement their application. See guidance documents on RFP website.

To be considered during the Concept Phase, proposers must submit their Concept Paper, which must be single-spaced, 1-inch margins, 11-point Arial font (or larger equivalent font), and a maximum of 4 pages (not including references); along with a short PowerPoint slide deck (maximum 5 slides), that adheres to the template provided for this project call at:

<https://www.niimbl.org/projects-programs/project-call-8-1/>. The Concept Paper, and Concept Slide Deck must be submitted via the NIIMBL Proposal Submission Hub by the deadline in Table 1.

Submitters invited to the virtual summit will be provided with further instructions for attendance.

For Technology development Concepts, the Concept BRL Appendix must also be submitted via the Submission Hub by the same deadline. There is no page limit for the Concept BRL Appendix.

Submitted concepts that do not adhere to the formatting and length limits will be considered non-compliant and will not be considered for further review.

The Concept Paper must include:

- Submitter name and organization
- Concept title
- Topic area to be addressed
- Identified project team partners and/or desired project team partners and expertise (if known)
- Background and significance of the problem to be solved
- Current state of the art; short summary of existing solutions to solve the problem
- Description of the proposed concept
- Value proposition to project partners, NIIMBL, the NIIMBL community, and/or the United States biopharmaceutical manufacturing industry. Considerations include: return on investment, time to impact in the industry, contribution to enhanced diversity within the ecosystem
- For technology development concepts: BRL justification of the proposed concept and planned BRL transition from at least BRL 4 to a higher BRL; this should be addressed in the Concept Paper, Slide Deck, and the Concept BRL Appendix (template available at: <https://www.niimbl.org/projects-programs/project-call-8-1/>.)

Table 2. Summary of Concept submission documents. Submission deadlines are listed in Table 1.

	Constraints
Concept Paper	Single-spaced 1-inch margins 11-point Arial font (or equivalent) Maximum of 4 pages File Type: .pdf only
Concept Slides	Maximum of 5 slides, adhering to template provided at: https://www.niimbl.org/projects-programs/project-call-8-1/ Standard size (4:3) File Type: .ppt or .pptx only
Concept BRL Appendix (if applicable)	No page limits adhering to template provided at: https://www.niimbl.org/projects-programs/project-call-8-1/ File Type: .doc or .docx
Video	90 seconds max 500 MB max Preferred format: MP4

3.3 Stage 2: Full Proposal

The proposal narrative must be no more than 14 pages single-spaced, 1-inch margins, 11-point Arial font (or larger equivalent font). When properly labelled, the full proposal is NIIMBL confidential except for the abstract, which will be released to the public if an award is made.

The full proposal must address and include the following:

1. Abstract (200 words max; not counted towards the page count)
2. Executive Summary (up to 1 page; not counted towards the page count)
3. Proposal Narrative (up to 14 pages)
4. Required Proposal Appendices (not counted towards the page count)

Appendix A	Biosketches
Appendix B	Quad Chart (.ppt or .pptx file – see template)
Appendix C	Project Plan (includes Work Breakdown Structure, Responsibilities Assignment Matrix, and Gantt Chart) (.doc file – see template)
Appendix D	Individual Organization Budgets (.xls file – see template)
Appendix E	BRL Evaluation (additional information will be provided to the invited Full Proposal teams upon invitation)

5. Additional Proposal Appendices (not counted towards the page count)

Appendix F	References
Appendix G	List of Acronyms
Appendix H	Tier 3 industry member partner exemption request
Appendix I	Project Partner Organization Identification Form

All documents listed above should be included in one .pdf file with the exception of Appendices B, C, D, and E, which should be uploaded separately in their appropriate file format. A proposal completion checklist can be found at: <https://www.niimbl.org/projects-programs/project-call-8-1/>.

Project Partner Organization Identification Form

Each unique project organization on the project proposal team 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 2 CFR 200 cost share are required to complete and submit the Subrecipient Commitment Form. Templates can be found on the Project Call website.

Industry partners who are only providing a leveraged cost share commitment, or volunteer participating organizations essential to completing the project should complete a Letter of Commitment documenting their desire to participate and describe the resources they will provide in support of the project.

Abstract

The abstract includes the names and information of the lead organization, each partner organization, the PI, all co-PIs, and a brief description of the proposal. This description is limited to 200 words. It will be released to the public if an award is made; therefore, teams are expected to ensure that it does not contain any confidential or proprietary information.

NOTE: The Abstract should be included in the pdf 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

Summarize the proposed work including the technology development objectives and how they are consistent with the Project Call topic area and NIIMBL goals, initial and anticipated final BRL level, and the projected impact of the project. The Executive Summary is limited to one page.

Proposal Narrative

The proposal narrative must include all the sections (1 to 4) described below (not including Appendix F).

1. Background and Significance

Technology Development proposals: Identify the project call Priority Topic area being addressed. Describe the specific problem or current state of the art within the context of the relevant Priority Topic area of this project call. Summarize prior work done in the area, preliminary results, and the starting and expected ending BRL of the work being proposed. Describe how this proposal is an improvement over the existing solutions or state-of-the-art and how the proposed project will uniquely contribute to solving the above-mentioned problem.

2. Project Description

Describe the project segments, tasks, deliverables, milestones, and go/no-go decision points, to include potential Material Transfer Agreement (MTA), and Institutional Review Board (IRB) reviews. Describe the success criteria / evaluation approach for the project, including metrics for measuring project success. Deliverables must be specific and quantitative.

NOTE: Appendix C the Project Plan must cross reference the page number(s) in the narrative where additional details can be found. Appendix C must contain a Responsibility Assignment Matrix (RAM) that will describe the project segments, tasks, deliverables, milestones, and go/no-go decision points, to include potential MTAs, and IRB reviews. Describe the success criteria / evaluation approach for the project, including metrics for measuring project success. Deliverables must be specific and quantitative. Describe how the responsibilities for the work will be shared and a Gantt Chart that will show how the work will be performed over time. Appendix C does not count towards the total page count.

3. Value Proposition

Summarize the impact of the proposed project on the overall goals and objectives of NIIMBL and describe the overall value proposition. This should be from the perspective of NIIMBL, as well as the broader NIIMBL community and/or the United States biopharmaceutical manufacturing industry. Show how the project will advance the BRL of the technology by addressing the questionnaire for exit from the current BRL. Examples of impact include technical impact on productivity, quality, efficiency, energy usage, efficacy, potency, safety, and/or any other important factors identified in the key areas below (see Section 6). Economic impact in this sector might include factors such as scalability of technical projects, the future of biomanufacturing, and/or estimated

economic impact on a company or on the industry broadly, or any other relevant measure. Describe how the project enhances diversity (e.g., socioeconomic, geographic, organizational/institutional, academic/professional backgrounds) within the NIIMBL member community and/or the broader United States biopharmaceutical manufacturing ecosystem. Measurable or quantifiable improvements are strongly encouraged.

4. Description of Team

Identify the Principal Investigator (PI) from the lead organization for the project proposal team, the co-PIs from other partner organizations, and other senior/key personnel. In addition, each project team must identify a Project Manager to manage and oversee the project execution. The Project Manager should not be the PI for the project. Describe the project management approaches to ensure synergistic work across project team members, particularly any handoff of work between organizations. Include how the team will ensure timelines, budget and risk will be actively managed and decisions will be made.

NOTE: Additional senior/key personnel (those team members who are not identified as the PI or co-PIs) may include staff whose participation and/or leadership is critical for the success of the project. Postdoctoral or graduate students or laboratory technicians should not be considered senior/key personnel. For all identified team members, include their responsibilities and roles in the project.

Required Proposal Appendices

Appendix A: Biosketches

Provide biosketches for the PI, all co-PIs, and Project Manager only. Biosketches are

Appendix B: Quad Chart

Complete a quad chart providing an overview of the proposal's methodology and approach, highlights from the work breakdown structure, the impact, team composition, and the total team budget. The quad chart is limited to one page and must be submitted as a .ppt or .pptx file. The NIIMBL template is available at: <https://www.niimbl.org/projects-programs/project-call-8-1/>.

Appendix C: Project Plan - Work Breakdown Structure, Responsibilities Assignment Matrix, and Gantt Chart

The Project Plan for the proposed project forms the foundation of the proposed project plan. Align the Project Plan with the Responsibility Assignment Matrix (RAM) to describe how responsibility will be shared across the identified Project Plan elements.



The Gantt chart will visually show how the work will be completed over time. One Project Plan is required for each project proposal team and must include all proposed work. The Project Plan must be submitted as a .doc or .docx file. A template is available for download at: <https://www.niimbl.org/projects-programs/project-call-8-1/>.

Appendix D: **Individual Organization Budget/Cost Justification**

Provide separate budget tables (.xlsx) and cost justifications (.docx) for the lead organization and each of the partner organizations requesting funding and/or committing 2 CFR 200 cost share. Leveraged cost share commitments have a separate commitment form and do not require a budget table. Budgets are to be organized by Project Plan Level 2 Segments. The budget template allows for 5 Project Plan Level 2 Segments. Any project proposal team with more than 5 Project Plan Level 2 Segments is asked to email projectcalls@niimbl.org for further direction on how to complete the budget forms. The budget template and separate cost justification templates are available for download at: <https://www.niimbl.org/projects-programs/project-call-8-1/>.

Project teams are encouraged to budget for travel to present at the NIIMBL National Meeting, which occurs in the summer in Washington, D.C.

Appendix E: **BRL Evaluation**

A detailed BRL assessment (insert link) will be required for all teams that are invited to Full Proposals when invitations are made and there will be special attention paid to technical readiness. More information will be made available at that time via the RFP website: <https://www.niimbl.org/projects-programs/project-call-8-1/>.

Additional Proposal Appendices

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: **Tier 3 industry member partner exemption request**

If a Tier 3 Industry Member is not a proposed project partner, then a required explanation must be submitted with the full proposal. The exemption request contains two components: 1. How do you know that there is no Tier 3 industry member

available for this project? 2. The basis upon which it was determined to be fair and reasonable not to include a Tier 3 industry member. If a Tier 3 industry member is part of the project team, this appendix is N/A. A template is available for download at: <https://www.niimbl.org/projects-programs/project-call-8-1/>.

Appendix I: **Project Partner Organization Identification Form**

Each unique project organization on the project proposal team must submit either a Subrecipient Commitment Form or a Letter of Intent. Templates are available for download at: <https://www.niimbl.org/projects-programs/project-call-8-1/>. Include Letters of Commitment from (a) volunteer participating organizations essential to complete the project or from an end user of the developed technology; (b) large industry members who are only committing leveraged cost share; (c) state cost share commitments.

4. Proposal Review and Evaluation

4.1 Stage 1: Concept Evaluation Criteria

NIIMBL Acceptance Criteria

Concept Papers, Slide Decks, and Showcase Videos must comply with requirements outlined in this RFP. Automatic rejection will occur if the submission is received after the published deadline or from a non-NIIMBL member.

Concept Paper, Concept Slide Deck and Showcase Video Review

NIIMBL will review submitted Concepts to ensure alignment with the NIIMBL mission (see Section 1 of this RFP), suitability of work within the Topic areas (see Section 6 of this RFP), and also the BRL 4-7 space for Technology Development Concepts.

NIIMBL industry members and Federal stakeholders will review concepts and provide feedback to NIIMBL that will be used to prioritize a subset of Concepts for invitation to Full Proposals.

The Concept Phase evaluation criteria for reviewers are:

1. The Concept's ability to address the topic's problem statement and a relevant industrial need.
2. The Concept's demonstration of awareness of existing solutions.
3. The Concept's ability to provide a clear value proposition for the project team, the broader NIIMBL community, and/or the biopharmaceutical manufacturing industry.

4.2 Stage 2: Full Proposal Evaluation Criteria

NIIMBL Acceptance Criteria

Full Proposals must comply with the requirements outlined in this RFP. Proposals will be assessed to ensure the budget/cost share commitment is appropriate and reasonable for the proposed work. All administrative requirements, terms and conditions, and other requirements will be assessed. NIIMBL also reserves the right to request information regarding senior/key personnel's current and pending support after the submission of the full proposal. By requesting this information, NIIMBL will be able to better assess the capability of the senior/key personnel to conduct the proposed scope of work.

Automatic rejection will occur if (a) the submission is received after the published deadline, (b) the project team includes only a single member organization; (c) all budget parameters are not met; (d) any member of the team is not a NIIMBL member or Federal Employee.

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:

Impact – 40%

- The proposal's ability to provide a solution to an industrial need.
- The proposed solution's difference than or complementarity to existing solutions or related initiatives.
- The speed with which the benefits of the project be realized.
- The proposal's ability to provide a clear value proposition for the project team, the broader NIIMBL community, and/or the biopharmaceutical manufacturing industry.

Technical Assessment – 60%

- The merit of the technical approach.
- Whether the project deliverables and timelines are realistic.
- The project's clarity of criteria for success.
- The team's inclusion of the needed technical expertise, including project management.

NIIMBL Technical Activities Committee Review of Technology Development Proposals

The NIIMBL Technical Activities Committee will perform an impact review using the following criteria:

- The proposal's ability to provide a solution to an industrial need.
- Whether the technical approach and project plan are likely to result in success.
- The proposal's ability to provide a benefit to NIIMBL members.
- Whether the project complements the existing NIIMBL technology portfolio.



NIIMBL Governing Committee

The NIIMBL Governing Committee will take into account the total Project Call funding that is available and perform a strategic review of the proposals. The GC will consider the following:

- Benefit to NIIMBL members
- NIIMBL sustainability
- Complementarity to existing NIIMBL project portfolio
- Cost and scope alignment with proposed benefits
- Cost share commitment
- Industry involvement
- For Technology development Proposals: starting BRL and expected progression of BRL.
- Increased geographic, organizational/institutional, academic/professional diversity within the NIIMBL member community and/or the broader United States biopharmaceutical manufacturing ecosystem

5. Reporting

Project reporting requirements will be outlined in the Project Award Agreement.

6. Project Call Topics

The narratives for each of the project topic areas below are not meant to be exhaustive. All approaches and concepts consistent with the overall goals described in the project topic areas will be considered. As the industry matures and deals with a diversity of products there is a continued need for improved platforms and better analytical technologies. These needs include novel process analytical technologies – particularly those that are product agnostic, flexible manufacturing platforms, and approaches that support enhanced process reliability. NIIMBL seeks proposal ideas aligned with these needs as described in the sections below.

6.1 Process Analytical Technology (PAT) and Control for Biopharmaceutical Manufacturing

Novel process analytical technologies (PAT) are essential to provide biopharmaceutical manufacturers with timely and accurate measurements of critical process parameters, quality attributes, and impurities. Proposals should focus on the application and timescales of information to maximize impact. Examples include but are not limited to:

1. In-line Monitoring and Multivariate Analysis (MVA):

- Technologies enabling real-time (in-line or at-line) monitoring of critical quality attributes (CQA) with a response time commensurate with what is being controlled and which may be combined with MVA deconvolution methods which

leverage libraries which can be shared to facilitate feedback/feedforward control methods.

2. **Real-time Analytical Technologies:**

- Tools for real-time measurement of protein, viral vector, or monoclonal antibody (mAb) glycosylation in bioreactors, integrating with process parameter data for adaptive control, enhancing product quality (CQAs) and yield by at least 20%.

3. **Advanced Sensors:**

Miniaturized Sensors: Development of sensors designed to operate within significantly smaller experimental setups (such as milliliters of culture volume rather than liters of culture volume, and/or utilizing smaller reaction surfaces, and/or requiring fewer materials or sample volumes). These sensors should be capable of delivering high levels of accuracy and precision in measurement, essential for the early phases of process development where rapid testing and cost-effective iteration are critical. The goal is to enable precise quantification of improvements in percentage terms, facilitating effective scaling and optimization from lab to production environments.

- **Single-Use, Robust Sensors:** Sensors compatible with gamma-irradiated systems, eliminating the need for calibration, and capable of measuring pH, dissolved oxygen, CO₂, and other critical parameters with accuracy and precision metrics and basis of any relative percent improvement.

By targeting specific improvements over current technology, funded projects will significantly enhance the efficiency, control, and quality of biopharmaceutical manufacturing processes. While a given project may not address in all of these in the given project period, successful proposals should provide a justification for which they are addressing and briefly provide a vision for how to address the other aspects in longer-term work. There is a particular interest in technologies that can be useful to address issues relevant to two or more modalities (i.e. modality-agnostic PAT).

6.2 **Manufacturing Platforms for Biopharmaceutical Products**

Manufacturers are focused on developing state-of-the-art custom and flexible bioreactors and scale-down models for biopharmaceutical manufacturing needs. This includes the design of scaffolds and bioreactors that: enhance in-process measurements and controls; substantially reduce cost of goods for manufacturing; are product-agnostic flexible manufacturing solutions; and provides lower carbon footprint. Examples include but are not limited to:

1. **Robust Analytical Tools:**

- Advanced analytics for full/empty capsid characterization, viral vector titers, genome copy number, and cell-based potency assays. These technologies must justify improvements relative to existing techniques based on, e.g., CQAs, material needs, throughput, etc.

- Implementation of multi-attribute methods, not necessarily limited to mass-spectrometry based methods, assessing quality attributes, reducing material requirements by 50% compared to current methods.
- Methods assessing multiple quality attributes simultaneously, reducing material requirements by at least 50%.

2. Expression Systems for Viral Vectors:

- Scale-up of expression systems for viral vectors to lower costs by at least 30% and increase yields by at least 50%.

3. Solid-phase Growth Factor Delivery Vehicles:

- Bioreactor-integrated delivery systems provide controlled, prolonged exposure to growth factors, reducing overall costs and enhancing cell growth efficiency.

4. Automated RNA and DNA Extraction Devices:

- Devices capable of online nucleic acid measurements to monitor and control transfection in bioreactors, with an operational efficiency of >95%.

5. Custom Bioreactors:

- Bioreactors with low shear stress, high mass transfer capabilities, and precise pH and O₂ control (as justified compared to current state of the art technology used for T-cell production). Proposals to include accuracy and precision metrics and basis of any relative percent improvement.
- Closed-loop control systems and integrated online sensors for real-time metabolite measurement and cell characterization.
- Integrated imaging capabilities to monitor cell growth in real-time, ensuring optimal culture conditions.

6. Efficient Cell Washing and Concentration Technologies:

- Technologies enabling high cell density operations (15-30 x 10⁶ cells/mL) and effective removal of residuals, achieving >3 logs removal efficiency.

These advancements aim to significantly improve the efficiency, control, and cost-effectiveness of biopharmaceutical manufacturing, ultimately enhancing product quality and scalability

7. Abbreviated List of Acronyms

1. BRL: NIIMBL Biomanufacturing Readiness Level
2. Co-PI: Co-Principal Investigator
3. FDP: Federal Demonstration Partnership
4. FFRDC: Federally Funded Research and Development Centers
5. GC: Governing Committee
6. IP: Intellectual Property
7. IRB: Institutional Review Board (for Human Subjects Research)
8. MTA: Material Transfer Agreement
9. NIIMBL: National Institute for Innovation in Manufacturing Biopharmaceuticals
10. PC8.1: Project Call 8.1
11. PI: Principal Investigator
12. RAM: Responsibility Assignment Matrix
13. RFP: Request for Proposals
14. PAT - Process Analytical Technology
15. CQA - Critical Quality Attributes
16. MVA - Multivariate Analysis
17. mAb - Monoclonal Antibody
18. T-cells - T Lymphocytes (a type of white blood cell)
19. RNA - Ribonucleic Acid
20. DNA - Deoxyribonucleic Acid