The National Institute for Innovation in Manufacturing Biopharmaceuticals

Quick Start Project
Request for Proposals

UPDATED: July 13, 2017

Proposals due: August 11, 2017

Please note: The original Request for Proposals was released on June 30, 2017. It was updated on July 13, 2017. This version (v071317) includes the following clarifications:

It is a requirement that at least 1 SME participate on project teams if the proposal requests more than $100,000 per year of NIIMBL funds AND the proposal is a Technology Project or a combined Technology and Workforce Project. Details can be found in section 4 on page 9.

No human or animal studies may be proposed as part of a response to this QSP call. Additional detail has been added in Section 5 of this RFP.

This document details the Quick Start Project (QSP) call issued by the National Institute for Innovation in Manufacturing Biopharmaceuticals (NIIMBL). **This QSP call requests proposals that address technology, workforce, and/or regulatory science issues in biomanufacturing, or projects that integrate two or more of these topics.** This QSP call serves to *accelerate the project launch process and return on investment* for stakeholders during the NIIMBL start-up phase. The guidelines, eligibility, limitations, availability, and public nature of this document will differ from future Project Calls. QSPs will help demonstrate and test the project call and launch process to prepare for the first Project Call. NIIMBL's first full Project Call is expected in Fall 2017.

NIIMBL

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1. About NIIMBL and the QSP Call

NIIMBL's mission 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.

As a member of the Manufacturing USA network, NIIMBL's Technology Development Projects, including those that will be launched under this QSP call, will be in the manufacturing readiness levels (MRL) 4-7:[1]

MRL 4: Capability to produce the technology in a laboratory environment

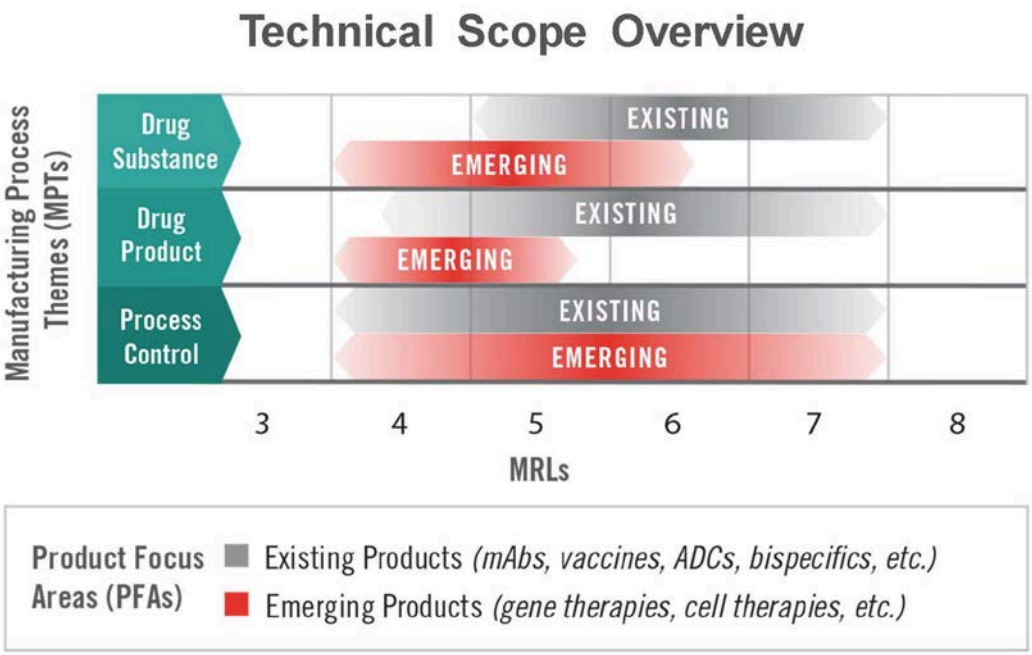
MRL 5: Capability to produce prototype components in a production relevant environment

MRL 6: Capability to produce a prototype system or subsystem in a production relevant environment

MRL 7: Capability to produce systems, subsystems, or components in a production representative environment

NIIMBL's technical space includes existing biopharmaceutical products (e.g. proteins, antibodies, vaccines, blood products, bi-specifics) and emerging biopharmaceutical products (e.g. gene therapies, cell therapies). The NIIMBL technical space addresses needs for production of drug substance, drug product, and process and product control, for both existing and emerging products.

[1] "Manufacturing Readiness Level (MRL) Deskbook." Version 2.0 OSD Manufacturing Technology Program, May 2011. 2-2 –2-4 & Appendix A. *OSD Manufacturing Technology Program*. http://www.dodmrl.com/MRL_Deskbook_V2.pdf



Successful QSP proposals are expected to have some (or all) of the following characteristics:

1. Address an industry-wide technical challenge, advance or create a resource for workforce training, and/or address a pressing regulatory science issue
2. Propose project teams that demonstrate the capability and preparedness to be agile in project launch
3. Demonstrate a high likelihood of success in the proposed period of performance based on the nature of the project, and the expertise and resources available
4. Articulate clear goals and implementation strategies, including realistic and measurable deliverables and milestones
5. Demonstrate opportunity for a quick return on investment for NIIMBL members, particularly industry members, for greatest impact
6. Commit a minimum 1:1 cost share, thus providing a mechanism to help project participants meet cost share obligations

2. Areas of Interest

Only NIIMBL Institute-Wide projects will be permitted.[2] No Partner-Specific projects will be considered as part of this QSP call. Such projects will be invited during NIIMBL's first full Project Call expected in Fall 2017. No human or animal studies may be proposed as part of a response to this QSP call. Such projects may be invited during NIIMBL's first full Project Call in Fall 2017. Proposal teams must identify their project as a Technology Development Project, a Workforce Development Project, or both, on the QSP Cover Sheet. Proposal teams must also identify their project as an existing product, emerging product, or both, on the QSP Cover Sheet.[3]

This QSP call solicits proposals in any area of biopharmaceutical manufacturing that fulfills the NIIMBL mission. To facilitate engagement, NIIMBL has conducted numerous surveys of stakeholder groups over the past 12 months and has identified some topics that appear to be of broad interest to the community. The methodology used in these surveys, the complete survey results, and executive summaries of both technology and workforce development surveys can be found in the NIIMBL website (http://www.niimbl.org/techNeeds.php and http://www.niimbl.org/eduWorkforce.php). This information is provided only to offer examples of interest areas. Proposals are not limited by the survey information collected and may be submitted on any topic that addresses the NIIMBL mission.

Example Technology/Regulatory Science Development Areas

Product Types:

Antibodies, proteins, antibody-drug conjugates (ADCs), bi-specific antibodies, vaccines, cell therapies, gene therapies, and oligonucleotides.

Topics of interest:

1. Cell line development, cell line engineering

   Increased productivity; alternative cell lines or platforms; cell line robustness

2. Analytical methods / process control

[2] Institute-Wide projects are defined in the NIIMBL Bylaws: "broadly inclusive research and development projects offered, funded all or in-part by NIIMBL, that address broad challenges faced by the biomanufacturing industry at large, with the goal of developing solutions that will benefit the overwhelming majority of manufacturers."

[3] As defined in the NIIMBL Bylaws: "Emerging Products" are currently manufactured at clinical trial-scale only, and include cell therapies and gene therapies. "Existing Products" are commercially manufactured today and include therapeutic proteins, mAbs, vaccines, blood factors and components, and enzymes that are widely used to treat a variety of diseases.

Real time or rapid methods, and in-line measurement methods; small volume and non-destructive methods for drug substance or drug product; predictive models and control algorithms; novel in-line and on-line sensors; rapid adventitious agent / bioburden testing; automation for cell testing and cell banking; extended characterization for excipient and raw material control and standardization; in vitro assays for clearance and biodistribution; device and container closure functionality measurements; industry wide automation and control platforms including mathematical methods, software, and analytics

3. Process development

   Process integration and intensification, including continuous and 'connected' processes; large-scale frozen bulk storage methods; novel and optimized unit operations; improved scale-up and scale-down approaches; high-throughput process design and development platforms; mathematical models for manufacturing-scale unit operations; mobile, autonomous clean rooms; novel single-use disposable systems; novel automation, data acquisition and data handling approaches; small volume drug product processes; personalized medicine production

4. Reference standards / regulatory science

   Acceptable limits for impurities and particles; science-based compliance standards, reference standards for testing process or product, including CHO-based mAb, excipients, and surfactants; cell-based standards; rapid surrogate assays; standardization of interfaces and connectors for single-use equipment; harmonization approaches for standards; reducing risk in regulatory evaluation of innovations for continuous and connected processes, combination products, and aspects of 'clonality'; multi-attribute methods; standardization of data handling / data exchange systems for automation and control; standardized extractables, leachables, and particle testing

5. Supply chain management / IT solutions

   Rapid raw materials testing and understanding; improved methods to determine shelf-life and stability of intermediates; tracking methods for cell and gene therapy products; rapid pandemic response; standardized software for – 'omics' data; cross-company knowledge pooling tools that support industry-wide interests and allow data analytical and support regulatory filings.

Example Education / Workforce Development Areas

There are several cross-cutting themes of interest:

1. On-site training modules
2. Virtual or online training modules, alone or in conjunction with hands-on training
3. Curriculum development for rapid retraining
4. Student training programs and internships in biomanufacturing and undergraduate capstone experiences
5. Hands-on capabilities in analytical testing, drug substance and drug product manufacturing
6. Cleanroom training
7. Coordinated linkages between universities and community colleges to support articulation and stackable credentials
8. Workforce resource mapping and evaluation and supply/demand analyses
9. Evaluation of effectiveness of a diversity of training programs and identifying best practices and designs

New training approaches to address the following needs for technicians, operators as well as professional scientists and engineers (students and incumbent workers) such as:

1. Training in GMP and working in a regulated environment
2. Training in risk analysis
3. Emerging therapies (e.g. cell or gene therapy)
4. Training in regulatory affairs
5. Advanced manufacturing technologies (e.g. continuous, single-use, automation)
6. Validation
7. New analytical technologies and control strategies
8. Leadership / management skills

Workforce Projects that meet the definition of human subjects research as found in 45 CFR Part 46 are not permitted. This limitation includes exempt studies. If you have questions about your project, please seek guidance from your local IRB and also contact qsp@niimbl.org.

3. Deadlines

August 4, 2017 – Notice of Intent due by 5:00pm Eastern Standard Time (EDT) from a single Lead Organization from each project team. Notices of Intent are required and must be submitted to QSP@niimbl.org.

August 4, 2017 - All Members of a proposal project team must have signed the NIIMBL membership agreement by 5:00pm EDT to be considered a project participant.

August 11, 2017 – Proposals due by 5:00pm EDT.

September 1, 2017 – Proposal leads and participating organizations notified of intention to fund the project. Award negotiations begin. Note: teams will have 30 business days to finalize award negotiations including the intellectual property (IP) Management Plan. A draft IP Management Plan will be available soon at http://niimbl.org/quickstart.php. If negotiations are not completed and agreements not executed by 30 business days, NIIMBL intends to withdraw the offer to launch the project.

September 18, 2017 – Earliest possible start date for Quick Start Projects.

Proposals in response to this QSP call must be submitted by project teams via Box.com folder by 5:00pm EDT on August 11, 2017. Specific guidance and instructions can be found below and also on the NIIMBL website at http://www.niimbl.org/quickstart.php.

4. Eligibility and Proposal Team Composition

To participate on a proposal team, an organization must have signed the NIIMBL Membership Agreement by 5:00pm EDT on August 4, 2017. This means that the organization must have returned their Membership Agreement, signed by their authorized representative. Information on how to join NIIMBL is available at www.niimbl.org.

NIIMBL will soon establish an on-line resource to facilitate the identification of relevant expertise for partnering purposes. Moreover, NIIMBL encourages organizations to host teaming workshops. NIIMBL will facilitate coordination and marketing of these events. If your organization is interested in hosting such a workshop please contact info@niimbl.org. Teams looking for specific expertise can also send email to info@niimbl.org.

It is a requirement that at least 1 Small-to-Medium Enterprise (SME) participate on project teams if both of the following apply:

1. the proposal requests more than $100,000 per year of NIIMBL funds AND
2. the proposal is a Technology Development Project or a combined Technology and Workforce Development Project (as designated on the QSP Cover Sheet).

Proposals that solely identify as Workforce Development Projects are exempt from the SME requirement for this QSP call.

Every project team must identify a Lead Organization to coordinate the proposal preparation efforts. This organization will serve as the primary point of contact with NIIMBL for all technical matters, and will provide leadership in the execution of the proposed project. Although there will be a Lead Organization, NIIMBL will directly issue subawards to all participating organizations on a project team, as appropriate and applicable. Thus, project teams will have to plan for careful coordination to ensure that project participants meet their technical project

obligations and that non-performance, or unsatisfactory performance, is addressed. The project lead will be responsible for technical reports.

For any questions about eligibility please contact QSP@niimbl.org

5. Award Information

QSP proposals are limited to a request of no more than $1,000,000 per year of funding from NIIMBL. All QSP proposals are required to have a minimum of 1:1 cost share annually from non-federal sources. Projects are limited to no more than 18 months in duration ($1,500,000 requested NIIMBL funds maximum plus minimum 1:1 cost share).

All proposed costs, both in the requested budget and in the proposed cost share budget, must be deemed allowable in accordance with the Department of Commerce Financial Assistance Standard Terms and Conditions (December 2014) and the Federal cost principles set forth in 2 CFR 200, Subpart E. Examples of allowable costs include salaries and associated fringe benefits for staff and students participating on the project, equipment, supplies, services, and travel in support of the project. In addition, federally negotiated facilities and administrative (F & A) costs will be reimbursed in accordance with 2 CFR 200.414. For inquiries related to cost share allowability, please contact QSP@niimbl.org.

Subject to the availability of funds, requested budgets, and quality of submissions, NIIMBL can commit up to $4,500,000 to support QSPs. NIIMBL will fund QSP proposals to a maximum of $1,500,000 per project, but proposals with lower budgets are also encouraged. Project Award Agreements will be issued to successful project teams in accordance with the NIIMBL Bylaws. For project team members requesting direct funding in support of their efforts on the project, NIIMBL will issue funding agreements directly to those organizations. The first NIIMBL Project Call is expected in Fall 2017.

Proposals that meet the definition of human subjects research as found in 45 CFR Part 46 are not permitted in this QSP call. This includes human subjects research that is determined to be exempt under these regulations. Proposals that include research activities involving live vertebrate animals are also not permitted in this QSP call. Because this QSP call is designed and intended to accelerate the project launch process and return on investment for stakeholders during the start-up phase, we are encouraging teams to submit proposals involving human subjects and/or vertebrate animals during our first full Project Call, which is expected in Fall 2017. Waiting until our next submission period will give more time to teams to develop their proposals, and to NIIMBL to prepare for the administrative review and approvals needed to authorize such projects. If you have questions about your project, please seek guidance from your local IRB/IACUC or also contact qsp@niimbl.org.

6. Proposal Preparation and Submission Process

NIIMBL will host a webinar, to be announced on the NIIMBL website and emailed to each member's designated administrative and technical contacts, to offer details and answer questions related to this QSP call. The member's contacts have responsibility to ensure that information is disseminated within the member organization. A FAQ will be posted on the website. To register for the webinar or to find out more details about a date and time, please email QSP@niimbl.org.

6.1 Required Notice of Intent

The Lead Organization of each proposal team is required to send a Notice of Intent to submit a QSP. The notice must be submitted via email to QSP@niimbl.org by 5:00pm EDT on August 4, 2017. The notice must include the following: the names of expected participating organizations, a draft proposal title (if known), and the names and contact information for all individuals requiring access to the project team's Box submission folder. While the notice is required, the information it contains about partners, the title, and the ultimate submission of a QSP proposal is non-binding.

Upon submission of the Notice of Intent, NIIMBL will create a private, secure folder on Box.com that is accessible only to partner personnel and organizations named in the Notice of Intent, and NIIMBL personnel. All users will have full access to the folder. At the submission deadline (5pm EDT, August 11, 2017), user access to the folder will be converted to view only. Therefore, no changes or edits may be made to the submitted proposal document after the deadline. Please direct questions about the submission process to QSP@niimbl.org.

6.2 Checklist for Submission

Each submission must consist of the following items and in the following sequence combined into a single PDF file. Failure to comply with all required proposal elements may result in the proposal being returned without review.

1. QSP Proposal Cover sheet (1 sheet for each participating organization on the team)
2. Abstract (suitable for public use)
3. Proposal Narrative (all content NIIMBL-confidential)
    a. Executive Summary (1-page maximum)
    b. Background and Significance
    c. Project Description
    d. Potential Project Impact
    e. Project Management Plan
    f. Description of Team
    g. Project Management Plan
4. Proposal Appendices limited to those specified in Section 6.6

5. Individual Organization Budgets
6. Consolidated Budget
7. Individual Organization Budget Justifications

Proposal elements 1-7 (above) must be uploaded to the project team's Box.com folder by 5:00pm EDT on August 11, 2017. Specific guidance and instructions are provided on the NIIMBL website (http://www.niimbl.org/quickstart.php).

6.3 QSP Proposal Cover Sheet

Download the template from http://niimbl.org/Downloads/QuickStartCoverSheet.pdf and complete all required fields. Each participating organization must complete its own proposal cover sheet.

6.4 Abstract

The abstract may be shared publicly. It is limited to 100 words. It must follow the template that is available online at http://niimbl.org/Downloads/QSPAbstract.docx. Be sure that the abstract does not contain any confidential or proprietary information.

6.5 Proposal Narrative

This section must be single-spaced, 11 point *Arial* font (or larger) with 1" margins and numbered pages. The font limitations do not apply to figures or tables. The Proposal Narrative must include all the sections described below and must not exceed 12 pages (including the Executive Summary).

A. Executive Summary (1-page maximum)

This is a confidential summary of the proposed work, the technology or workforce development objectives and how they are consistent with NIIMBL goals, and the projected impact of the project. The Executive Summary is limited to one page.

B. Significance and Background

Describe the problem being addressed. Summarize prior work done in the area, preliminary results, and the estimated Manufacturing Readiness Level of the technology being proposed. The Introduction should also summarize the overall objectives of the project, methodology to be used, regulatory considerations, and significance of this project for the industry.

C. Project Description

Describe the research or workforce development methodologies and approaches to be used, tasks to be completed by project participant, milestones or deliverables

and timelines, and metrics for success. A Gantt chart showing proposed milestones and deliverables by quarter is recommended.

D. Potential Project Impact

Summarize the impact of the proposed project to the overall goals and objectives of NIIMBL. For example, describe any potential increases in productivity, quality, efficiency, energy savings, efficacy, potency, safety, and/or any other important factors related to the production of biopharmaceuticals that may be derived from the project as well as any impact on domestic competitiveness in this sector such as the development of a highly trained workforce, the future of domestic biomanufacturing, and/or estimated economic impact on a company or on the industry broadly or any other relevant measure.

E. Description of Team

Identify the principal investigator from the Lead Organization for the proposal team, and also identify additional organizations' principal investigators and any other senior/key personnel. Include their responsibilities and roles in the project. If known, postdoctoral scientists, staff members and / or students' names should be included.

F. Project Management Plan

Describe approaches to be taken to ensure that the work of the project team members will be synergistic and how information among the various teams will be shared. Describe how issues of material and technology transfer will be addressed. Note that each project will be assigned a NIIMBL Project Manager to facilitate and monitor project progress.

6.6 Proposal Appendices - limited to only the following items

1. References
2. Two-page biosketches (Required for each organization's lead Principal Investigator and all senior personnel. Proposers are encouraged to use the NSF format which is described at https://www.nsf.gov/pubs/policydocs/pappg17_1/pappg_2.jsp#IIC2f.)
3. List of acronyms
4. Quad chart (1 page) based on the template provided: http://niimbl.org/Downloads/QuadChartTemplate.pptx.

6.7 Budget

Each organization requesting funding and/or committing cost share must complete its own budget spreadsheet, which is available for download at

http://niimbl.org/Downloads/QSPBudgetTemplate.xls. The lead organization must also provide a combined budget for all project costs.

The combined budgets from each project team must not exceed $1,000,000 per year of requested NIIMBL funding. The combined budgets from each project team must commit a minimum of 1:1 cost share. Additional cost share over the required minimum will be considered favorably during the review process.

All proposed costs must be deemed allowable in accordance with the Department of Commerce Financial Assistance Standard Terms and Conditions (December 2014) and the Federal cost principles set forth in 2 CFR 200, Subpart E. Examples of allowable costs include salaries and associated fringe benefits for staff and students participating on the project, equipment, supplies, services, travel, infrastructure modifications, analytical services, and associated overhead in support of the project. Costs to support construction are not allowable. Costs to support renovations require prior approval.

Project work should preferably take place within the United States. Prior approval must be obtained for any activities taking place outside of the United States, including foreign travel.

In addition, funding from NIIMBL will only be available to organizations and institutions that are Tier 1, 2, and 3 academic or industry members and have agreed to comply with all aspects of confidentiality and intellectual property considerations described in the NIIMBL Membership Agreement and Bylaws.

6.8 Budget Justification

This section should provide a clear description of all budget items to support and justify the expenses. Each organization requesting funding and/or committing cost share must complete its own budget justification. The lead organization is not required to provide a combined budget justification for all project costs. There is no page limit for the budget justifications.

7. Evaluation Process

Proposals will be scored using the following rubric:

Project Significance: 25 points maximum

The extent to which the project addresses the NIIMBL mission. Also, the degree to which the project aligns with the characteristics of a successful QSP as described in Section 1 of this RFP.

Technical Merit: 20 points maximum

Technical projects are based on sound scientific research principles, fall within MRL 4-7 range, and provide clear and achievable milestones or deliverables. Workforce development projects

are based on state of the art approaches to education and training and have a clear target audience and well-defined metrics for success.

Project Potential for Impact on Industry: 35 points maximum

The potential for the project to realize significant and expedient returns for the industry in productivity, quality, efficiency, energy savings, efficacy, potency, safety, economic impact and/or any other important factor related to the production of biopharmaceuticals with an emphasis on solutions that will be implementable in a cGMP manufacturing environment. Workforce development projects should accelerate the education and training of a globally-competitive biomanufacturing workforce.

Team Expertise: 20 points maximum

The degree to which the experience and expertise of the principal investigators and senior/key personnel, as well as the qualifications of the participating organizations who will carry out project, is expected to help the project achieve project objectives.

In addition, the following non-quantitative criteria that will be considered are:

1. The total amount of cost share in excess of 1:1
2. The degree of Tier 3 Industry member (SME) participation.

Upon project start, teams will be assigned a Project Manager.

The Technical Activities Committee (TAC) will evaluate proposals involving a significant technology effort. Subject matter experts, that may include participants from the Regulatory Considerations Committee (RCC) or outside of NIIMBL, may be used to evaluate proposals. The Workforce Activities Committee (WAC) will evaluate proposals involving a significant workforce effort. Subject matter experts, that may include participants from the RCC or outside of NIIMBL, may be used to evaluate proposals. Depending on the number and nature of proposals received, joint meetings of members of the TAC, RCC, and WAC may be used to evaluate submissions. The evaluations and all proposals will be distributed to the Governing Committee (GC) to make final funding decisions.

8. Reporting

Reporting requirements will be outlined in the Project Award Agreement, but will involve both technical and financial reporting. Individuals and organizations on funded projects will be required to comply with the outlined reporting requests found in the Project Award Agreement.