The National Institute for Innovation in Manufacturing Biopharmaceuticals

Project Call 4.1G
Request for Proposals

Concept Papers due: October 22, 2020

Full Proposals due: February 4, 2021

VERSION October 1, 2020

NIMBL

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1. Executive Summary

The NIIMBL Global Health Fund (GHF) was established by NIIMBL with funding contributed by the Bill & Melinda Gates Foundation (BMGF) to develop and implement innovative technologies for vaccine and biological manufacturing that will accelerate development timelines, lower the cost of manufacturing, secure supply for the Global Alliance for Vaccines and Immunization, and ensure appropriate product profiles for their geographies, all in furtherance of BMGF's charitable objectives (the "Purpose"). To advance the Purpose, NIIMBL and BMGF worked with subject matter experts from leading vaccine manufacturers and other NIMBL stakeholders to identify key needs for advanced manufacturing technologies that are the focus of this RFP. The Bill & Melinda Gates Foundation does not control the selection of the recipient of the award(s). The Bill & Melinda Gates Foundation will not be a party to the funding agreement(s), if awarded. Any awards that are made will be controlled, made and managed solely by NIIMBL.

Funding Opportunity Title: Project Call 4.1G (Global Health Fund)

Stage 1: The Concept Phase includes the submission of a Concept Paper limited to 4 pages (not including references) and a short slide deck (see details below). No teaming, detailed budget, or cost share information is required at this stage. Concept Phase submissions must be submitted via the NIIMBL Proposal Submission Hub. All submissions must be received no later than 5:00 p.m. Eastern Time **Thursday, October 22, 2020**. Submissions received after the deadline, or that are not compliant with the page / slide limits, will not be considered.

Following submission of Concepts, each will be reviewed by subject matter experts to prioritize those Concepts that have the potential for the highest industry impact and likelihood of success. Factors for invitation to full proposals include the feedback from industry, alignment with prioritized areas noted in this RFP (see below), and the readiness level of a given Concept. The Concept Phase (Stage 1) concludes with invitations or declinations issued for submit a Full Proposal in Stage 2 of the process.

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. Proposals must be received no later than 5:00 p.m. Eastern Time **Thursday, February 4, 2021**. Submissions received after the deadline, or otherwise non-compliant with the submission requirements (see below) will not be considered.

This Phase concludes with a decision to fund or not fund the proposal by the GHF Steering Committee.

EVENT	DATE
RFP Release	October 1, 2020
Concept Paper Due	October 22, 2020
Invite for Full Proposal	Expected by December 1, 2020

Full Proposal Due	February 4, 2021
Proposal Review	February - March 2021
Award Decisions Made	Expected end of March, 2021

Funding Opportunity Description

Further details on project topics are found in Section 6.

PC4.1 Global Health Fund (GHF) projects are expected to enhance the ability to manufacture and release vaccines to, among other things, serve low- and lower-middle income countries. The following project priority areas have been selected for PC4.1G:

1. Drying technologies and associated fill-finish for production of vaccine drug products.
2. Rapid release assays for vaccine drug products.
3. Alternative hosts for higher yield to lower cost and provide more rapid vaccine production.

The top priority topic is listed first. Both the second and third topics are of equal interest but are each considered secondary priorities. It is recognized that this is a broad area so proposals will likely focus on a sub-set of these opportunities

Total Amount to be Awarded

NIIMBL expects to make available up to $1,500,000 to fund proposals submitted in response to the PC4.1G request for proposals, subject to GC approval. It is anticipated that up to three projects will be funded.

2. Project Requirements and Eligibility Criteria

Project Types

Global Health Fund projects are designed to support advancements of global health related to biopharmaceutical manufacturing. Unlike projects funded by other NIIMBL RFPs (including PC4.1T and PC4.1W), projects funded by PC4.1G are expected to be managed in such a way as to ensure the broadest possible access to those most in need. See section below on Global Access Commitment, IP and Publication for more information. Partner Specific projects as defined in the NIIMBL Bylaws are not permitted for PC4.1G proposals. Global Health Fund project proposals shall be within NIIMBL Biomanufacturing Readiness Level (BRL) 4-7. More information on BRL can be found at: http://www.niimbl.org/project-call-4-1.

Period of Performance

Proposals must not exceed 18 months.

Proposer Eligibility

Stage 1: Unlike other NIIMBL project calls, NIIMBL members, non-members, and Federal employees are permitted to submit Concepts in response to PC4.1G. Note that only NIIMBL members or Federal employees are permitted to submit Concepts in response to PC4.1T and PC4.1W.

Stage 2: To participate on a project Full Proposal team, the lead project proposer AND all members of the proposed project team must be a NIIMBL member or a Federal employee. To be considered a NIIMBL member, an organization must be a member or have submitted a partially-executed NIIMBL Membership Agreement by **5:00 p.m. Eastern Time on Thursday, January 28, 2021.** Information on how to join NIIMBL is available at niimbl membership-information.

Budget

Project teams are required to meet a minimum 1:1 (NIIMBL:partners) cost share requirement.

Indirect cost recovery is limited for proposals submitted in response to PC4.1G. See Section 3.3 for more information

Cost Share

All committed cost share must be from non-Federal funding sources. There is no requirement to have cost share documented or planned at the Concept Phase. However, 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 NIIMBL Bylaws and Membership Agreements.

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. 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.

Project teams requesting State cost share funding may require additional review and approval from those State organizations to secure their commitment for cost share funding. Project proposal teams with state funding are encouraged to include confirmation of the support (Appendix I). Project proposal teams must contact the appropriate State organization for additional information:

Delaware: Contact Marta Rosario (martar.udel.edu) by 5:00 p.m. Eastern Time on January 15, 2021 to request state cost share. The request should include a 1-paragraph description of the project, partners, and budget narrative.

Massachusetts: Massachusetts applicants planning to submit a full proposal and requesting cost-share from the Massachusetts Life Sciences Center should reach out to NIIMBLMA@masslifesciences.com early in the application process to confirm requirements and dates. MA applicants will be required to submit a draft application to NIIMBLMA@masslifesciences.com the week of January 4, 2021. Selected applicants will present their proposal in person to the Massachusetts Life Science Center mid-January 2021.

North Carolina: Contact Jon Horowitz (jmhorowi@ncsu.edu) at the NC State Office of Research and Innovation. Requests need to reach this office by 5:00 p.m. Eastern Time on December 15, 2020.

Teaming

There is no requirement to have partners identified during the Concept Phase, but if partners have been identified they should be noted in the Concept Paper.

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 highly encourages inclusion of Tier 3 industry members. 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. 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 PC4.1 Guide Information for Federal Stakeholders available at: http://www.niimbl.org/project-call-4-1

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 is available at: http://www.niimbl.org/project-call-4-1.

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 at: http://www.niimbl.org/project-call-4-1.

Global Access Commitment; IP and Publication

Global Access Commitment

All projects shall be conducted in a manner that ensures Global Access, and the Global Access commitments will survive the term of the funded project. “Global Access” is a BMGF policy requiring that (a) the knowledge and information gained from the project will be promptly and broadly disseminated; and (b) the Funded Developments will be made available and accessible at an affordable price (i) to people most in need within developing countries, or (ii) in support of the U.S educational system and public libraries, as applicable to the project. “Funded Developments” means the products, services, processes, technologies, materials, software, data, other innovations, and intellectual property resulting from the project (including modifications, improvements, and further developments to Background Technology). “Background Technology” means any and all products, services, processes, technologies, materials, software, data, or other innovations, and intellectual property created by a project participant, or a third party prior to or outside of the project, used as part of the Project.

Humanitarian License

Subject to applicable laws and for the purpose of achieving Global Access, the project participants shall be required to grant NIIMBL and BMGF a nonexclusive, perpetual, irrevocable, worldwide, royalty-free, fully paid up, sublicensable license to make, use, sell, offer to sell, import, distribute, copy, create derivative works, publicly perform, and display Funded Developments and Essential Background Technology. “Essential Background Technology” means Background Technology that is: (a) owned, controlled, or developed by a project participant, or in-licensed with the right to sublicense; and (b) either incorporated into a Funded Development or reasonably required to exercise the license to a Funded Development. Project participants shall be required to certify that they have retained sufficient rights in the Funded Developments and Essential Background Technology to grant

this license. The project participants must ensure this license survives the assignment or transfer of Funded Developments or Essential Background Technology. On request, the project participants must promptly make available the Funded Developments and Essential Background Technology to NIIMBL or BMGF for use solely under this license.

Publication

Consistent with the Global Access commitments, if the project description specifies Publication or Publication is otherwise requested by NIIMBL or BMGF, project participants shall be required to seek prompt Publication of any Funded Developments consisting of data and results. "Publication" means publication in a peer-reviewed journal or other method of public dissemination specified in the project description or otherwise approved by NIIMBL and BMGF in writing. Publication may be delayed for a reasonable period for the sole purpose of seeking patent protection, provided the patent application is drafted, filed, and managed in a manner that best furthers Global Access. If project participants seek Publication in a peer-reviewed journal, such Publication shall be under "open access" terms and conditions consistent with the Foundation's Open Access Policy available at: www.gatesfoundation.org/How-We-Work/General-Information/Open-Access-Policy, which may be modified from time to time. Nothing in this section shall be construed as requiring Publication in contravention of any applicable ethical, legal, or regulatory requirements.

Intellectual Property Reporting

During the term of the project award agreement associated with the funded project, and for five (5) years after, project participants will be required to submit to NIIMBL and BMGF upon request annual intellectual property reports related to the Funded Developments, Background Technology, and any related agreements using NIIMBL's and/or BMGF's templates or forms, which may be modified from time to time.

3. Proposal Instructions

3.1 General Instructions

Submissions

Stage 1: Concept Paper submissions must be submitted via the NIIMBL Proposal Submission Hub. All submissions must be received no later than 5:00 p.m. Eastern Time **Thursday October 22, 2020**. Submissions received after the deadline, or otherwise not compliant with the requirements for a compliant proposal, will not be considered (see below for full requirements)

Stage 2: Full Proposal submissions must be submitted via the NIIMBL Proposal Submission Hub. Proposals must be received no later than 5:00 p.m. Eastern Time **Thursday, February 4, 2020**. Submissions received after the deadline, or otherwise not compliant with the requirements for a compliant proposal, will not be considered (see below for full requirements).

Confidentiality

Teams are expected to mark their Full Proposal submissions "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

The Concept Phase is designed to give proposers the opportunity to propose their project ideas for consideration by reviewers comprised of industry representatives and Federal stakeholders. Proposers will provide their concepts in the form of a written Concept Paper, a short Concept Slide Deck, and a Concept BRL Appendix. Following this submission, NIIMBL will facilitate review of the Concept Papers and Concept Slide Decks by subject matter experts from industry members, federal stakeholders, and BMGF stakeholders. The feedback from those reviews will identify the Concepts that are best aligned with industry needs and priorities and will inform the selection of invitations issued to submit a Full Proposal in Stage 2 of the process.

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 PC4.1G at http://www.niimbl.org/project-call-4-1. The Concept Slide Deck may not include recorded voiceover. The Concept Paper, Concept Slide Deck and Concept BRL Appendix must be submitted via the NIIMBL Proposal Submission Hub by 5:00 pm Eastern Time **Thursday, October 22, 2020**. Submitted concepts that do not adhere to the formatting and length limits for both the Concept Paper and the Concept Slide Deck will be considered non-compliant and will not be considered for further review. There is no page limit for the Concept BRL Appendix.

The Concept Paper must include:

- Submitter name and organization
- Concept title
- Topic area to be addressed
- Identified project team partners 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
- BRL of the proposed concept and short justification; this should be addressed in the Concept Paper and Slide Deck, and also must be addressed via the submission of the Concept BRL Appendix (see template at http://www.niimbl.org/project-call-4-1 for Concept stage)

- Value proposition to project partners, NIIMBL, the NIIMBL community, and the global health market, including expected benefits to people in low- and lower-middle income countries. Considerations include return on investment, time to impact in the industry, and planned BRL transition.

	Submission	Constraints
Concept Paper	October 22, 2020, via NIIMBL Proposal Submission Hub	Single-spaced 1-inch margins 11-point Arial font (or equivalent) Maximum of 4 pages File Type: .pdf only
Concept Slides	October 22, 2020, via NIIMBL Proposal Submission Hub	Maximum of 5 slides, adhering to template provided (http://www.niimbl.org/project-call-4-1 Standard size (4:3) File Type: .ppt or .pptx only
Concept BRL Appendix	October 22, 2020, via NIIMBL Proposal Submission Hub	No page limits adhering to template provided (http://www.niimbl.org/project-call-4-1 File Type: .doc or .docx

3.3 Stage 2: Full Proposal

The full proposal narrative must be no more than 14 pages. 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. Project Partner Information Form(s), or Letter(s) of Intent (not counted towards the page count)
2. Abstract (200 words max; not counted towards the page count)
3. Executive Summary (up to 1 page; not counted towards the page count)
4. Proposal Narrative (up to 14 pages)
5. 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 Questionnaire (.doc file – see template)

6. 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	Letter(s) of commitment

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 http://www.niimbl.org/project-call-4-1.

Project Partner Information Form(s)

Each unique project organization on the project proposal team must submit either a Project Partner Information 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 Project Partner Information Form. Industry partners who are only providing a leveraged cost share commitment should complete a Letter of Commitment (see Appendix I). All project proposal team organizations must be NIIMBL members or a Federal entity. Templates for the Project Partner Information Form and the Letter of Intent are available at: http://www.niimbl.org/project-call-4-1.

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, GHF alignment, 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 be single-spaced, minimum 1 inch margins, 11-point Arial font (or larger equivalent font). The proposal narrative must include all the sections (1 to 4) described below and must not exceed 14 pages (not including references, which is Appendix F).

1. **Background and Significance**

Identify the project call topic area being addressed and describe the specific problem or current state of the art. Summarize prior work done in the area, preliminary results, and the starting/ending BRLs 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 and advance the Purpose defined above.

2. Project Description

Describe the project segments, tasks, milestones, deliverables, and go/no-go decision points. Describe the success criteria for the project, including metrics for measuring project success. Milestones must be specific and quantitative whenever possible.

NOTE: Appendix C will cross reference the Work Breakdown Structure (WBS) with the page number in the narrative where additional details can be found. Appendix C will also contain a Responsibility Assignment Matrix that will 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. Potential Project Impact & Value Proposition

Summarize the impact of the proposed project to the overall goals and objectives of NIIMBL, including the Purpose defined above. Describe the overall value proposition and the positive impact on developing countries. This should be from the perspective of NIIMBL, as well as the broader NIIMBL community and/or the United States biopharmaceutical manufacturing industry. Examples 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. 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 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 the

synergistic work across project team members, in particular 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 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 limited to two pages each, and while no format is prescribed, proposers are encouraged to use the NSF format as prescribed in PAPPG 20-1: https://www.nsf.gov/bfa/dias/policy/nsfapprovedformats/biosketch.pdf

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 budget information. The quad chart is limited to one page and must be submitted as a .ppt or .pptx file. The NIIMBL template is available at: http://www.niimbl.org/project-call-4-1.

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

The WBS for the proposed project forms the foundation of the proposed project plan. Align the WBS with the Responsibility Assignment Matrix to describe how responsibility will be shared across the identified WBS 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: http://www.niimbl.org/project-call-4-1.

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

Provide individual budget table (.xlsx) and cost justification (.docx) for the lead organization and each of the partner organizations requesting funding and/or committing cost share to the proposed project. Budgets are to be organized by WBS Level 2 Segments. The budget template allows for 5 WBS Level 2 Segments. Any project proposal team with more than 5 WBS 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 template are available for download at: http://www.niimbl.org/project-call-4-1.

Proposals submitted in response to PC4.1G must closely consider the indirect costs (also called Facilities and Administrative Costs) that are included in the Individual Organization Budget. Indirect costs budgeted must adhere to the Indirect Cost Policy of the Bill & Melinda Gates Foundation, which can be found at https://docs.gatesfoundation.org/documents/indirect_cost_policy.pdf, in addition to the federal guidance found at 2 CFR 200.414. The Bill & Melinda Gates Foundation places restrictions on the maximum indirect cost rates that can be charged, which are driven by the type of institution:

1. Government agencies and other private foundations may not charge indirect costs.
2. U.S. universities and community colleges may not charge indirect costs in excess of 10% of total direct costs.
3. For-profit organizations, non-governmental organizations, and multilateral organizations may not charge indirect costs in excess of 15% of total direct costs.

The federal government requires that an organization have a federally negotiated rate or limit their indirect cost recovery to no more than 10% of modified total direct costs. Project partners are encouraged to carefully review both guidance and determine the appropriate rate to charge that would ensure compliance with both policies. Please email projectcalls@niimbl.org with any questions about how to determine the correct indirect cost rate.

Project teams are encouraged to budget for travel to a kickoff meeting and to present at the NIIMBL National Meeting, which occurs in late spring in Washington, D.C.

Appendix E: **BRL Questionnaire**

Answer each of the questions in the provided template regarding the NIIMBL Biomanufacturing Readiness Level(s) of the key aspects of the technology to be demonstrated in the proposed work (instructions included with template). Supporting documentation, if needed, must be available upon request by NIIMBL. The BRL Questionnaire is available for download at: http://www.niimbl.org/project-call-4-1.

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: http://www.niimbl.org/project-call-4-1.

Appendix I: **Commitment Letters**

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. If Commitment Letter(s) are not needed, this appendix is N/A.

4. Proposal Review and Evaluation

4.1 Stage 1: Concept Evaluation Criteria

NIIMBL Acceptance Criteria

Concept Papers and Concept Slide Decks must comply with information requirements outlined in this RFP. Concepts will be non-compliant and not considered further if they include either a Concept Paper the excludes the maximum 4 pages, or a Concept Slide Deck that exceeds the maximum 5 slides. All administrative requirements, terms and conditions, and other appropriate disclosures will be assessed for completeness.

Automatic rejection will occur if the submission is received after the published deadline.

Concept Paper and Concept Slide Deck Review

NIIMBL will review submitted Concepts to ensure that they comply with the intended outcomes of this Project Call (see Section 1), suitability of work within the BRL 4-7 space, industry interest, and alignment with the goals of the Global Health Fund.

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

For GHF projects, the Concept Phase evaluation criteria are:

1. The Concept Paper ability to address the topic's problem statement and a relevant industrial and global health need.
2. The Concept Paper's demonstration of awareness of existing solutions.
3. The Concept Paper's ability to provide a clear value proposition for the project team, the broader NIIMBL community, and/or the biopharmaceutical manufacturing industry, and the global health market.
4. The BRL of the concept falling within the NIIMBL mission space.

4.2 Stage 2: Full Proposal Evaluation Criteria

Full Proposals that are submitted will follow an evaluation process that relies on subject matter experts from NIIMBL member companies and the expertise of the relevant NIIMBL committees and stakeholders. Final decisions on which subgrantees to award rests with NIIMBL.

NIIMBL Acceptance Criteria

Full Proposals must comply with information requirements outlined in this RFP. Proposals will be assessed to ensure the budget is appropriate and reasonable for proposed work. All administrative requirements, terms and conditions, and other appropriate disclosures 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) budget parameters are not met, such as the maximum project budget and minimum cost share ratio.

NIIMBL Subject Matter Expert Review Panel

GHF 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 an innovative solution to critical global health needs for safe, potent, and readily accessible vaccines for infectious diseases that, among other things, benefit people most in need in developing countries
- The speed with which the benefits of the project will be realized
- The proposal's ability to provide a clear value proposition for the project topic area
- The proposal's ability to reduce time, costs, resources and accelerate implementation timelines for vaccine production for developing countries vaccine manufacturers.

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 – provide a transition pathway to *in vitro* testing, predict key quality attributes necessary for product safety and efficacy
- The team's inclusion of the needed technical expertise, including project management

NIIMBL Governing Committee

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

- The proposal's ability to provide a solution to critical global health needs for vaccines addressing infectious diseases
- Whether the technical approach and project plan are likely to result in success
- The proposal's ability to provide a benefit to NIIMBL members and people most in need in developing countries
- Whether the initial/final BRL falls within the NIIMBL mission space

Additionally, the NIIMBL Governing Committee will take into account the total Project Call 4.1G funding that is available and perform a strategic review of the proposals. The Committee will consider the following as well:

- Benefit to NIIMBL members and the mission of Bill & Melinda Gates Foundation
- NIIMBL sustainability
- Cost and scope alignment with proposed benefits
- Cost share commitment
- Industry involvement

5. Reporting

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

6. Project Call 4.1 Topics

1. Drying Technologies and Associated Fill-Finish for Production of Vaccine Drug Products

The focus of this topic area is to demonstrate improved technologies for the production of dry-product drug substance forms of vaccine (bulk dry powder, in situ lyo, etc.), particularly to support the development of dual-chamber injectable applications. More specifically to address one or more of the following challenges: (i) reduce processing times with a target of 12 hours for existing, mature drying technologies (e.g., lyophilization) without jeopardizing key quality attributes of existing vaccines or those in development (e.g., final moisture content, structural integrity of the active molecular species, and long-term stability of the product); (ii) for less mature drying technologies, achieve drying times less than those of

mature technologies (e.g,. 6 hours) while achieving key quality attributes such as noted for (i); (iii) provide reliable indication of room-temperature stability of at least 1 year duration, while being scalable to a fully commercial process for existing vaccines of high priority for the GHF; (iv) bulk dry-powder fill-finish processes that enable low cost, dual-chamber injectable devices for delivery of labile vaccines to eliminate the need for in-vial lyophilized products (e.g., approaches could include amorphous powders, particles, tablets, etc. that are compatible with filling a dual chamber device with dry vaccine, and must address challenges associated with filling of commercial products).

The desired technologies can be specific to individual vaccine modalities, but technologies applicable across multiple modalities are preferred. A particular vaccine target of interest for the PC4.1 Global Health fund will be the Measles-Rubella (MR) vaccine. Proposals should include details of analytical assays that will be performed to ensure that CQAs are not compromised in the drug product. For example, preservation of content and potency must be ensured. It is anticipated that the choice of assays will depend on the particular vaccine modality.

2. Rapid Release Assays for Vaccine Products

Demonstrate improved and faster assays for critical quality attributes to remove major bottlenecks in release of vaccine products. Prioritized areas of interest are (1) *in vitro* potency assays, (2) sterility test and (3) viability/integrity of individual antigens in multi-antigen vaccines. In all cases, a significant reduction in assay performance time, compared to currently accepted assays, must be achieved and, for (1) and (2) a 5-fold saving in time should be demonstrated. A prioritized area of vaccines is live attenuated viruses (LAV). Precision and accuracy of *in vitro* LAV potency assays should be improved over currently approved assays. Proposals for DNA/RNA and viral vector- based vaccines, focusing on *in vitro* assays as indicators of *in vivo* expression of relevant antigen(s), will also be considered. In all cases, proposals should outline a path towards regulatory approval.

3. Alternative Hosts for Higher Yield to Lower Cost and Provide More Rapid Vaccine Production

Demonstrate robust, alternative host cells for producing human vaccines that do not require mammalian cell culture and provide significantly lower cost and/or more rapid vaccine production compared to current industry standards. Specific targets include: (i) reduced development time for stable strains to less than one month; (ii) at least 5-fold improvement in yield of stable, active vaccines relative to current industry standards for a given vaccine and/or vaccine modality; (iii) at least 5-fold reduction in COGS, including due to lower CAPEX via smaller production facility footprint, and ability to scale-out to local production facilities globally. Successful proposals will focus on expression systems that have established industrial use that will help address questions of future regulatory acceptance and ease of process development.

7. List of Acronyms

1. BMGF: Bill & Melinda Gates FoundationCo-PI: Co-Principal Investigator

2. BRL: NIIMBL Biomanufacturing Readiness Level
3. CAPEX: Capital Expenses
4. COGS: Cost of Goods Sold
5. CQAs: Critical Quality Attributes
6. DNA: Deoxyribonucleic Acid
7. FDP: Federal Demonstration Partnership
8. FFRDC: Federally Funded Research and Development Centers
9. GC: Governing Committee
10. GHF: Global Health Fund
11. IP: Intellectual Property
12. NIIMBL: National Institute for Innovation in Manufacturing Biopharmaceuticals
13. NSF: National Science Foundation
14. PAPPG: Proposal & Award Policies & Procedures Guide
15. PC4.1G: Project Call 4.1 Global Health Fund
16. PI: Principal Investigator
17. QC: Quality Control
18. RFP: Request for Proposals
19. RNA: Ribonucleic Acid
20. WBS: Work Breakdown Structure

8. Release

The Bill & Melinda Gates Foundation assumes no responsibility for costs to respond to this RFP. Applicant agrees not to bring a legal challenge of any kind against the Bill & Melinda Gates Foundation relating to any matter arising from this RFP.