Innovations for Exceptionally Low-Cost Monoclonal Antibody (mAb) Manufacturing

This Challenge is in Honor of our late colleague, Dr. Steve Hadley, former Senior Program Officer at the Gates Foundation, who long championed the reduction of mAbs manufacturing costs to make them affordable to low- and middle-income countries.

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Before applying, applicants should familiarize themselves with the supporting documents for this Grand Challenge, including the descriptive White Paper, Rules and Guidelines, Application Instructions, and Frequently Asked Questions.

Background

Monoclonal antibodies (mAbs) are one of the most powerful tools in modern medicine, offering a highly specific and effective treatment for a range of conditions - from infectious diseases like COVID-19 to chronic illnesses such as cancer and autoimmune disorders. These biologic therapies provide targeted interventions that can save lives and improve the quality of life for millions of patients globally. Yet, the high production costs associated with mAbs limit access to these lifesaving treatments for patients in low- and middle-income settings.

With efforts to improve technology and affordability, mAb costs have decreased significantly in the last 30 years and have stagnated at around $50-100 per gram. These high costs are driven by the complexity of the manufacturing process, which involves sophisticated methods, strict regulatory compliance, expensive raw materials, and significant infrastructure investments. Reducing production costs is critical, as many applications of anti-infective antibodies may require doses on the order of hundreds of milligrams (as seen for the antibodies that achieved emergency use authorization and/or approvals for COVID-19). In order to improve mAb affordability in low- and middle-income countries, we will need to reach a final drug substance cost-of-goods of $10 per gram - a goal long championed by our late colleague, Dr. Steve Hadley, former Senior Program Officer at the Gates Foundation.

To reach our goal, we will need to draw on innovation and novel approaches from a wide range of scientific and engineering disciplines. While those in the biopharmaceutical field are already deeply engaged in the challenge of reducing mAb manufacturing costs, there is tremendous potential for breakthroughs as we incorporate learnings from adjacent industries, such as dewatering and filtration, blood fractionation, industrial enzymes, and food and beverages. By bringing together diverse expertise and encouraging out-of-the-box thinking, we believe it is possible to achieve this ambitious goal.

The Grand Challenges family of initiatives seeks to source and seed innovations and accelerate the development of transformational solutions. The Gates Foundation, in collaboration with LifeArc, a self-funded medical research charity in the UK, is calling on innovators, scientists, engineers, and entrepreneurs- whether they are seasoned experts in biologics or pioneers in related fields- to join us in this Grand Challenge. Together, we can unlock new pathways to reduce costs, enhance production efficiency, and ultimately expand access to life-saving treatments for all.

This Grand Challenge is calling for proposals that are bold in their vision and approach, offering clear pathways to achieving the $10 per gram target. This is not just a technical challenge; it is an opportunity to make a lasting impact on the lives of millions of people worldwide. We invite you to bring your expertise, creativity, and passion to this effort and help shape a future where the best medical treatments are available to everyone, everywhere.

The Challenge

The Gates Foundation and LifeArc are soliciting proposals to develop proof-of-concept for manufacturing platforms that produce monoclonal antibodies at a final drug substance cost-of-goods of $10 per gram (Option A). The goal is to catalyze and accelerate multiple, diverse, innovative bioprocessing approaches that hold the promise of low cost-of-goods mAbs.

Additionally, the Gates Foundation is interested in hearing from organizations that have already completed proof-of-concept work that could result in cost-of-goods of $10 per gram and may be interested in additional support (Option B).

Applicants can apply with solutions meeting the criteria for **either Option A or Option B** but should not submit entries to both options.

Option A: Proof-of-Concept

The primary outputs of this challenge will be (1) development of a conceptual facility design, and (2) generation of bench or lab-scale process data with sufficient analytical data to demonstrate the ability to produce an antibody at a final drug substance cost-of-goods of $10 per gram that could meet requirements for human applications and would support a rigorous cost-of-goods assessment by a third-party organization (chosen by the Foundation). A full physical demonstration that the manufacturing platform meets specific manufacturing cost targets is not required at this stage. If the success criteria from this process are met and if additional funding is available, Option A applicants may be eligible for further support in a follow-on phase of work.

To apply for the Option A opportunity, please click the "Apply Now" button at the top of this page, or visit this link.

Option B: Operationalization and Economic Viability

Independent of the Proof-of-Concept (Option A), the Gates Foundation recognizes that some organizations may already have proof-of-concept data that could support a final drug substance cost-of-goods of $10 per gram and would like to partner for further development funding. If you have existing data meeting Technical Readiness Level 3-5 (POC Defined, Lab Scale Demonstrated, or Pilot Scale Demonstrated) please share a solution with additional information listed below, as well as any non-confidential data demonstrating Technical Readiness Level 3-5 for production of a monoclonal antibody at a final drug substance cost-of-goods of $10 per gram. The proposal review committee will evaluate this information and reach out to you if there is interest in exploring further. **To apply for the Option B opportunity, please visit this link.**

Objectives of the challenge (both Option A and Option B)

- **Advance innovative and bold ideas** that enhance production efficiency and improve overall process economics for mAb production, resulting in a final drug substance cost-of-goods of $10 per gram. This includes, but is not limited to:
    - **Alternative hosts to mammalian cell culture**
    - **Alternative to standard downstream purification methods**
    - **Reduction in material costs**
- **Push the boundaries of current technology** by harnessing disruptive innovations, possibly from parallel industries, and identify process improvements to reduce manufacturing costs
- **Rethink existing methods of working** such as release testing process and costs, high-quality and affordable raw materials and critical reagents

Funding Level

Option A: The Gates Foundation and LifeArc will consider several proposals for awards of up to $750,000 USD for each project, with a grant term of up to 18 months. Each organization will make coordinated but independent award decisions. Application budgets should be commensurate with the scope of work proposed.

Option B: Potential funding and grant terms will be evaluated on a per-project basis. The funding and timeline are intentionally open given that the work is exploratory at this time. Application budgets should be commensurate with the scope of work being proposed.

Eligibility Criteria – Options A and B

This initiative is open to nonprofit organizations, for-profit companies, international organizations, government agencies and academic institutions. We particularly encourage applications involving projects led by women / in collaboration with women-led organizations, and/or applications from / in collaboration with institutions based in low- and middle-income countries. Only individuals who are applying through a legally recognized corporate entity are eligible.

We are looking for proposals that:

- Would work with the MAM01 malaria antibodies (Option A applicants) or malaria, RSV, or HIV antibodies (Option B applicants) requiring high doses
    - We are focused on applications capable of producing antibodies at volumes of a metric ton per year and are modeled assuming tonnage demand (1000 kg per year)
- Include fully loaded costs inclusive of reagents, consumables, labor, facility-related costs, QC/QA (quality control, quality assurance) costs, fill-finish, and licensing costs

- Outline solutions with specific steps and/or end-to-end solutions
- Provide technological solutions to reach the target rather than solutions relying upon multi-use facilities, brown-field facilities and other non-technological solutions
    - For the purposes of calculating costs, assume a "green-field" facility producing just a single product
- Clearly outline the capabilities of the team, including a level of demonstrated applicability to a related problem and/or credibility for pharmaceutical applications
- Demonstrate technical quality and the ability to generate data within 12 months
- Include a justification of costs, which will also be analyzed by an external third-party
- We encourage applications that may include a number of collaborators who each bring specific expertise. If applicants need partners with specific expertise, please identify so within your proposal submission and we will consider areas to encourage collaboration amongst different applicants to enable end-to-end solutions
- Articulate solutions that could enable manufacturing in LMICs
- For applicants interested in Option B: Please share any non-confidential data sharing that technical readiness level 3-5 has been met for low-cost production of HIV, RSV, or malaria antibodies

For this challenge we are not seeking proposals that:

- Include changes to an existing licensed molecule
- Require changes to the coding of sequence of standard human- or humanized-IgG1s.
    - Since the foundation is separately funding the development of protein molecules with improved affinity and potency, this particular RFP is focused on manufacturing solutions
- Are focused on solutions for lower-cost delivery and administration of antibodies
    - This RFP is focused on drug substance only so applications on DP (drug product), filled container and alternative administration routes (oral, nasal, ID, etc.) are outside the scope of this RFP
- Are focused on technologies like in-vivo expression of antibodies using nucleic acid and gene delivery
    - The Gates Foundation is pursuing alternative paths to these technologies, and they are outside the scope of this RFP
- Include cost reductions resulting from price negotiations (e.g., buying materials in bulk)
- Are focused on stepwise or incremental improvements that result in nominal cost reductions
- Are not applicable to global-health target diseases

*The **Option A** (Proof-of-Concept) part of this Grand Challenge is a collaboration between the Gates Foundation and LifeArc, however each funder will make independent funding decisions. Following the RFP process, organizations with successful applications will be invited to submit their proposal on Gates Foundation or LifeArc standard proposal templates in alignment with each potential funder's due diligence process as applicable.*

*The Gates Foundation is accepting proposals for **Option B** independently from LifeArc.*

Initiative: Grand Challenges

Date Open: Nov 17, 2024, 11:00 am PST

Deadline: Jan 31, 2025, 11:30 am PST

Supporting Materials:

- Low-Cost mAb Manufacturing - RFP
- Low-Cost mAb Manufacturing - Rules and Guidelines
- Low-Cost mAb Manufacturing - Application Instructions
- Low-Cost mAb Manufacturing - Budget Template
- Low-Cost mAb Manufacturing - White Paper
- Low-Cost mAb Manufacturing - Frequently Asked Questions (FAQs)