Request for Assistance:

Establishing a current Good Manufacturing Process (cGMP) small-scale manufacturing process for microarray patches (drug-specific) and preparing a chemistry, manufacturing, and controls (CMC) data package for a pre-Investigational New Drug (IND) submission

MAPs for PrEP project: Dissolving microarray patches (MAPs) for long-acting HIV and pregnancy prevention

This project is made possible by the generous support of the American people through the United States Agency for International Development (USAID) through the United States President’s Emergency Plan for AIDS Relief (PEPFAR), under the terms of Cooperative Agreement #AID-OAA-A-17-00015. The contents are the responsibility of PATH and do not necessarily reflect the views of USAID, PEPFAR, or the United States government.
Request for Assistance (RFA) – REVISED text in green

Establishing a current Good Manufacturing Process small-scale manufacturing process for microarray patches (drug-specific) and preparing a chemistry, manufacturing, and controls data package for a pre-Investigational New Drug submission

MAPs for PrEP Project

RFA 2020-006

Table 1. Schedule and deadlines - REVISED

<table>
<thead>
<tr>
<th>Event</th>
<th>Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Request for assistance (RFA) re-released</td>
<td>February 27, 2020</td>
</tr>
<tr>
<td>Expression of interest due by email, including signed non-disclosure agreement (NDA) and organizational description, and any questions about this RFA (see details in Step 1 below)</td>
<td>March 10, 2020</td>
</tr>
<tr>
<td>Confidential technical information is sent organizations which have successfully submitted an expression of interest</td>
<td>March 12, 2020</td>
</tr>
<tr>
<td>PATH emails RFA questions and answers to all organizations</td>
<td>March 16, 2020</td>
</tr>
<tr>
<td>Application/proposals due (see details in Step 2 below)</td>
<td>March 31, 2020</td>
</tr>
<tr>
<td>Proposal evaluation complete</td>
<td>April 9, 2020</td>
</tr>
</tbody>
</table>

*PATH reserves the right to adjust the schedule, if necessary. All interested parties will be notified as soon as possible.

PATH statement of business

PATH is the leader in global health innovation. An international nonprofit organization, we save lives and improve health, especially among women and children. We accelerate innovation across five platforms—vaccines, drugs, diagnostics, devices, and system and service innovations—that harness our entrepreneurial insight, scientific and public health expertise, and passion for health equity. By mobilizing partners around the world, we take innovation to scale, working alongside countries primarily in Africa and Asia to tackle their greatest health needs. Together, we deliver measurable results that disrupt the cycle of poor health. Learn more at www.path.org.

Background

Health need

Women and adolescents in low- and middle-income countries are at greatest risk of HIV infection and need acceptable products that provide long-acting protection against HIV. Microarray patches (MAPs; also known as micronneedle patches) are an easy-to-use, discreet delivery technology, which could improve adherence to HIV pre-exposure prophylaxis (PrEP)—an acknowledged challenge for current HIV PrEP regimens.

Project objective

With United States Agency for International Development (USAID) funding, PATH is collaborating with Queen’s University Belfast (QUB) and ViiV Healthcare to develop dissolving MAPs for delivery of cabotegravir (CAB) for HIV prevention. Due to the dose required to be delivered, the CAB MAPs will be significantly larger than MAPs used for vaccine and high-potency drug delivery. Based on rat pharmacokinetic data and human population-based pharmacokinetic modelling data, we estimate the total
microneedle array area of a human size patch would be ~20 cm² to 40 cm²—likely multiple individual arrays applied simultaneously.

**Purpose of this Request for Assistance**
PATH is seeking a contract manufacturing organization (CMO) to establish a small-scale manufacturing process for CAB MAPs that could be used in the future to produce cGMP CAB MAPs for a Phase 1 proof-of-concept clinical trial. We expect production can be non-aseptic for clinical trial use.

**Scope of this work**

**Description.** PATH is seeking a cGMP CMO to conduct process development of dissolving MAPs formulated with CAB. Technology transfer will take place from QUB to the CMO, including transfer of analytical methods and formulation details. The CMO may need to travel to Belfast, Ireland, or members of the QUB team may need to travel to the CMO to ensure a successful technology transfer. Once agreements are in place and technology transfer is complete, the CMO will conduct a gap analysis and draft plans for establishing a small-scale GMP manufacturing process, which QUB and PATH will review. The CMO will then conduct process development and produce a non-GMP test batch of dissolving MAPs. A key deliverable for this project is a chemistry, manufacturing, and controls (CMC) data package that can be presented to the United States Food and Drug Administration (FDA) to inform an initial pre-Investigational New Drug (pre-IND) consultation with the FDA. The CMO should be ready to work with PATH, QUB, and PATH’s regulatory advisors to prepare for and participate in the pre-IND consultation. The CMO should expect to lead regular meetings with QUB, PATH, and the regulatory advisors to align all collaborators. The CMO should also expect to engage QUB, PATH, and the regulatory advisors for input on activities and documentation, as well as address recommendations, advice, and revisions from the project team. At the end of the project, the CMO will write a document that describes the manufacturing process in detail and complete a CMC data package; both documents should be provided to PATH and QUB (see Deliverables section). The test batch of GMP-like CAB MAPs will provide proof-of-concept evidence for the technical feasibility of clinical-scale and commercial-scale MAP production but will not be used in clinical trials (therefore, the test batch does not have to meet full GMP requirements and sign-off).

**Budget and duration.** Up to US$1,000,000. Budget should be detailed, reasonable, and realistic. The estimated duration of this work is 14 months; Table 2 shows the estimated timeline.

**Table 2. Estimated timeline.**

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Complete RFA process.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Select CMO, request USAID approval, and establish agreements.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tech transfer from Queen’s University Belfast to CMO.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Conduct gap analysis and draft plans for establishing a small-scale GMP manufacturing process.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Conduct process development.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
--- | --- | --- | --- | --- | --- | ---
Produce test batches of GMP-like material. |  |  |  |  |  |  
Complete CMC data package (in collaboration with PATH, QUB, and regulatory advisors) that will be required for an initial pre-IND consultation with the FDA. |  |  |  |  |  |  
Meet with and present to the FDA (regulatory advisors, not CMO, will drive the meeting forward, but CMO should expect to be active contributor and participant during the meeting). |  |  |  |  |  |  
Complete project documentation for GMP manufacturing process and CMC package and provide to PATH. |  |  |  |  |  |  

**Technical details**

**Viscosity of the formulation.** The formulation is viscous, like honey. Details about the API and required excipients will be provided upon signature of a mutual non-disclosure agreement (NDA).

**Expected doses.** The MAP dosage and size for testing in future human clinical trials (which are beyond the scope of this project) is still to be determined, but we do expect the MAPs to be large (approximately 20 cm² to 40 cm²). CMO should be prepared for dosage flexibility by developing a plan to assemble multiple microneedle arrays (e.g., 2 cm x 2 cm) to produce a single MAP.

**Dry time.** Once the liquid formulation is dispensed into MAP molds, there is a two-step drying process that can take up to 24 hours each at room temperature. Details about the dry time will be provided upon signature of the NDA.

**Manufacturing steps.** MAPs are currently formulated on the bench (lab-scale) in a two-step fabrication process, where the MAP molds are filled with a drug in the tips, the dried, and then filled again with a drug-free layer in the needle shafts. We are looking for a CMO to adapt the current lab-scale production process and develop a potentially scalable cGMP production process. Details about the current lab-scale manufacturing process will be provided upon signature of the NDA.

**Material Safety Data Sheet (MSDS) for cabotegravir.** We will provide a copy of the MSDS upon signature of the NDA.

**Equipment and technology.** QUB will conduct a complete tech transfer, including analytical methods, to the selected CMO. Table 3 and Table 4 show the equipment and technology needed at the CMO.

**Table 3. Equipment and technology needed for MAP projections/arrays.**

<table>
<thead>
<tr>
<th>Process step</th>
<th>Equipment/technology needed</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prepare polymeric gel</td>
<td>Double jacket tank, up to 100°C, mechanical mixture</td>
</tr>
<tr>
<td>Prepare drug-polymer gel</td>
<td>High shear mixer</td>
</tr>
</tbody>
</table>
| Fill MAP mold | • Drug-polymer gel micro-dispensing machine with homogenizer  
• Positive pressure chamber (up to 5 bar)  
• Scraper machine |
| Dry | Oven with shelves, up to 50°C |
Table 4. Equipment and technology needed for analytical methods.

<table>
<thead>
<tr>
<th>Type of analysis</th>
<th>Equipment/technology needed</th>
</tr>
</thead>
<tbody>
<tr>
<td>Quantitative</td>
<td>High-performance liquid chromatography (HPLC) with ultraviolet (UV) detector</td>
</tr>
<tr>
<td>Qualitative</td>
<td>Fourier-transform infrared spectroscopy (FTIR)</td>
</tr>
<tr>
<td>Thermal</td>
<td>Differential scanning calorimeter (DSC), thermal gravimetric analyzer (TGA)</td>
</tr>
<tr>
<td>Gel viscosity</td>
<td>Rheometer</td>
</tr>
<tr>
<td>Particle size</td>
<td>Particle size analyzer</td>
</tr>
</tbody>
</table>

**Deliverables for this work**

- Review, agree to, and sign an existing project confidentiality agreement (6-way) with current project partners.
- Fully executed materials transfer agreement with QUB.
- Molds procured and plans drafted for small-scale GMP production of CAB MAPs.
- Test batch of GMP-like placebo MAPs produced.
- Test batch of GMP-like CAB MAPs produced.
- CMC package for pre-IND consultation.
- Collaborate with PATH, QUB, and project regulatory advisors to prepare for and participate in pre-IND consultation with the FDA.
- Final CMC package, manufacturing procedures, and quality control (QC) test method documentation.

**Required qualifications and accomplishments**

1. Experience establishing novel cGMP manufacturing processes for novel dosage forms, including experience that could directly translate into development of a cGMP manufacturing process for large, dissolvable MAPs.
2. Team, facilities, and equipment needed to manufacture cGMP MAPs of various sizes (including large MAPs up to 40cm²) in a pilot production setting in preparation for a future Phase 1 clinical trial.
3. Regulatory (FDA) experience, including generation of a CMC package.
4. Demonstrated success planning, budgeting, and completing collaborative projects within budget and on time.
5. **DUNS number.** To be considered for this work, which is supported by US government funds, organizations **must** provide their DUNS number to PATH.
   - If organizations do not already have a DUNS number, they must immediately request one (at no cost) via this link: [https://fedgov.dnb.com/webform/newReq.do](https://fedgov.dnb.com/webform/newReq.do).
   - Step 1 below requires a DUNS number or proof of a DUNS number request (screen captures or receipt of request). Step 2 requires an assigned DUNS number.
   - Learn more at: [https://www.dnb.com/duns-number/get-a-duns.html](https://www.dnb.com/duns-number/get-a-duns.html).

**Application evaluation criteria**

1. Confirmation of eligibility for US government funding (verification conducted by PATH using DUNS number).
2. Completeness of application/proposal.
3. Technical capability, expertise, and previous experience.
4. Suitability of facilities, staff, and equipment to complete the scope of work.
5. Appropriateness of detailed budget; reasonable and realistic cost details.

How to respond to this Request for Assistance

NOTE: please do not submit proprietary/confidential information.

Step 1. Expression of interest. Email mapsforprep@path.org by the deadline (listed in Table 1. REVISED Schedule and deadlines) to express your interest, and include the following:
   a. Signed NDA (file included with this RFA).
   b. Organizational description (location, number of staff, mission, expertise, etc.).
   c. DUNS number or proof of request for a DUNS number (screen capture or request receipt).
   d. Answer to question: Has the organization ever received US government funding (directly or indirectly)?
   e. Questions about this RFA.

Step 2. Application/proposal. Email mapsforprep@path.org by the deadline (listed in the Schedule and deadlines table), and include the following:
   a. Technical capability (up to 1 page)
      ▪ Describe your organization’s manufacturing capabilities, types of facilities, location of manufacturing, technical certifications, etc.
      ▪ Past performance references: provide company name, contact name, and email address of two previous or current clients for whom you have produced MAPs.
   b. Technical proposal (up to 3 pages)
      ▪ Describe how your organization meets the needs listed in the Required qualifications and accomplishments section, and how you would work with PATH and its partners to achieve the deliverables.
   c. CVs (for relevant personnel only; no page limit).
   d. Detailed budget (use template provided).
   e. Budget narrative (no page limit). This document should describe how you arrive at your total dollar amount in each line item of your detailed budget.
   f. DUNS number, if not provided in Step 1. See number 5 in the Required qualifications and accomplishments section.

Step 3. Agreement. Upon selection of the regulatory services organization, PATH will work with the regulatory services organization to execute the required agreements to implement the work.
Terms and conditions of the Request for Assistance

A. Notice of non-binding solicitation

PATH reserves the right to reject any and all bids received in response to this solicitation and is in no way bound to accept any application. The applications submitted through this RFA process are the responsibility of the submitters and do not necessarily reflect the views of the United States Agency for International Development (USAID), the United States government, or PATH.

B. Confidentiality

All information provided by PATH as part of this solicitation must be treated as confidential. In the event that any information is inappropriately released, PATH will seek appropriate remedies as allowed. Applications, discussions, and all information received in response to this solicitation will be held as strictly confidential, except as otherwise noted.

C. Conflict of interest disclosure

Suppliers bidding on PATH business must disclose, to the contacts listed in the RFA, any actual or potential conflicts of interest. Conflicts of interest could be present if; there is a personal relationship with a PATH staff member that constitutes a significant financial interest, board memberships, other employment, and/or ownership or rights in intellectual property that may be in conflict with the supplier’s obligations to PATH. Suppliers and PATH are protected when actual or perceived conflicts of interest are disclosed. When necessary, PATH will create a management plan that provides mitigation of potential risks presented by the disclosed conflict of interest.

D. Communication

All communications regarding this solicitation shall be directed to appropriate parties at PATH. Contacting third parties involved in the project, the review panel, or any other party may be considered a conflict of interest and could result in disqualification of the application.

E. Acceptance

Acceptance of an application does not imply acceptance of its terms and conditions. PATH reserves the option to negotiate on the final terms and conditions. We additionally reserve the right to negotiate the substance of the finalists’ applications, as well as the option of accepting partial components of an application if appropriate.

F. Right to final negotiations

PATH reserves the option to negotiate on the final costs and final scope of work, and also reserves the option to limit or include third parties at PATH’s sole and full discretion in such negotiations.

G. Third-party limitations

PATH does not represent, warrant, or act as an agent for any third party as a result of this solicitation. This solicitation does not authorize any third party to bind or commit PATH in any way without our express written consent.

H. Application validity

Applications submitted under this request shall be valid for 90 days from the date the application is due. The validity period shall be stated in the application submitted to PATH.