



Request for Quote RFQ # 2017-007

Drug Product Manufacture: GMP Fill/Finish of Monoclonal Antibody

I. Summary of Deadlines

Release of Request for quote	Feb 13, 2017
Confirmation of interest due by	Feb 20, 2017
Fact-finding questions received by	Feb 27, 2017
Response to fact-finding questions by	Mar 6, 2017
Proposals due by	Mar 30, 2017
Selection of short-listed suppliers by	Apr 28, 2017
Conclusion of process by	June 30, 2017

Note that PATH reserves the right to modify this schedule as needed. All parties will be notified of any changes simultaneously by email.

II. 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.

MVI

Created in 1999 through a grant from the Bill & Melinda Gates Foundation, the PATH Malaria Vaccine Initiative (MVI) is a focused vaccine development program. MVI's mission is to accelerate the development of promising malaria vaccines and catalyze their availability and accessibility in the developing world.

As part of this mission, MVI is implementing targeted partnerships with scientists, vaccinologists, and development projects. MVI works to link government, industry, and academia partners with field trial sites in malaria endemic countries as early as feasible in the development process. To help ensure access

to the eventual vaccine(s), MVI works with vaccine programs, vaccine development partners, and the GAVI Alliance to identify strategies that will maximize public health sector availability in countries most affected by malaria.

For more information, please visit www.malariavaccine.org.

III. Project Background and Purpose of RFQ

A. Project background and objective of RFQ

PATH is developing two human monoclonal antibodies for phase I clinical trials in the US and Europe. In each case, the manufacturing of drug substance has begun and is expected to be completed by Jan 2018. PATH is seeking a GMP contractor to fill these products. The antibody drug substance will be delivered to you at a slightly higher than target drug product concentration in a frozen liquid form at -80°C. In addition to manufacturing (under cGMP) the drug product, we require release testing and stability studies to be performed. We are also inquiring your availability for frozen storage of drug product. The batches will require primary labeling and bulk packaging before shipment. The target fill volume is 10 mL and the batch size is 1,000-3,000 vials. Vials are anticipated to be borosilicate glass with rubber stopper and crimp seal, however the CMO may indicate appropriate container/closures available at their facility.

The complete project will include the following matrix for your proposal and budget purposes. It is understood a CMO may not be able to provide all the capabilities listed below and proposals are still highly encouraged for those capabilities within a CMO's scope.

<i>Activity</i>	<i>Fill/Finish of 1000-3000 vials of DP</i>	<i>Interim/interim release of DP to include compendial methods</i>	<i>Full release testing of DP to include antibody specific assays</i>	<i>DP Storage</i>	<i>Stability testing of DP</i>	<i>Regulatory/CMC support</i>	<i>IV Bag Compatibility study</i>
RFQ Module	Module I	Module I	Module II	Module III	Module IV	Module V	Module VI
Monoclonal Antibody #1	X	X	Optional	Optional	Optional	Optional	Not required
Monoclonal Antibody #2	X	X	Not required	Optional	Not required	Optional	Optional

B. Technology Transfer:

At the beginning of activities with the candidate CMO, you may assume the following activities will take place

- ~400g of frozen bulk drug substance will be shipped to you. Drug substance should be stored prior to fill/finish at -80°C.
- DS would have been tested for at least endotoxin and bioburden. The DS may be provided under quarantine status for further manufacturing.
Antibody specific analytical methods (non-compendial) will be provided.

Minimum scope of activities with candidate CMO

- A quality agreement will be drafted and negotiated between PATH and CMO during contracting and prior to commencement of GMP activities.
- Formulation fill finish of Drug Product under cGMP (two monoclonal antibodies total)
- Minimum release of two Drug Products under compendial methods

Optional in-scope activities with candidate CMO:

- Full DP release testing of monoclonal antibody #1 including antibody specific assays
- Drug product storage and distribution
- Conduct stability program for Drug product
- Writing relevant section of CTD
- Conduct IV-bag compatibility study

Out of scope activities not be considered or quoted:

- Lyophilization
- Extractable and leachable study
- Filling of Placebo

C. Proposed Project Timeline

There are 2 monoclonal antibodies to be filled; 2 distinct projects with 2 different project plans

Contract negotiations	3Q2017
Tech transfer activities to commence	4Q2017
Target cGMP of drug product manufacturing	1-2Q2018

IV. Scope of Work and Deliverables**Module I: Formulation Fill Finish**

Assumptions:

- You may assume the product is stable to be handled at room temperature.
- MVI will conduct a minimum of one onsite audit of the CMO.
- It is also the expectation that PATH shall be permitted a man-in-plant or on premises during critical activities including GMP activities.

In your description of the scope of work, please include (but not limited to) the following points

- Your receiving /quarantine process for drug substance and raw materials
- Your approach to minimize line loss
- In process assay: protein concentration, vial inspection, fill weight check
- Container closure preparation method (e.g. if materials are sourced sterile/depyrogenated or if they are washed, sterilized, and depyrogenated onsite).
- Type of container/closure you have validated and have media fill on file for. If a media fill is required, please clearly indicate in your proposal
- Raw material test release procedure
- Formulation buffer preparation procedure. Assume final volume of <50L
- Primary labelling, including if the facility/labeling allows for individual vial numbers.
- Bulk packaging
- BR preparation and approval process
- What has been/will be performed for sterility assurance
- What has been done to prevent cross contamination between lots/products

- Minimum release criteria for each drug product to leave facility including compendial testing available for both monoclonal antibodies. Such as:
 - Appearance (100% vial inspection)
 - Density/Fill weight
 - pH
 - Sterility
 - Endotoxin

DELIVERABLES

1. Minimum of 1000 vials, maximum of 3000 vials (budget should be reflective of 3000 vials, however final fill count will be dependent upon drug substance manufacture and yield).
2. Completed batch record
3. Interim release monoclonal antibody drug products

Module II: Optional full release testing of DP (required for monoclonal antibody #1)

- The product specific assays will be transferred from DS manufacturer. Please assume at a minimum the following types of assays will be available for transfer:
 - Capillary electrophoresis (SDS CE and cIEF)
 - ELISA
 - HPLC-SEC
- In your proposal, please indicate method transfer and qualification costs and appropriate timelines.
- Please provide proposed release assays and criteria in the proposal assuming a standard monoclonal antibody.

DELIVERABLES

1. QA released COA for drug product including relevant product specific assays for monoclonal antibody #1

Module III: Optional DP storage for up to 3 years

- Please provide your frozen storage (-80°C) and distribution availability
- Please indicate costs in a per year basis
- Please include brief description of temp monitoring, compliance of facility and emergency backup systems available.

Module IV: Optional stability testing of DP

Please provide DP stability proposal (3 yr real time and one accelerated condition for 6 months) and the available temperatures of your stability chambers.

DELIVERABLES

1. Stability results and final report

Module V: Support in CMC sections of regulatory filings with the FDA to include Pre-IND and IND (Optional)

- PATH retains the services of consultants and contractors to support full regulatory filings in eCTD format. However, the CMO should allocate appropriate resources to assist in preparation of CMC sections as appropriate for both Pre-IND and IND filings.

- During preparation of regulatory filings, one of our representatives may visit during regulatory dossier preparation to gather documents/work on critical aspects of the document including flow diagrams, material flows, etc.

Module VI: IV bag compatibility study (Optional)

- Please provide a proposal

V. Proposal Requirements - Financial

Provide itemized costs for the total scope of this project, based on the scope of work and deliverables outlined in Section IV. The final scope of work may be subject to negotiation; however, bidder selection will be made against the original scope of work. Bids should include itemized costs for key elements of the scope of work, as follows:

- The CMO proposal should clearly indicate costs associated for each monoclonal antibody drug product fill/finish and associated activities outlined in previous table. If a media fill is required, please indicate costs as a separate line item.
- Distinct activities (e.g. fill/finish, release, etc.) should be represented as distinct activities with a total budget reflected for each monoclonal antibody (refer to prior table for summary of activities for each monoclonal antibody). It is understood each CMO may not be able to perform all activities as outlined.
- Percent participation in total level of effort according to key staff.
- Rates of key staff.
- Estimated total level of effort and associated costs.
- Itemization of all other costs, e.g., agency costs, agency fees, service tax, administrative costs, supplies, etc.
- Estimated schedule of other anticipated expenses (travel, sub-contracted resources, supplies, outside resources, etc.)
- Detailed description of any subcontracted costs including work to be performed, rates, and whether the subcontract and budgeted figure is confirmed or projected. For any subcontract exceeding \$25,000, a copy of the proposed subcontract budget (by budget line item) should be included with the submission.
- Anticipated raw materials cost or appropriate budget is required and clearly represented as line items. This may also be represented as a maximum anticipated budget.
- Budget narrative describing costs, cost calculations, and rationale.

VI. Proposal Requirements – Technical

Provide a narrative on your technical approach to accomplish the Scope of Work and Deliverables per section IV. **Please make sure the following components are sufficiently addressed in the proposal.**

Please do not submit a draft legal agreement in format for consideration. PATH is conducting a request for quotation, for which based on a proposal a CMO will be selected and a final SoW (As determined between PATH and CMO) will be negotiated and drafted.

- Description of technical approach including:
 - Overall capability and capacity related to the scope of work
 - Brief narration of technology transfer of analytical methods including:
 - Management of technology transfer process and general flow of activities

- Transfer of DS into the facility
 - List of proposed analytical in-process tests and release tests. The list of release assays should then clearly indicate which are in-house and which are sub-contracted activities/assays
 - Stability study management (including storage and analytical testing)
- Provide a brief description of quality control and assurance procedures and systems in-place related to production and release testing for cGMP DP
- Brief discussion of project management and roles of project team
- Time line to meet the deliverables
 - If a candidate CMO is not available in the projected timelines provided they should include anticipated later availability.
- Potential obstacles and plan to overcome them
- Identification of major internal and external resources(subcontracts)
- Location from which the project would be managed. Location from which manufacture will occur.

Provide information on your overall qualifications, including:

- Formulation fill finish capability specific to monoclonal antibodies including line capacity and types of vials/closures available.
- Storage capabilities (of GMP product)
- Number of years in business; Annual Revenue and financial stability
- Inspection history
- Regulatory experience (e.g. number of candidates produced and support provided in regulatory filings). Note regulatory agency (e.g. FDA, EU, etc) and type of product (e.g. *E.coli* produced recombinant protein, mAb, etc).

VII. Proposal Evaluation Criteria

The following is a list of significant criteria against which proposals will be assessed. This list is not exhaustive or 100% inclusive, and is provided to enhance a company's ability to respond with substance:

- A. Technical. Compatibility and capability of CMO to handle monoclonal antibodies under the volumes and line capacity anticipated.
- B. Demonstrated experience with monoclonal antibodies
- C. Costs
- D. Timeline (Estimated timeline for completion; and availability for GMPfill/finish)

Note: PATH reserves the right to include additional criteria.

VIII. Instructions and Deadlines for Responding

A. PATH contacts:

Procurement Contact: Marie Zinck (mzinck@path.org)

Technical/Program Contact: Shwu-Maan Lee (smlee@path.org)

Financial Contact: Trevor Lutzenhiser (tlutzenhiser@path.org)

B. Confirmation of interest:

Please send a statement acknowledging receipt of this solicitation and your intent to respond or not respond no later than **Feb 20, 2017**. Send the confirmation to the contacts listed above. ***Proposals might not be considered if confirmation of interest is not received by the date indicated above.*** Expressing confirmation of interest is non-binding. There are no consequences if subsequent to confirming interest, you decide against submitting a proposal.

C. Fact-finding questions:

Questions on this solicitation will be accepted via email to the contacts listed above through **Feb 27, 2017**. Questions and answers to all questions will be provided to all participants who confirmed interest per Section VIII.B by **Mar 6, 2017**. Please note that responses will **not** be confidential except in cases where proprietary information is involved. Inquiries after this date cannot be accommodated. Questions and answers may be sent out in a number of rounds depending up until Feb 27, 2017 on the number and nature of the questions.

D. Proposals due: March 30, 2017

Completed proposals should be submitted by email to the contacts listed above. The subject line of the email should read: **RFQ 2017-007: Drug Product Manufacture: GMP Fill/Finish of Monoclonal Antibody**

We advise that you send files in commonly recognized MS or PDF formats. We will not accept responsibility for resolving technical transmission problems with proposals. A hard copy of the proposal should not be sent. Your proposal should only include information specific to accomplishing the scope of work. Additional information submitted outside of the proposal requirements will be reviewed at PATH's discretion only. Elaborate materials, artwork or other information not directly related to the scope of work are not suggested.

E. Selection of short-list

PATH reserves the right to select a short list from the bids received. PATH has the option to interview and discuss specific details with those candidates who are on the short-list.

F. Conclusion of process

Applicants will be notified of PATH's decision by June 30, 2017. Final award is subject to the terms and conditions included in this solicitation, as well as successful final negotiations of all applicable terms and conditions affecting this work.

IX. Terms and Conditions of the Solicitation

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 proposal.

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.

Proposals, discussions, and all information received in response to this solicitation will be held as strictly confidential, except as otherwise noted.

C. Communication

All communications regarding this solicitation shall be directed to appropriate parties at PATH indicated in Section VIII. A. 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 proposal.

D. Acceptance

Acceptance of a proposal 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' proposals, as well as the option of accepting partial components of a proposal if appropriate.

E. 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.

F. 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.

G. Proposal Validity

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