Production of Sabin Poliovirus Master and Working Seeds to Ensure Future Production of both Live and Inactivated Polio Vaccines

Request for Proposal (RFP)
The purpose of this Request for Proposal (RFP) is to enter into a contractual agreement with a successful bidder and, through a transparent process, select a suitable Contractor to produce and test Sabin poliovirus master and working seeds, including (but not limited to):

- Production of master Sabin viral seed (SO+2) from the current Sabin original (SO+1) WHO stock and for type 3 from the widely used Pfizer sub-strain (RSO1).
- Production of working Sabin viral seed (SO+3) to be prepared from the produced SO+2 master seed.
- Provide evidence that the seeds meet quality control specifications as outlined in the WHO Recommendations for the production and control of poliomyelitis vaccine (oral) (TRS, No 904 and 910, 2002) and relevant additional quality control tests (see section 2.3.3.).

WHO is an Organization that is dependent upon Member State funding for its activities. Therefore, it is vitally important that non health-related items that provide infrastructure support for the delivery of health services be cost-effective. For this reason, Vendors are requested to propose the best and most cost-effective solution to meet WHO requirements, while ensuring a high level of service.

Introduction

The Sabin strains of poliovirus used in the production of oral poliovirus vaccine (OPV) have been shown to yield vaccines that are both immunogenic and highly attenuated when administered orally to susceptible children and adults. Live vaccines prepared from the Sabin strains of poliomyelitis viruses of types 1, 2 and 3 were introduced for large-scale immunization in 1957. From then until 1972, Dr Albert Sabin himself distributed his strains to manufacturers; in 1972 he donated his strains to WHO to manage the distribution of the viral seeds for vaccine production.

Master seeds were generated from the original viruses produced by Sabin and were described as Sabin Original plus one passage level (SO+1). Working seed lots (SO+2) were also produced from the WHO master seeds. Although WHO has taken every possible precaution to ensure that these seeds meet the Recommendations for Poliomyelitis Vaccine (Oral), it is the responsibility of manufacturers and national control authorities in producing countries to ensure the quality and safety of the vaccines produced from the WHO seeds.

As mentioned above, WHO is the custodian of the Sabin master seeds used in the production of OPV. In addition, a sub-strain was rederived by RNA plaque purification (Pfizer sub-strain) and a master seed was established (RSO1). The RSO1 has been widely used for the production of the type 3 component. Given the interest of many manufacturers to produce inactivated poliovirus vaccines (sIPV), WHO predicts an increase in demand for these viral seeds during the coming years. Therefore, there is a need to produce more master and working seeds in order to handle the current and future demand.

WHO is requesting manufacturers of OPV to submit proposals for the production of master and working seeds from the current WHO Sabin poliovirus strains SO+1 for type 1 and 2 and the RSO1 for the production of type 3 poliovirus.

WHO will provide the Sabin original viral seed (SO+1) to the selected contractor to be used for the production of master and working seeds for type 1 and 2. For the production of master and working seeds for type 3, it is expected that the manufacturer will provide the RSO1.

The selected Contractor will develop a project including the production stages and testing activities according to their current master/working seed production procedures. The project plan should be used to track work and, if necessary, reflect changes in delivery time(s) of the produced master and working seeds during the course of the project.

Requirements
WHO requires the successful bidder, the Contractor, to carry out the production and quality control testing of master and working Sabin viral seeds.

The Contractor should be a manufacturer of WHO pre-qualified oral poliovirus vaccine that is produced in a continuous cell line (e.g. Vero or MRC-5). The manufacturer should be compliant with the cGMP.

**Eligibility information**

- The contractor shall be a manufacturer of OPV produced in a continuous cell line (e.g. Vero or MRC-5 cell lines)
- The contractor should be in a position to provide the RSO1 for the production of type 3 Sabin poliovirus seeds.
- The OPV produced by the Company must be a WHO pre-qualified vaccine
- Demonstrated compliance with current Good Manufacturing Practices (cGMP)
- Previous experience in producing and testing master and working Sabin viral seeds
- Trained and qualified personnel to perform the task under cGMP conditions

**Project deliverables**

The contractor should provide WHO with the new master and working Sabin viral seeds together with all relevant batch records and quality control test documentation.

The following tests should be performed to ensure the new viral seeds comply with the WHO Recommendations (TRS, No 904, 2002 and No 910, 2001) and with additional specifications:

<table>
<thead>
<tr>
<th>QC test (production in cell lines)*</th>
<th>Specification</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Cell cultures</strong></td>
<td></td>
</tr>
<tr>
<td>Test of control cell cultures</td>
<td>No abnormalities</td>
</tr>
<tr>
<td>Test for haemadsorbing viruses</td>
<td>Absence</td>
</tr>
<tr>
<td>Tests for other adventitious agents (supernatant)</td>
<td>Absence</td>
</tr>
<tr>
<td>Identity</td>
<td>Identity confirmed relevant to the cell line used</td>
</tr>
<tr>
<td><strong>Cell cultures for vaccine production</strong></td>
<td></td>
</tr>
<tr>
<td>Tests for adventitious agents</td>
<td>Absence</td>
</tr>
<tr>
<td>Tests for bacteria, fungi and mycoplasmas</td>
<td>No growth</td>
</tr>
<tr>
<td><strong>Control of single harvest</strong></td>
<td></td>
</tr>
<tr>
<td>Tests of neutralized single harvests for adventitious agents</td>
<td>Absence</td>
</tr>
<tr>
<td>Sterility tests</td>
<td>No growth</td>
</tr>
<tr>
<td>Test for molecular consistency of</td>
<td>Pass</td>
</tr>
</tbody>
</table>
production for type 3 (MAPREC)
Neurovirulence on monkeys**
RCT 40-Marker
Identity (seroneutralization)
Detection of retrovirus by PERT assay
Detection of SV40 by PCR

<table>
<thead>
<tr>
<th>Test</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>No significant difference vs the reference standard</td>
<td></td>
</tr>
<tr>
<td>Not less than 5.0 log10 between 36 and 40°C</td>
<td></td>
</tr>
<tr>
<td>Positive</td>
<td></td>
</tr>
<tr>
<td>Negative</td>
<td></td>
</tr>
<tr>
<td>Negative</td>
<td></td>
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</table>

* according to the WHO Recommendations TRS 904 and 910, 2002
** or current WHO requirement (e.g. transgenic mouse neurovirulence test) at the actual time of production of the new seeds.

Approval letter from the National Regulatory Authority will be needed and should be submitted to WHO together with the production information for master and working seeds including quality control test results outlined in section 2.3.3.

**Amount of master and working seeds needed.**

WHO estimates that within the next 20 years there will be a need for $48 \times 10^{10}$ doses based on the current usage of OPV and the potential development of inactivated poliovirus vaccines based on Sabin strains (sIPV) using the current manufacturing process for OPV (prior to inactivation in the case of a sIPV product).

Given the differences in the production process that each manufacturer has (e.g. initial viral inoculum in terms of MOI, efficiency of the purification and inactivation steps etc) it is not possible to accurately estimate the quantity of master and working viral seeds required for the next 20 years since this amount is product-specific and the information is not available to WHO. Therefore, WHO would like to request that the bidder manufacturers provide in their proposal the amount of master and working seeds that will be required to support the production of $48 \times 10^{10}$ doses according to their current manufacturing process for OPV. WHO understands that there will be limitations on the production capacity of the manufacturers to provide enough viral seeds to support the estimated doses, alternative approaches, including reduction of the proposed amount, may be included in the proposal for WHO consideration.

**Performance monitoring**

WHO will be in contact with the contractor to discuss any unexpected issues encountered during the production of the master and working viral seeds. However, the Contractor should inform WHO of any problems or delays expected in meeting the requirements of the proposal.

**Format and content**

- Executive Summary (one page) must be provided which describes the approach the manufacturer proposes to meet WHO’s requirements. Major elements of the Proposal should be listed clearly and concisely as well.

- The proposal may not exceed 30 pages (font 12). Annexes including CV’s etc are not included in the 30-page limit. There is no specific template for the proposal, however, the proposal should address the following points in the following order:
1. Project Plan

- Describe the plan of activities that will be performed
- Identify potential problem areas and discuss how these may be addressed
- Identify timelines, milestones and production plans

2. Management Plan

- Identify plans for the administration and management of the proposed activities, including plans on management of the funding if received, reporting and monitoring of activities and auditing of expenditures.

3. Budget justification

- Provide a budget justification, indicating production costs etc

Additional information such as Curricula Vitae, organizational charts etc will not count towards the 30-page limit.

Submission of proposals

- Electronic copies of the Proposal (in English), must be clearly marked “Production of Sabin Poliovirus Master and Working Seeds - Request for Proposal- should be sent by electronic mail to:

  Attn: Dr. David Wood
  World Health Organization
  20, Avenue Appia
  CH-1211 Geneva 27
  Switzerland

  E-mail address: woodd@who.int

- Electronic copies must be received by Dr. David Wood by midnight (Geneva time) Monday September 28, 2009. After this date no proposal can be considered for inclusion.

  A duly signed paper copy should be sent by regular mail and received by WHO in Geneva (address above) no later than October 15, 2009.

- Proposals submitted by any other method and/or in any other way will be rejected.

- At any time prior to the Closing Date for receipt of Proposals, WHO may, for any reason, modify the request for proposal and associated documents by amendment. All designated manufacturers will be notified in writing of these amendments, if any and any possible related extension of the Closing Date.

- WHO reserves the right to:
  o Award the Contract on the basis of the Organization's particular objectives
  o Award the Contract to a manufacturer of its choice
  o Award separate Contracts for parts of the work, components or items to one or more manufacturers of its choice
  o Not award any Contract at all

- The final decision on the selection of successful candidates will rest solely and exclusively with WHO. The submission of a Proposal does not entitle the party submitting such Proposal to claim compensation, financial or otherwise, from WHO.
• The technical evaluation of proposals will be accomplished by a Selection Panel. The Selection Panel will evaluate all proposals which have passed the Preliminary Examination of Proposals according to:

  o the quality of the overall proposal;
  o the appropriateness of the proposed approach;
  o the management strategy/plan detailed in the document;
  o the experience of the firm in carrying out related projects;
  o the qualifications and competence of the personnel proposed for the assignment;
  o the proposed timeframe for the project;