Polio Eradication Initiative

Call for Expressions of Interest (EoI)
Developing Sabin-Inactivated Polio Vaccine (sIPV)

The World Health Organization's Polio Eradication Initiative (WHO/POL) is looking for Expressions of Interest from private or public sector vaccine manufacturers in developing countries[1] interested in collaborating with WHO and the National Institute for Public Health and the Environment (RIVM) in the development, manufacture and distribution of a safe effective and affordable Sabin Inactivated Polio Vaccine (sIPV), that can be produced securely in developing country settings.

Further to Resolution WHA 61.1, directing WHO to develop safer processes for the production of inactivated poliovirus vaccine and affordable strategies for its use in developing countries, WHO is collaborating with RIVM in the implementation of a project which is aimed at:

- developing a safe and effective Sabin-IPV for the vaccination of humans against polio, including the establishment of a technology platform, compiling all necessary quality control tests for sIPV, standard operating procedures and documentation, and evaluating the safety and immunogenicity of a candidate vaccine; and
- transferring that technology to developing country vaccine manufacturers capable of securely producing sIPV.

Pursuant to this collaboration, RIVM has so far produced clinical lots of sIPV under Good Manufacturing Practices (GMP), established the technology platform, compiled all necessary quality control tests for sIPV and conducted a pre-clinical study on toxicity. RIVM has also compiled standard operating procedures and other documentation needed for the transfer of technology related to the production and quality control of sIPV. RIVM is currently conducting a phase I/II study in infants in Poland, in parallel with a real-time stability test and is working on further optimizing its production process

Following a first and second Call for Expressions of Interest in 2010[2] and 2011[3], respectively, WHO, in consultation with RIVM, is calling for a third round of Expressions of Interest from private or public sector vaccine manufacturers in developing countries interested in collaborating with WHO and RIVM in the development, manufacture and distribution of safe, effective and affordable sIPV targeted to and appropriate for public sector use in developing countries.

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[1] Developing country means any country classified or listed as such by the United Nations, i.e. any country other than Andorra, Australia, Austria, Belgium, Canada, Denmark, Finland, France, Germany, Greece, Iceland, Ireland, Italy, Japan, Luxembourg, Monaco, the Netherlands, New Zealand, Norway, Portugal, San Marino, Spain, Sweden, Switzerland, the United Kingdom, and the United States of America, it being understood that the status of any republic, previously included in the former Union of the Soviet Socialist Republics and the former Federal Socialist Republic of Yugoslavia, as well as Albania, Bulgaria, the Czech Republic, Hungary, Poland, Romania, and the Slovak Republic, shall be determined by the first document emanating from the United Nations system classifying or listing it as either a developed, a developing, or least developed country. Republics classified or listed in such document as a developing or least developed country shall be deemed as a developing country.

[2] A first Call for Expressions of Interest for Developing Sabin-Inactivated Polio Vaccine was issued on 1 June 2010 and resulted in the selection of two manufacturers for technology transfer.

[3] A second Call for Expressions of Interest for Developing Sabin-Inactivated Polio Vaccine was issued on 7 July 2011 and resulted in the selection of a further two manufacturers for technology transfer.

In this respect, it is intended that RIVM enter into bilateral technology transfer agreements with selected manufacturers, and provide training, capacity-building and assistance to such manufacturers for the in-country registration of sIPV for the vaccination of humans against polio. Any transfer of technology as aforesaid will be subject to the condition that: (1) the developing country manufacturers concerned have and continue to have the capability to produce securely [4] the licensed sIPV; and that: (2) RIVM may require each such manufacturer:

(i) to pay RIVM a modest compensation for the use of any pre-existing proprietary know-how of RIVM incorporated in the license; and

(ii) to reimburse RIVM for any costs, reasonably incurred by RIVM in actually transferring technology (it being understood that RIVM shall make every effort to limit such costs to the greatest extent possible).

With the exception of any pre-existing know-how of RIVM incorporated in the licensed method, the licensed method will be free of any applicable industrial property rights and will not necessitate the granting of licenses relating to proprietary know-how and information for the manufacture, use and distribution of the sIPV.

Subject to the above and as otherwise agreed by WHO and RIVM, the terms and conditions of the bilateral technology transfer agreements will be negotiated in good faith between the selected manufactures and the RIVM. In the event RIVM and a selected manufacturer fail to conclude a bilateral technology transfer agreement as aforesaid within a period of six months from the date of final selection of the manufacturer in question, WHO may -at its sole discretion- decide to cancel the selection of that manufacturer.

WHO will provide technical advice and assistance to the selected manufacturers in the development work and in collaboration with the relevant national regulatory authorities, be responsible for monitoring continued compliance by these manufacturers with requirements for secure production.

Interested private or public sector vaccine manufacturers must meet following "minimum criteria":

a) be located in a developing country;
b) have or be capable of readily acquiring in-house know-how on virus processing techniques, and have or be capable of readily investing in all utilities, facilities and other requirements needed for clinical development and large scale production of sIPV;
c) be committed to collaborating with WHO and RIVM in a manner consistent with the principles of WHO's global access strategy for sIPV;
d) agree to comply with and meet all current and future guidelines to produce sIPV securely, including the Global Action Plan (GAP) III requirements, in particular Annex IV ("Biorisk management standard for essential poliovirus facilities")[5], as and when such guidelines are adopted by WHO;
e) from the date of conclusion of the bilateral technology transfer agreement with RIVM, undertake to diligently produce clinical lots, initiate clinical trials within a period of 24 months, and use all reasonable efforts to apply for registration of the product in the country in which they are established within a period of 48 months;

[4] "produce securely" means production which after global OPV cessation meets the current requirements for post–eradication IPV production, as published in the WHO Technical Report Series, no 926, 2004 – "*Guidelines for safe production and quality control of inactivated poliomyelitis vaccine manufactured from wild polioviruses*". This definition of "produced securely" will be supplemented by any and all future updates and revisions of the aforesaid *Guidelines*. WHO's *Biorisk management standard for essential poliovirus facilities* and any and all updates and revisions thereof, as well as any future editions, updates and revisions of the WHO Global Action Plan for Laboratory Containment of Wild Polioviruses.

[5] Please refer to "WHO global action plan to minimize poliovirus facility-associated risk in the post-eradication/post-OPV era" (http://www.polioeradication.org/content/publications/GAPIIIWORKINGDRAFT_07.pdf)

f) have the capability to supply, or be able to readily make arrangements for the supply of, sIPV products to the public sector of developing countries in sufficient quantities to make a meaningful contribution to meeting global demand (e.g. at least 20 million doses annually);
g) agree to supply, or make arrangements for the supply of, sIPV products to the public sector of developing countries at a preferential and affordable price.

Interested parties should also:

1. preferably:

a) produce vaccine products that are regulated by one or more National Regulatory Authorities (NRAs) which have been assessed by WHO as functional[6]; and
b) have experience in manufacturing cell-culture derived vaccines, preferably OPV produced from viral seed strains;

2. ideally:

a) manufacture at least one WHO pre-qualified vaccine product, i.e. in particular pentavalent (DTP-Hib-HepB) product or OPV (either produced from viral seed or filled from supplied prequalified bulk);
b) have supplied prequalified product(s) to UNICEF and/or other UN procurement agencies in 2009-2011;
c) agree and be ready to allow for the technology transfer process to be initiated by Q3 2013 (e.g., training of production and QC staff, at small scale);
d) agree to develop both sIPV-combination and sIPV standalone products; and
e) agree to collaborate with WHO and RIVM in the conduct of possible future research if necessary (e.g., product optimization, manufacturing process improvement).

All expressions of interest should include information and supporting documentation on:

- The status, structure, main activities and location of the entity;
- CVs of key staff who would be responsible for the project;
- A copy of the entity's annual accounts over the last 5 years;
- Other records demonstrating the entity's sound financial standing;
- A list of the vaccine products licensed by one or more NRA(s), which have been assessed by WHO as functional;
- A list of cell-culture derived vaccine products manufactured by the entity (including those in development);
- A list of WHO pre-qualified products that are currently supplied to UN procurement agencies;
- An overview of: (i) WHO pre-qualified products which the entity has in the past supplied to UNICEF and/or other UN procurement agencies; and of (ii) other products, which the entity has in the past supplied to developing country markets
- Availability of suitable facilities to conduct large scale vaccine production;
- A checklist as per the attached format to demonstrate sufficient in-house technical expertise to securely produce and control sIPV;
- A commitment that the entity will from the date of conclusion of the bilateral technology transfer agreement with RIVM, undertake to diligently produce clinical lots, initiate clinical trials within a period of 24 months, and use all reasonable efforts to apply for registration of the product in the country in which it is established within a period of 48 months;

[6] See http://www.who.int/immunization_standards/national_regulatory_authorities%20/offices/en/index.html

- A commitment to comply with and meet all current and future guidelines to produce IPV securely, including GAP III requirements, in particular Annex IV ("Biorisk management standard for essential poliovirus facilities") [7], as and when such guidelines are adopted by WHO;
- A statement to indicate the entity's understanding of, and willingness to collaborating with WHO and RIVM in accordance with, the principles of WHO's global access strategy for sIPV, specifically by agreeing to:
  a) Develop vaccine targeted to and appropriate for public sector use in low- and middle- income developing countries
  b) Publish and disseminate the results arising out of the development work in consultation with WHO and without prejudice to any proprietary rights
  c) Grant WHO and any interested manufacturers in developing countries so designated by WHO, an irrevocable, non-exclusive, royalty-free, worldwide, license to any results which have not been so published or otherwise released in the public domain
  d) Support -on reasonable terms- subsequent transfer of the sIPV technology generated through this collaboration to other suitable manufacturers in developing countries so designated by WHO
  e) Make the vaccine available, or make arrangements for the availability of the vaccine, to the public sector of developing countries: (i) in sufficient quantities to make a meaningful contribution to meeting global demand (e.g., at least 20 million doses annually); and (ii) at a preferential and affordable price
- All other information and documentation that may be needed to demonstrate responsiveness to the requirements of this Call for Expressions of Interest

Manufacturers, which have submitted an EoI in response to the first and/or the second Call for Expressions of Interest, should submit all required information and documentation again, with a cover letter highlighting any changes from their responses to the previous Call(s).

On the basis of the Expressions of Interest received by it, WHO intends to invite selected candidates to submit a more detailed "business plan", for consideration by WHO. This business plan will need to include timelines for the sIPV development work, a detailed development plan of standalone and combination sIPV products, and a plan to share the technology with other manufacturers (More details will be communicated to those who will be invited to submit such a detailed business plan). WHO may also invite selected manufacturers for further discussions and/or to submit further information and documentation.

Subject to the terms of this Call for Expressions of Interest, WHO intends to select (in its sole discretion) two manufactures for technology transfer to take place in 2013. More manufacturers may be selected in subsequent years, based on a new Call for Expressions of Interest to be issued by WHO.

To promote wide geographical distribution and availability of sIPV, WHO aims to select two manufacturers from different countries, preferably in two different regions.

Interested entities are invited to submit their expressions of interest to WHO by **15 June 2012** at the latest, addressed as indicated in the box below.

[7] Please refer to "WHO global action plan to minimize poliovirus facility-associated risk in the post-eradication/post-OPV era" (http://www.polioeradication.org/content/publications/GAPIIIWORKINGDRAFT_07.pdf)

Any information considered by interested entities as confidential must be clearly marked as "confidential".

Incomplete expressions of interest and expressions of interest submitted after the deadline will, in principle, be disregarded (unless WHO, in its sole discretion, decides otherwise in respect of any such incomplete or late application).

WHO reserves the right to freely decide on the selection of those entities who will be invited for further discussions and/or for the submission of a more detailed business plan, in WHO's sole discretion, and without having to provide any justification to entities who will not be so invited. WHO further reserves the right not to follow up on any expression of interest at all.

WHO may request interested entities to submit further information and documentation. Any request for further information and documentation and any invitation for further discussions and/or for the submission of a more detailed business plan will be exploratory only, to evaluate the merits of a possible collaboration. Such discussions may be subject to appropriate safeguards of confidentiality.

WHO will advise all entities who have submitted an expression of interest whether or not they will be invited for further discussions and/or for the submission of a more detailed business plan. However, no explanation for the selection or rejection of any expression of interest will be provided, and the selection process will not be subject to any claims or appeal. WHO will not in any circumstances reimburse any costs or expenses associated with the submission of an expression of interest (including possible complementary information and documentation), nor any costs associated with possible further discussions and/or the possible submission of a more detailed business plan. The submission and selection process set forth in this document will not be subject to claims for financial compensation of any kind whatsoever.

Finally, it should be noted that although WHO welcomes collaboration with industry in the interest of promoting public health, WHO does not endorse any specific companies or branded products over others. In this regard, the WHO name and emblem may not be used for commercial or promotional purposes.

As noted above, the deadline for the receipt of applications is 15 June 2012

EXPRESSIONS OF INTEREST SHOULD BE SUBMITTED VIA E-MAIL AND COURIER MAIL TO:

Dr. HIROMASA OKAYASU
POLIO ERADICATION INITIATIVE
WORLD HEALTH ORGANIZATION,
20 AVENUE APPIA
1211 GENEVA 27
SWITZERLAND

EMAIL: polioresearch@who.int
And also visit the website http://www.polioeradication.org/

Appendix: a checklist for technical expertise

Processing techniques	Experience with processing techniques	Processing technique available for sIPV project				Remarks[8]
		Techniques readily available	(If techniques not available), willing to invest?	Funding available?	If funding not available, how do you propose to ensure such funding?	
Cell cultivation (on micro carriers) and harvesting	Yes ☐ No ☐	Yes ☐ No ☐	Yes ☐ No ☐	Yes ☐ No ☐		
Virus cultivation	Yes ☐ No ☐	Yes ☐ No ☐	Yes ☐ No ☐	Yes ☐ No ☐		
Clarification of virus containing medium	Yes ☐ No ☐	Yes ☐ No ☐	Yes ☐ No ☐	Yes ☐ No ☐		
Concentration techniques (i.e. ultrafiltration)	Yes ☐ No ☐	Yes ☐ No ☐	Yes ☐ No ☐	Yes ☐ No ☐		

[8] Please clarify the experience and available capability (lab scale or production scale, research or commercial purposes; products involved; used techniques etc.)

Company:
Date:
Name, designation:
Signature:

Processing techniques (continued)	Experience with processing techniques	Processing technique available for sIPV project				Remarks[9]
		Techniques readily available	(If techniques not available), willing to invest?	Funding available?	If funding not available, how do you propose to ensure such funding?	
Size exclusion chromatography	Yes ☐ No ☐	Yes ☐ No ☐	Yes ☐ No ☐	Yes ☐ No ☐		
Ion exchange chromatography	Yes ☐ No ☐	Yes ☐ No ☐	Yes ☐ No ☐	Yes ☐ No ☐		
Inactivation	Yes ☐ No ☐	Yes ☐ No ☐	Yes ☐ No ☐	Yes ☐ No ☐		
Sterile filtration and filter testing's	Yes ☐ No ☐	Yes ☐ No ☐	Yes ☐ No ☐	Yes ☐ No ☐		
Formulation and aseptic final product filling	Yes ☐ No ☐	Yes ☐ No ☐	Yes ☐ No ☐	Yes ☐ No ☐		

[9] Please clarify the experience and available capability (lab scale or production scale, research or commercial purposes; products involved; used techniques etc.)

Company:
Date:
Name, designation:
Signature:

Quality control tests	Experience with quality control tests	Testing capacity available for sIPV project				Remarks[10]
		Testing capacity readily available?	(If testing capacity not available), willing to invest?	Funding available?	If funding not available, how do you propose to ensure such funding?	
Animal testing (potency of vaccines)	Yes ☐ No ☐	Yes ☐ No ☐	Yes ☐ No ☐	Yes ☐ No ☐		
Neurovirulence Testing (safety of vaccines)	Yes ☐ No ☐	Yes ☐ No ☐	Yes ☐ No ☐	Yes ☐ No ☐		
ELISA techniques	Yes ☐ No ☐	Yes ☐ No ☐	Yes ☐ No ☐	Yes ☐ No ☐		
Inactivation testing	Yes ☐ No ☐	Yes ☐ No ☐	Yes ☐ No ☐	Yes ☐ No ☐		

[10] Please clarify the experience and available testing capability (on which product, routine testing or incidental testing and details on tests and experience)

Company:
Date:
Name, designation:
Signature:

Utilities and facilities requirements	Experience with utilities and facilities	Utility and facility available for sIPV project				Remarks[11]
		Utilities and facilities readily available?	(If utilities and facilities not available), willing to invest?	Funding available?	If funding not available, how do you propose to ensure such funding?	
HVAC	Yes ☐ No ☐	Yes ☐ No ☐	Yes ☐ No ☐	Yes ☐ No ☐		
Autoclaving (both for sterilization and destruction)	Yes ☐ No ☐	Yes ☐ No ☐	Yes ☐ No ☐	Yes ☐ No ☐		
WFI system	Yes ☐ No ☐	Yes ☐ No ☐	Yes ☐ No ☐	Yes ☐ No ☐		
Clean steam system	Yes ☐ No ☐	Yes ☐ No ☐	Yes ☐ No ☐	Yes ☐ No ☐		
Kill tank	Yes ☐ No ☐	Yes ☐ No ☐	Yes ☐ No ☐	Yes ☐ No ☐		
Biosafety level (2 or 3)	Yes ☐ No ☐	Yes ☐ No ☐	Yes ☐ No ☐	Yes ☐ No ☐		

[11] Please clarify the experience and available capability (specify techniques, numbers of unites and indication of scale; biosafety level if applicable)

Company:
Date:
Name, designation:
Signature:

Other requirements	Experience with requirements	Capacity available for sIPV project				Remarks[12]
		Capacity readily available?	(If capacity not available), willing to invest?	Funding available?	If funding not available, how do you propose to ensure such funding?	
QA Is there a general Quality Assurance system in place at your facility?	Yes ☐ No ☐	Yes ☐ No ☐	Yes ☐ No ☐	Yes ☐ No ☐		
GMP Is there a GMP system in place?	Yes ☐ No ☐	Yes ☐ No ☐	Yes ☐ No ☐	Yes ☐ No ☐		
Validation To what extent do you have experience with the validation of equipment, utilities and processes?	Yes ☐ No ☐	Yes ☐ No ☐	Yes ☐ No ☐	Yes ☐ No ☐		
Clinical trial expertise Phase I Phase II Phase III	Yes ☐ No ☐	Yes ☐ No ☐	Yes ☐ No ☐	Yes ☐ No ☐		
Post marketing surveillance	Yes ☐ No ☐	Yes ☐ No ☐	Yes ☐ No ☐	Yes ☐ No ☐		

[12] Please clarify the relevant experience and available capacity in details

Company:
Date:
Name, designation:
Signature: