



**IMMUNIZATION, VACCINES AND BIOLOGICALS (IVB)
INITIATIVE FOR VACCINE RESEARCH (IVR)**

APPLICATION FOR SUPPORT FOR A COLLABORATIVE RESEARCH PROJECT

GENERAL INFORMATION AND INSTRUCTIONS

1. Eligibility and review of proposals

Only proposals submitted on the requisite application form will be considered. All research proposals received by WHO will be treated in confidence and are subject to external review. WHO will, in its sole discretion, decide on the selection of any projects for funding, and reserves the right not to select or fund any proposal at all, to require the amendment of project proposals in order to be eligible for funding, and/or to provide partial funding. In addition, WHO reserves the right to amend the project requirements at any time prior to the completion of the selection process, by communicating the amended requirements to all applicants. WHO will advise all entities who have submitted a proposal whether their proposal has been accepted or rejected. WHO may, but shall not be held to, provide any explanation in this communication as to the reasons for the selection or rejection of any proposal. The selection process will not be subject to any further correspondence, claims or appeal.

2. Financing of approved projects

Approved projects will be funded through Technical Services Agreements, or similar contracts (the "Agreement") between WHO and the entity responsible for the project, including inter alia the conditions described in the Request for Proposals and this document. Projects may, subject to availability of funds and other considerations, receive an approval in principle for a period of one or two years. However, funding is always provided on a yearly basis and any extension of support for a second year is subject to satisfactory progress and to the availability of funds.

3. Payments

3.1 Payments are made in accordance with the Agreement which shall specify the schedule of payments to be made over the contract period, e.g. annually or biannually.

3.2 Agreements may provide for various methods of payment which may be subject to change in the course of implementation of the project. WHO reserves the right to request the return to WHO of any unused funds following completion or termination of the project.

3.3 A financial report on the use of funds shall be submitted to WHO as part of the annual progress and final reports required by paragraph 11 below. Financial reports shall be submitted under the signature of the entity's principal finance officer. Financial reports are subject to audit by WHO's auditors or audit by its designee, at WHO's discretion. In order to facilitate such financial reporting and audit, the entity shall keep accurate and systematic accounts and records in respect of the project and shall permit WHO to inspect them upon request.

4. Principal Investigator and Entity

4.1 The Principal Investigator is the individual who shall be responsible to the Entity for all technical aspects of the work referred to in the Agreement. The principal investigator will be associated with and responsible to the entity.

4.2 WHO policy does not permit salary support for Principal Investigators. If the proposal requires the collaboration of scientists in other entities, evidence of their willingness to collaborate should be attached to the application.

5. Equipment and supplies

5.1 Consumable supplies and equipment for the project being supported, including chemicals, reagents, animals, animal foods and other special items, may be purchased from WHO funds. Normally the Programme will not support the purchase of substantial items of equipment.

5.2 However, if the availability of such equipment is critical for the execution of the work, funds up to a maximum of US\$10 000 may be provided. The Programme does not support the establishment of new laboratories or the purchase of computers.

5.3 Arrangements can be made for WHO to hold funds awarded for the purchase of supplies on behalf of investigators/entities from non-OECD countries. However, WHO is obliged to institute certain limitations on the time during which purchases of supplies and equipment can be ordered through the Organization with such and held in trust. Accordingly, any balances under Agreements which have not been used for purchases within one year of the funds being made available, will revert to WHO on the following 31 December.

6. Administrative and overhead costs

WHO will consider financial support only for activities, services or materials clearly itemised and justified in the budget accompanying the proposal. Requests for "overhead", "administrative" or "miscellaneous" expenses will not be considered.

7. Other financial regulations

Funds provided cannot be used for the construction of buildings. They may not be used for meetings, unless specified in the agreement. Travel may be paid only if it is essential to the successful execution of the work and itemised in the approved budget.

8. Reports

8.1 The Principal Investigator shall submit to WHO an annual progress report and financial statement (see paragraph 3.3) in the required format, at the time specified. This report forms a part of the project evaluation and is essential for continuation of the support for the project.

8.2 Final reports should summarize the course of the research and give in some detail the positive and negative findings of the work in relation to the objectives of the Programme. WHO must be informed promptly of any major changes or significant deviation from the activities covered by the Agreement.

9. Access to results, release of results in the public domain and publication

In light of the recognized public interest benefits which may be achieved through the publication of new scientifically valuable information, entities and principle investigators may generally publish the results of research funded by WHO, except when and to the extent it is deemed necessary to maintain such results in confidence in order to promote the development of those results into a useful health related product, including inter alia through protection by property rights. Publication can be made in any journal, although publication in refereed journals is preferred. The responsibility for the direction of the work should not be ascribed to WHO. All publications will include a footnote as follows (unless WHO advises otherwise):

"This investigation received financial support from the Initiative for Vaccine Research (IVR), WHO Department on Vaccines and Biologicals (V&B)".

In the event of publication by the entity, two off-prints or copies should be sent to WHO.

10. Departure or change of Principal Investigator

Should the Principal Investigator leave the entity with which the Agreement is concluded, or cease to actively direct the project, the entity must notify WHO, who shall have the right to terminate the Agreement. If another Principal Investigator is appointed by the entity, the project may be continued, provided the approval of WHO is obtained.

11. Employer's liability

When staff are paid from WHO funds, WHO does not assume any liability as an employer and the employees work under the entity's normal regulations and discipline. Such staff are not entitled to describe themselves as WHO staff.

12. Research involving the use of laboratory animals

The entity shall undertake that living vertebrate animals required for use in research pursued under the Agreement with WHO will be handled in accordance with locally existing statutes and/or generally accepted principles for humane treatment of such animals. In all cases the avoidance of unnecessary suffering will be mandatory.

13. Research involving human subjects

13.1 Ethical aspects of the project

It is the responsibility of the entity and the Principal Investigator to safeguard the rights and welfare of human subjects involved in research supported in whole or in part by funds from WHO in accordance with the appropriate national code of ethics or legislation. WHO funds may be used only to support investigations where (a) the rights and welfare of the subjects involved in the research are adequately protected, (b) freely given informed consent has been obtained and (c) the balance between risk and potential benefits involved has been assessed and deemed acceptable by a panel of independent experts at the entity. The investigator must submit to WHO the written approval of an institutional ethical review panel to carry out the proposed research involving human subjects, together with a copy of the Informed Consent. For countries with national ethical review bodies for research involving human subjects, written agreement from such a body must be submitted to WHO with the research proposal. In the absence of national ethical review bodies, the investigator shall be guided by the Declaration of Helsinki supplemented by the revised and extended version of the Declaration adopted by the Twenty-ninth World

Medical Assembly in Tokyo (October 1975) and Article 7 of the International Covenant of Civil and Political Rights, adopted by the United Nations General Assembly on 16 December 1966. Before a final approval is given for WHO funding, the proposal should be reviewed and approved by the WHO Secretariat Committee on Research Involving Human Subjects (SCRIHS). WHO will, on request, advise scientists regarding the ethical aspects of planned research projects.

13.2 Regulatory requirements for drugs and devices

It is the responsibility of the entity and the Principal Investigator to comply with national regulations pertaining to clinical studies of drugs or devices. WHO shall, on request, arrange to make available information in WHO's possession as may be required by national regulatory agencies.

13.3 Security measures

It is the responsibility of the entity and the Principal Investigator to ensure that the safety and environmental aspects of projects involving live organisms are considered and covered and a statement to that effect must be included in the application for support. For projects involving DNA research, a statement that safety regulations have been met, signed by the Director of the entity, must accompany the application.

13. National requirements

In instances where national approval is required, the entity and Investigator are responsible for obtaining any review and approval of proposed projects by national authorities, prior to formal submission of the proposal to WHO. A document indicating such approval must accompany the submission of the proposal to WHO.

14. Project description (Page 6 of application form)

15.1 Objectives

State clearly the objectives of the project and indicate the hypothesis to be tested and questions to be answered.

15.2 Rationale and relevance

- (a) outline the rationale in relation to: the requirements set forth in the RFP
- (b) outline the present status of scientific knowledge relevant to the proposed project, and similar current research within the entity or elsewhere. Indicate why the project is scientifically feasible within the estimated time and resources requested.

15.3 Experimental design and methodology

Include all relevant details on experimental design, methodology and statistical methods as well as an approximate schedule for each part of the proposed plan of work. This plan and schedule should indicate clearly the logical progression of the work towards the objectives of the project. Please note the following guidelines:

- (i) For laboratory studies:

The following should be clearly outlined:

- experimental design
- statistical design and proposed analysis
- standard methodology to be employed (with relevant literature references); include information on whether:

it is already established in the laboratory
personnel are adequately trained
equipment and its maintenance are adequate
reagents are readily available

- new methodology; include information on:

detailed procedure(s) proposed
equipment available and whether new equipment is required
personnel available and required
alterations in facilities required (e.g. cold room, fume cupboard, small animal room)
other information to enable an expert reviewer to assess the proposed approach

(ii) For clinical studies

(a) Protocol design

Outline clearly and include:

- type of protocol (e.g. controlled, double-blind, etc.)
- the number of treatment groups
- the characteristics of the study population and each group therein
- the kind and frequency of observations
- the frequency, timing and route of administration of the proposed agent or drug
- the statistical design and analyses to be carried out

(b) Protocol operation

Describe how the trial will be carried out and include:

- Inclusion and exclusion criteria for subject selection

Describe the origin of the study population (e.g. school children, village residents, medical students, nurses, laboratory assistants, etc.). Specify in detail all characteristics required for participation in each observation or treatment group (e.g. age limits, special physical or physiological requirements, such as height, weight, haemoglobin level). Provide in detail the specific contraindications for admission to the study;

- Admission procedure

Attach a copy of the admission form, showing details of history to be taken, physical examination and laboratory tests;

- Subject allocation

State the method of allocation to the observation group or treatment

group, e.g. random allocation using random table, open allocation (physician's choice, subject's choice), etc.;

- Criteria for discontinuation

(1) of individual subject in study: specify all the conditions that would require dropping the subject from the study (e.g. specific side-effects, loss of follow-up, etc.);

(2) of the study itself: the criteria for premature termination of the study should be spelt out, e.g. lower than 94% confidence limits for cure or prevention rates in an efficacy study or side-effect rates in a study on safety;

- Follow-up

Attach a copy of the follow-up form showing details of history, physical examination and laboratory tests.

(iii) For field studies:

(a) Indicate the study area and give description of, or reference to, geography and climate.

(b) Describe the sociological and cultural background of the human population involved. When their active cooperation will be sought, indicate ease of linguistic communication or language training needs, as well as how the proposed studies will be explained to them.

(c) The estimated duration of:

- planning and preparation phase (pre-testing questionnaires, purchase and organization of material and logistics);
- actual data collection in the field;
- compilation of data results from laboratory studies (serology, etc.);
- data analysis

(d) Description of methodology:

- method of definition of the population, cohort or sample e.g. mapping and census, randomization, etc.;
- detailed methods of data collection, e.g. standardized questionnaires, physical examination, serological tests, etc.;
- methods of data recording, e.g. laboratory books, direct recording on computer-oriented records;
- methods of data analysis, e.g. computer programming and analysis, manual calculator.

(e) Indicate available personnel and equipment (i.e. vehicles, permanent apparatus).

(iv) Ethical considerations for projects involving human subjects

(a) Protocols for projects involving human subjects must be reviewed and approved by an independent institutional ethical body prior to formal submission to WHO (attach documentation of approval).

(b) National ethical bodies for the regulation of human experimentation, if they exist, should review and clear the proposal prior to formal submission to WHO (attach documentation of approval).

- (c) For all protocols or projects involving human subjects:
- Indicate the benefits and any known risks or inconveniences to the subjects involved in the study.
 - Describe precisely the information which will be conveyed to potential subjects of the study and the manner, oral or written, by which this information ¹ is to be conveyed. If a written consent form is to be used, attach a sample. The name(s) and status of the project staff member(s) who give(s) this information to potential subjects and who ascertain(s) that it is understood and that the consent is given freely by the subject, must be included.
 - Indicate any special incentives or treatment the subjects received for their participation (e.g. money for transport, stipends for participation, food or medication, etc.). Whenever payment is involved, specify amounts, manner and timing.
 - Indicate how the confidentiality of all information obtained during the course of the study, relating to participants included in the study, will be maintained.
- (d) List all drugs, vaccines, diagnostic or other procedures to be used, regardless of whether these are registered, unregistered, new or already in current use, in the country in question or elsewhere. State the manufacturers of each compound, vaccine or agent ².

NEW DRUGS: for new drugs, vaccine or agents being used for the first time on man or still at an early stage of clinical study, or being used by a new route or dose schedule, state the chemical composition of the drug, the source of the drug to be used in the study, amount present per dose, and the tests undertaken to establish and control the quality of the drug to be administered.

The Investigator should describe concisely the main pharmacological actions of the compounds to be used and provide appropriate safety data including results of studies already conducted in humans, if these are available. For new drugs, this type of information is required, not only for the active compounds but also for the vehicle or carrier of such drugs, e.g. an adjuvant in the case of a vaccine.

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- 1 Examples of information to be given to potential subjects include: aims of the research, the procedures which are experimental, any known short- or longer-term risks, possible discomfort, anticipated benefits from the procedures to the subject or others, expected duration of the study, alternative methods of treatment available if the study is a treatment procedure, and the freedom of the subject to withdraw from the study at any time.
- 2 For drugs or vaccines already widely used, the investigator should give the proprietary names, composition, doses to be administered and the name and address of the manufacturer.

15. Budget guidelines

15.1 The budget should be developed directly from the activities which will be carried out and the costs of the resources required to accomplish these activities. For example, carrying out the protocol for a clinical trial to establish the effective dose of a new therapeutic agent may require, for each subject in the study:

- interviews
- complete history and physical examination
- initial laboratory tests
- repeated history and physical examination
- repeated laboratory tests
- long-term follow-up including history, physical examination and laboratory tests.

15.2 The activities could involve visits to the subjects' homes to obtain better follow-up. Data analyses will also have to be provided. Such a trial could be costed on a per patient basis by adding the activities and averaging the cost per patient. Costs, especially for laboratory-oriented research, could be broken down into total numbers of man-months (e.g. technician: 6m/m; secretary: 4 m/m), rental or purchase of equipment and its maintenance, purchase of supplies and chemicals, special patients' costs (e.g. travel, incentives to participate, reimbursement of lost income, etc.), transport for follow-up home visits, purchase of animals and their maintenance, etc.

15.3 The funds requested must be justified by the research activities to be carried out, regardless of the method used to develop the budget. Therefore, for each item in each category, state how the cost figures were derived in relation to the activities to be undertaken.

15.4 The following constraints should be noted:

- (a) personal support for the principal investigator will not be considered;
- (b) major equipment will not normally be considered;
- (c) travel will be considered only if clearly essential to the successful implementation of the project;
- (d) overhead costs will not be accepted.

All applications should be addressed to:

Initiative for Vaccine Research (IVR)
Vaccines and Biologicals
Health Technology and Pharmaceuticals
World Health Organization
20, Avenue Appia
1211 Geneva 27
Switzerland

Facsimile numbers:

WHO General: (41.22) 791 07 46
IVR Direct: (41.22) 791 48 60
Email: fishern@who.int