

CONRAD

Guidelines for Submitting Applications

Updated July 2008

The CONRAD program is conducted under a Cooperative Agreement with the United States Agency for International Development (USAID) to develop, evaluate and obtain approval for improved and/or new reproductive health (RH) technologies that provide contraception and/or prevent the sexual transmission of HIV/AIDS and other infections. To this end, CONRAD supports timely and high-quality subprojects conducted by collaborating investigators at universities, research institutes, and private companies worldwide. Priority is given to moving promising leads through Phase I and II clinical trials. This may include appropriate preclinical studies which contribute directly to the development of specific contraceptive products. Research to develop contraceptives that reduce transmission of human immunodeficiency virus (HIV) and other STD pathogens is also of interest.

Funding for research is provided through cost-reimbursed Subproject Agreements which require financial reports quarterly and technical reports semiannually. A collaborative approach between the investigator and the CONRAD program staff is used in assessing progress and targeting future studies. Substantial involvement of CONRAD staff may be appropriate depending on the nature of the subproject.

SUBMISSION OF APPLICATIONS

All potential applicants are strongly encouraged to consult the CONRAD program staff before preparing an application for research support, and to submit a brief Preliminary Proposal before preparing a Full Proposal. Submission of the Preliminary Proposal is not mandatory, but is intended to assist the applicant.

All application materials should be written in English, typed single-spaced on 82 x 11 inch or A4 paper in 10-12 point type, and submitted in duplicate.

U.S. citizenship is not required for applicants.

Preliminary Proposals: The Preliminary Proposal should be brief (no more than five pages) and describe the research being considered for submission, including:

1. a clear statement of the objectives and expected results
2. an outline of the approach and methods to be used
3. an estimated budget, and
4. a brief curriculum vitae or summary of the investigator's qualifications

These Preliminary Proposals will be reviewed by the CONRAD Program staff, and comments will be returned in a timely manner. Those investigators whose Preliminary Proposals are

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considered appropriate for further consideration will be invited to submit Full Proposals, as described below, for complete peer review of programmatic and scientific merit.

Full Proposals: Full Proposals may be submitted to CONRAD for either Pilot Subprojects or Regular Subprojects, and must follow the complete format for Full Proposals that is provided below.

Pilot Subprojects are generally of one year or less in duration, have a total budget of up to \$25,000 (U.S.), and are intended to demonstrate feasibility and produce preliminary results on which future research proposals to CONRAD or other agencies may be based. Applications for Pilot Subprojects may be submitted at any time and must address each section of the Full Proposal format, but may be relatively brief. Applications for Pilot Subprojects will receive timely review by CONRAD staff and consultants.

Regular Subprojects should be fully justified based on existing data and should address all sections of the Full Proposal format in detail. Applications for Regular Subprojects may also be submitted at any time.

All application materials, and any administrative questions regarding the preparation of the application materials, or technical questions regarding the scientific aspects of the proposed research, should be directed to:

CONRAD

1911 North Fort Myer Drive, Suite 900
Arlington, VA 22209
USA

Phone: (703) 524-4744

Fax: (703) 524-4770

Internet: info@conrad.org

FORMAT FOR PREPARATION OF FULL PROPOSALS

All Full Proposals should address each of the relevant sections indicated below.

1. **Cover Page**

- A. Brief descriptive title of the proposed subproject
- B. Names of the proposed investigator(s) and institution(s)
- C. Indication that the application is being made to the CONRAD Program
- D. Date of submission

2. **Title Page**

- A. Subproject title
- B. Name, academic degrees, title, mailing address (and street address for deliveries, if different), telephone number, fax number, and signature of the:
 - 1) Principal investigator (P.I.)

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- 2) Official authorizing the P.I. to submit the application (e.g., department chairperson or dean)
 - 3) Official authorized to bind the institution contractually (i.e., who will sign the Subproject Agreement for the institution)
- C. Proposed duration of subproject with annual and total costs requested
 - D. Statement indicating that it is understood that the application, if approved and funded, is to be administered under a cost-reimbursed Subproject Agreement (not a grant) with the CONRAD Program
 - E. Name of the institution to which reimbursement checks are to be made payable (Reimbursement checks cannot be made payable to individuals.)
 - F. Exact address to which checks should be mailed, including the name of any person to whose attention the checks should be directed
 - G. Tax Payer ID Number for the recipient institution
3. **Table of Contents**

Indicate page locations for each of the principle sections of the proposal.
 4. **Summary** (no more than two single-spaced pages)

Provide a Summary of the proposed research, including:
 - A. A concise statement of the General Objectives
 - B. How the objectives contribute to the mission of the CONRAD Program to improve or develop new contraceptive products for developing countries
 - C. The general approach proposed, and
 - D. A list of the Specific Aims
 5. **Description of the Proposed Research** (no more than ten single-spaced pages, exclusive of appendices)
 - A. ***For Preclinical Studies:***
 - 1) **Introduction and Background** - Describe:
 - a. The overall design of the proposed subproject
 - b. The relationship of the proposed subproject to present knowledge in the field
 - c. Relevant work by the applicant(s) and others in the field, including results of any preliminary studies and complete citations for all published information

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Relevant publications or other materials may be included as appendices but should not be substituted for a complete discussion in the Introduction and Background section.

- 2) Detailed Description of the Proposed Studies - Describe:
- a. The experimental design, with an explicit rationale for each step
 - b. The methods to be used, with an evaluation of their feasibility and limitations, and complete references
 - c. All data to be collected, with statistical justification of proposed sample sizes
 - d. The method of analysis
 - e. All potential obstacles, scientific or other, with proposed solutions
 - f. A schedule for completing each phase of the proposed studies

As above, relevant publications, etc., may be appended but should not be substituted for a complete description of the proposed studies.

- 3) Anticipated Results - Describe all of the expected results from the proposed subproject, including data, chemical or pharmaceutical agents, devices, publications, actions undertaken relative to regulatory agencies, and others.

B. *For Clinical Studies (Phase I and II Clinical Trials):*

Ordinarily, the principal investigator for subprojects involving human subjects in a clinical study will assume the roles of both a sponsor and an investigator. In multicenter studies organized by the CONRAD Program, however, only the responsibilities of an investigator will be applicable.

Sponsors are responsible for:

- Selecting qualified investigators (in this case, sub-investigators)
- Providing investigators with the information needed to conduct investigations properly
- Ensuring proper monitoring of the investigation(s)
- Ensuring that the investigations are conducted in accordance with the General Investigational Plan and protocols contained in an Investigational New Drug Exemption (IND) or Investigational Device Exemption (IDE) from the U.S. Food and Drug Administration (FDA)
- Maintaining an effective IND or IDE with respect to the investigations

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- Ensuring that the FDA and all participating investigators are promptly informed of significant new adverse effects or risks with respect to the drug or device, and
- Having the drug or device under investigation shipped only to qualified investigators participating in the study

Investigators are responsible for:

- Ensuring that an investigation is conducted according to the signed investigator statement, the General Investigational Plan, and all applicable regulations
- Protecting the rights, safety, and welfare of subjects under the investigator's care, and
- Controlling the distribution of drugs and devices under investigation

More detailed information regarding the responsibilities of sponsors and investigators may be found in 21 CFR 312 (drugs) and 812 (devices) (available from the Superintendent of Documents, U.S. Government Printing Office, Washington, DC 20402, or from the CONRAD Program).

- 1) IND/IDE Information - Relevant IND/IDE information should be included in all applications for clinical studies to be conducted in the U.S., or to be conducted outside the U.S. but investigating a drug or device manufactured in the U.S. Information to be provided should include the IND/IDE Title, Number, date filed, and the date of expiration for the 30-day waiting period. In some cases, the IND/IDE may be obtained by CONRAD or another agency.
- 2) Protocol - The Protocol should include:
 - a. Protocol Title Page, with the Protocol Title, Protocol Number (if any), and date
 - b. Protocol Table of Contents
 - c. Statement of Objectives for clinical study or trial
 - d. Background and Introduction, including rationale for conducting the proposed study and relationship to present knowledge, with previous work in the area by the applicant and other investigators
 - e. Description of test article: Summarize information provided in Section 5.B.3, below, Description of the Drug or Device

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- f. Design:
 - i) Phase of study
 - ii) Type of study, e.g., open, comparative, or controlled (parallel, crossover)
 - iii) Number of centers, with addresses and names of investigators
 - iv) Number of subjects receiving the drug or device under investigation.
 - v) Use and number of control subjects or subjects receiving alternative treatment
 - vi) Prevention of bias, e.g., blinding or randomization procedures
- g. Selection of subjects:
 - i) Population from which subjects will be drawn
 - ii) Inclusion/exclusion criteria
 - iii) Post-admission withdrawal criteria, including Lost To Follow-Up criteria
 - iv) Rules regarding concomitant medications
- h. Study procedures for each visit, including:
 - i) Informed Consent procedures
 - ii) Dose, frequency, timing, and route of treatment
 - iii) Lab work
 - iv) Compliance monitoring
- i. Criteria for discontinuation (premature termination) of study
- j. Study materials:
 - i) Packaging of drug or device under investigation, including control or placebo articles
 - ii) Plans for shipping drugs or devices to the investigation sites
 - iii) Disposition of returned study drugs or devices
- k. Management of intercurrent events:
 - i) Protocol deviations
 - ii) Adverse event recording and reporting
 - iii) Pregnancy
 - iv) Subjects who discontinue (and replacement policy)
 - v) Modifications of Protocol
- l. Statistical considerations:
 - i) Justification of sample size
 - ii) Rules for termination of study
 - iii) Data analysis plan, including outcome variables and anticipated results
- m. Schedule for conducting the proposed study
- n. Protocol supplements (append special procedures, patient instructions, etc.)

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o. References

- 3) Description of the Drug or Device - For drugs or devices already marketed, provide an appendix with the proprietary name, chemical composition, amount of drug present per dose, name and address of manufacturer.

For new drugs or devices, give complete composition of the drug or device, the source, manufacturing data and amount present per dose, as well as a statement on the availability of such materials. Summarize all relevant preclinical investigations in animals. Describe concisely the main pharmacological actions of the compound and appropriate toxicological data. If available, give results of studies already conducted in humans. The above information should be provided for all active compounds, as well as for all vehicles or carriers.

- 4) Data Collection Forms - Append copies of all Case Record Forms to be used in collecting data for each subject and visit.
- 5) Protection of Human Subjects (Informed Consent) - All investigators (U.S. and non-U.S.) are expected to comply with U.S. FDA regulations regarding the protection of human subjects and informed consent (21 CFR 50).

Append a copy of the Informed Consent Form. If any subjects will receive an Informed Consent Form in a language other than English, a certified English translation of the Informed Consent Form should be included.

- 6) Institutional Review - All investigators (U.S. and non-U.S.) are expected to comply with U.S. FDA regulations requiring Institutional Review Board (IRB) approval of studies involving human subjects (21 CFR 56).

Since the welfare of human subjects is a matter of concern to CONRAD and the Eastern Virginia Medical School, advisory groups, consultants, and staff may review all research involving human subjects and prohibit research which presents unacceptable hazards. This provision, however, shall not derogate in any manner from the responsibility of the investigator's institution.

For U.S. institutions with an IRB having a Department of Health and Human Services (DHHS) Assurance Number: Append documentation showing the DHHS Assurance number, the IRB identification number, and a letter from the Chair of the IRB indicating approval of the study. Protocols will be reviewed by the CONRAD staff and will be forwarded to

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the IRB of the Medical College of Hampton Roads only if concerns or questions remain.

For U.S. institutions with an IRB not having a DHHS Assurance Number: Append a letter from the Chair of the IRB indicating approval of the study. In addition, include documentation of the IRB membership, composition, and operating procedures. Protocols will be reviewed by the CONRAD Program staff and will be forwarded to the IRB of the Medical College of Hampton Roads only if concerns or questions remain.

For non-U.S. institutions: Append a letter from the Chair of the IRB indicating approval of the study. In addition, include documentation of the IRB membership, composition, and operating procedures. All protocols will be reviewed by the CONRAD Program staff and forwarded to the IRB of the Medical College of Hampton Roads for review and approval.

- 7) Additional regulatory requirements for clinical studies outside the U.S. - Studies with unmarketed drugs or devices which are conducted outside the U.S. must be performed in accordance with the regulations applicable in the country where the study is conducted, and a summary should be appended describing these regulations and identifying the relevant regulatory agencies. Evidence of compliance with all applicable regulations must be provided to CONRAD, including documentation that the protocol has been reviewed and approved by the appropriate regulatory agency and copies of all correspondence between the investigator and the relevant regulatory agencies.
- 8) Liability Insurance - All institutions or organizations conducting clinical studies should have professional liability insurance and a statement to this effect from the responsible official must be appended. For subprojects developing new drugs or devices, a statement on the existence of liability insurance for such products should also be included.

6. **Scientific Personnel and their Qualifications**

Provide curricula vitae with pertinent publication lists as appendices for all scientific personnel.

7. **Facilities and Equipment**

Describe the existing facilities and equipment that will be used for the proposed studies.

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Investigators are expected to have access to all equipment that is necessary for the proposed studies. If not, the investigator's institution is expected to purchase equipment as a cost-sharing measure. If new equipment must be requested in this application to CONRAD, a full description and a strong justification will be required (see Section 9 below). Any equipment costing over \$2,500 (U.S.) will require that three competitive bids be submitted to CONRAD for approval.

8. **Collaborations**

For all studies involving more than one principal investigator, academic department, or institution, or involving other collaborative arrangements, describe the nature of the collaboration proposed, the relative responsibilities, and the mechanisms for assuring efficient interaction.

When unique materials, services, consultations, or other collaboratively obtained resources are essential to conducting the proposed studies, appropriately detailed and signed Letters of Collaboration from the individuals or other parties involved should be included as appendices.

9. **Line-item Budget with Justification**

A detailed budget, as in the sample below, must be included with each proposal, with a complete justification for each line-item. If a multi-year subproject is proposed, the budget submitted should include a separate annual budget for each year. Any proposed subcontracts must have a separate budget with the same format.

SAMPLE BUDGET:

<u>Category</u>	<u>Year 1</u>	<u>Year 2</u>	<u>Total Years 1-2</u>
Key Personnel (listed individually with % time)			
Support Personnel (as above)			
Fringe Benefits (with rates)			
Consultants			
Equipment			
Laboratory Supplies			
Animals			
Human Subject-related Costs			
Travel			

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Office Supplies and Services
Publication Costs
Other Direct Costs

SUBTOTAL

Indirect Costs

TOTAL REQUESTED

The budget section should include a complete justification for each line-item in the budget. Attention should be paid to the following:

- A. **Personnel** - Key personnel are those individuals whose contribution is unique and essential to the conduct of the proposed study, and cannot be changed without approval from CONRAD. Support personnel generally have technical or administrative responsibilities which can be met by other appropriately trained individuals, and can be changed by the investigator.
- B. **Consultants** - A list of consultants, their curricula vitae, the number of days needed, and the proposed daily fee should be specified. CONRAD will provide the necessary forms which must be completed by each proposed consultant.
- C. **Equipment** - List the cost and justify the need for each item. (Note Section 7, Facilities and Equipment, above.)
- D. **Laboratory Supplies** - Include all chemicals, glassware, disposable laboratory items, etc., with their intended use.
- E. **Animals** - Specify all purchase, maintenance, and other animal-related costs.
- F. **Human Subject-related costs** - Specify costs involved with human subject participation including advertising, subject reimbursement, clinical supplies, and lab tests, as well as other costs which are human subject-related but not included in other categories.
- G. **Travel** - Limited travel support will be considered for the investigator's attendance at meetings directly related to the proposed studies. Support for foreign travel may be included, but may require an additional request for approval approximately three months before the anticipated departure.
- H. **Office Supplies and Services** - Appropriate costs for supplies, as well as mail, telecommunications, and photocopying, etc., may be included.

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- I. **Publication Costs** - Anticipated publication costs, including purchase of reprints, may be included.
- J. **Other Direct Costs** - Any other anticipated direct costs not included above.
- K. **Indirect Cost** - Consistent with the Cooperative Agreement which provides funds to CONRAD, and the expectation that the investigator's institution will cost-share overhead expenses, Indirect Costs for subprojects are limited to up to 15% of Total Direct Costs.

10. **Other Activities and Research Support**

List any current support or pending applications for the proposed or related research for each individual involved with the proposed studies. Include the research topic, current or pending source of funds, amount of support awarded or requested, and the percent of time devoted to other research projects. The allocation of funds for any potentially overlapping research must be clearly delineated.

11. **Technology Transfer and Patents**

All potential recipient institutions must document their technology transfer capability, including:

- A. A statement of already existing patent rights relevant to the proposed studies
- B. The patent policy of the potential recipient institution
- C. Any written procedure for processing invention disclosures

All Subproject Agreements contain a patent clause in which the recipient institution is granted patent rights for invention disclosure; however, certain rights are reserved by the U.S. Government. CONRAD also reserves the right to share in intellectual property rights when substantive input has been contributed by CONRAD Program staff

12. **Requirements for Research Involving Laboratory Animals**

CONRAD requires that the use of all vertebrate animals in research be governed by the Principles for Use of Animals and also, in the case of warm-blooded vertebrates, the Guide for the Care and Use of Laboratory Animals. These documents are available from the Office for Protection from Research Risks, National Institutes of Health, Bethesda, MD 20892, USA. The Principles provide for humane treatment and care of animal research subjects. Animals are not to suffer unnecessary discomfort, pain or injury and are to receive proper care and maintenance.

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All U.S. applicant institutions proposing the use of animals in research must indicate that the applicant institution has filed with the Department of Health and Human Services a written assurance which commits it to following the standards established by the Animal Welfare Acts and above documents. All U.S. applicant institutions must also have or establish a review committee to assist in meeting the commitment to humane treatment and care. Investigators working outside the U.S. are expected to apply similarly high standards for the humane treatment and care of animals used in research.

13. **Requirements for Research Involving Risk of Exposure to Bloodborne Pathogens**

All research involving potential exposure to Human Immunodeficiency Virus (HIV), Hepatitis B Virus (HBV), or other bloodborne pathogens must comply with the OSHA/VOSH 1910.1030 Bloodborne Pathogen Standard [Federal Register Vol. 56, No. 235, Dec. 6, 1991; OSHA Department of Publications, U.S. Department of Labor, Room N3101, 200 Constitution Ave., NW, Washington, DC 20210, USA; Phone (202) 523-9667].

This standard is intended to minimize or eliminate exposure to bloodborne pathogens by a combination of engineering and work practice controls, personal protective clothing and equipment, training, medical surveillance, Hepatitis B vaccination, signs, labels, and other provisions.

All U.S. and non-U.S. institutions conducting research involving risk of exposure to bloodborne pathogens must provide written assurance to CONRAD that full compliance is being maintained with this Standard. Appropriate measures should also be taken to insure against infection by agents of nonhuman origin (including Simian Immunodeficiency Virus among others), and corresponding assurance that these measures are being taken should also be provided to CONRAD.

14. **Requirements for Research Involving Human Subjects not Enrolled in Clinical Trials**

CONRAD requires IRB approval for all research that involves collection of human blood, semen, or cervical mucus; biopsy of human tissues; sampling of human surgical tissues; or similar procedures (see Section 5.B.6).

Informed consent of the human subjects involved is also required (see Section 5.B.5, and append the Informed Consent Form), unless the tissues to be used were collected for another purpose (e.g., for another study or for diagnostic use) and are used anonymously.

In the latter case, the manner in which the proposed study methods ensure the subjects' right to confidentiality must be explained in the application.