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ETHICS
in HIV-Related Research
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INTRODUCTION

As more CRS programs enlarge their HIV programming to include aspects of Operations Research (OR), it has become imperative that some materials exist to assist country programs to navigate through the minefield of ethics-related issues that accompany all research projects. As HIV programming inevitably works with vulnerable populations and health-related interventions, it is eminently important that all programs engaging in OR understand the basic principles of ethics and the minimum standards required by CRS to conduct this research.

In general, ethics within CRS can be defined as a system or code of conduct that is based on universal moral duties and obligations that indicate how one should behave. It deals with the ability to distinguish good from evil, right from wrong, and propriety from impropriety (Velasquez et al., 1987). The Church has a centuries-long history of contributing both theological thinking and practical applications to the field of ethics, which it calls moral theology. In the last few decades, it has engaged deeply with modern bioethics. Based on the principle of respect for life and the value and dignity of the human person, Catholic bioethicists endorse the principles contained in this paper regarding ethics and research.

CRS programs should always be aware of the ethical considerations in HIV-related OR and understand the moral implications of the research, as well as follow the basic code of conduct for CRS HIV-related OR. This document provides a brief overview of several components that many Country Programs (CPs) face as they engage in OR. This is by no means comprehensive, but should be used as a guide to address several key issues that CPs currently face. Numerous additional references and resources are cited in this folder for those interested in gaining additional in-depth understanding on any of the topics here.

The document also provides guidance for CPs on CRS' ethical requirements for all HIV-related OR. These guidelines would also apply to any health-related interventions outside of HIV. If a CP requires additional guidance beyond that mentioned here, they should contact Shannon Senefeld (ssenefel@crs.org) or Sr. Phyllis Hughes (phughes@crs.org).

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BACKGROUND OF ETHICS IN HUMAN SUBJECT RESEARCH

The history of modern day ethics began with the development of guidelines, the Nuremburg Code, when dealing with human subjects[1] following the Nuremberg trials in 1945. Nuremberg trials revealed massive human experimentation and medical abuse during World War II. As new medical and research advances grew, the need for improved guidelines emerged, culminating with the 1964 Declaration of Helsinki.

In 1979, following a long US history of human subject research abuses, culminating in the revelation of 30-year Tuskegee Syphilis study in which rural black men were left untreated for diagnosed syphilis, even after the discovery of treatment, the US government established a commission for the protection of human subjects of biomedical and behavioral research. This commission published recommendations known as the Belmont Report.

The Belmont Report (1979) laid out three general ethical principles that should govern human subjects' research:

1. **Respect for persons:** This principle focuses on the need to treat research participants as autonomous individuals and that those persons with diminished autonomy are protected. The principle is designed to protect the autonomy and privacy rights of participants. This principle influences the "informed consent" concepts.
2. **Beneficence:** This principle focuses on the treatment of people in an ethical manner by not only respecting their decisions and protecting them from harm, but also by making efforts to secure their well-being. As such, this principle has two general rules: (1) do no harm and (2) maximize possible benefits and minimize possible harms. This means that researchers are obliged to give forethought to the maximization of benefits and the reduction of risk that might occur from the research investigation.
3. **Justice:** This principle deals with the fair and just distribution of benefits and risk among persons and groups participating in the research. The selection of research subjects needs to be scrutinized in order to determine whether some groups are being systematically selected simply because of their easy availability, their compromised position, or their manipulability, rather than for reasons directly related to the problem being studied. This principle is closely linked to control group decisions.

1 Human subjects will also be referred to as research participants within this text.

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CONTROL AND EXPERIMENTAL GROUPS

To test the effectiveness of an intervention, studies often use control and experimental groups. Control groups are held constant or "controlled". Experimental groups receive the intervention (services, products or activities) that is being studied. The control groups do not receive the intervention. The two groups are often very similar in all other attributes apart from receiving the intervention. At the end of the study, the two groups are compared.

Control groups are a useful and effective standard for comparison. Control groups provide a mechanism by which a researcher can determine the effectiveness, impact and/or success of an intervention.

In health-related studies, the use of control and experimental groups involves many delicate issues. Researchers ultimately have the responsibility to protect their research subjects' rights and welfare, which must take precedence over research findings or science. As such, if an intervention is determined to be harmful, to any degree, it is incumbent upon researchers to adhere to standards of research and principle of "do no harm". To do otherwise is unethical. Likewise, it can be deemed to be unethical to withhold an intervention from the control group if it proves highly effective.

There are many recent examples of HIV-related studies being halted due to ethical concerns that emerged as a result of using control and experimental groups:

- **Microbicide trial stopped:** A Phase III study of the candidate microbicide cellulose sulfate to prevent HIV transmission in women was stopped prematurely because of a higher number of HIV infections in the experimental group compared with the control group. The study was sponsored by CONRAD and conducted in Benin, India, South Africa and Uganda. A second study on the same product sponsored by Family Health International conducted in Nigeria was also stopped because of the safety concerns in the first trial. (WHO and UNAIDS, 2007)
- **Male circumcision trial halted:** A South African study examining the role of male circumcision in HIV prevention was stopped in March of 2005, after initial results indicated a 60% protective effect in the group that received the intervention (circumcision), on the grounds that it would be unethical to further delay circumcision to the control group assigned for delayed circumcision (Auvert et al., 2005).

CRS Guidance Regarding the Use of Control and Experimental Groups

All CRS OR programs should carefully consider the full ethical concerns of control and experimental groups.

Hypothetical example: you design a nutrition program to decrease child malnutrition in pediatric HIV cases. You obtain funding from an external donor to pilot this program over a two-year period. You want to see if this program is actually successful in decreasing child malnutrition in these cases, so you use a control and experimental group, collecting monthly data from both groups. The control group does not receive the intervention, but the experimental group does. After six months, you begin see dramatic differences in anthropometrics between the two groups. By the one year mark, you see that the experimental group not only has significantly greater anthropometric outcomes, but also significantly higher survival outcomes overall. You do the appropriate analyses and believe that the nutrition program is the real, driving reason behind these differences. At this point, you ethically need to expand the program to include the control groups. You cannot ethically continue to withhold the nutrition program from these children. However, the donor has not provided additional programming funds to expand to this other group.

In examples such as the one above, CRS programs should fully consider the implications of carrying out HIV-related operations research with live people and how they will address any ethical considerations that might arise. There are many times when control groups are the best option. However, there are other options available as well, and all programs should consider when control and experimental groups are truly the best option. In those cases where these groups are used, CRS should be prepared to deal with any ethical concerns that might arise during the actual research.

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ETHICAL REVIEW BOARDS

Ethical review boards are independent review boards. They are comprised of individuals with experience in the subject matter being researched, individuals who are not experienced in the subject matter, community members and members of various genders, ethnic groups and ages. Generally speaking, members of the ethical review board have an equal voice in the determination of the ethical nature of the research.

Many funding organizations have their own ethical review boards, often referred to as Institutional Review Boards (IRB) or Independent Ethics Committees (IEC) including WHO, various US funding agencies, and universities from around the world.

Though ethical review boards were initially established to protect participants in medical and psychological research, many institutions require ethical review for social and behavioral research. Initially, it may appear that social and behavioral science research pose little or no threat to participants, closer inspection reveals various opportunities for harm.

An ethical review board should review any project that has the potential for serious effects including the following (National Science Foundation, 2007):

- ***Emotional or psychological harm,*** for example when a research interaction causes upset, or worry about breach of confidentiality.
- ***Social harm*** due to stigma or other negative social outcomes of breach of confidentiality.
- ***Physical harm*** if revelations about others get back to those persons, particularly when researchers study domestic violence, gang activity, political activity in a conflict zone, or other phenomena concerning violence-prone individuals.
- ***Financial harm*** if revelations result in loss of employment or insurance coverage.
- ***Legal harm*** when illegal activities are disclosed.
- ***Moral harm*** when participation in research strengthens subjects' inclinations to behave unethically.

No special review or protection is required when the harm is considered commensurate with daily life. This specifically refers to mere inconvenience when a survey or other research interaction is administered at an inconvenient time or place or simply takes a long time to administer (National Science Foundation, 2007).

CRS Guidance Regarding Ethical Review

If you are not certain if you need an ethical review for your research, please contact Shannon Senefeld **(ssenefel@crs.org)** or Sr. Phyllis Hughes **(phughes@crs.org)** for assistance and guidance. In general, if you use control groups, conduct an experimental design, or if you are engaged in operations research that is outside of your normal project parameters, you should consult with an ethical review board.

CRS does not have an official, in-house ethical review board for the agency. However, all strategy-funded operations research projects will undergo a thorough review by a review team before funding is allocated to the study. This review will include an emphasis on possible ethical concerns. This same review process will be made available to other donor-funded projects as requested.

All projects that require an ethical review board, should also seek review externally. Whenever possible, a local review board should be consulted to ensure that local ethical considerations are undertaken. In all cases, local laws and procedures for review must be followed. In some countries, the Ministry of Health has guidelines on the types of review required and approved ethical review boards. ***Country programs should consult with the local Ministry before beginning any research to determine the requirements for the country where the research is occurring.***

In those areas where the local review boards are weak or non-existent, there are commercial review boards that provide this service for a fee. These can be quite expensive however and should be carefully considered. If a country program is partnering with a university, they also have IRB that will meet the ethical review requirement.

A list of US approved review boards is available on the website of the National Institute of Health: **http://ohrp.cit.nih.gov/search/asearch.asp.** Any US government-funded study must be approved by a US approved review board.

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INFORMED CONSENT

Informed consent is the voluntary consent to participate in research. This consent should be documented. This verification is requested only after complete, objective information has been given about the research, including an explanation of the study's objectives, potential benefits, risks and inconveniences, alternative therapies available, and of the subject's rights and responsibilities in accordance with the current revision of the Declaration of Helsinki. Informed consent is considered by most to be a fundamental necessity in ethical research.

According to researchers, there are four main elements of informed consent (Pedroni & Pimple, 2001):

1. Information.

For true informed consent, research participants must be given all information relevant to make a knowledgeable decision to participate in the research or not. Relevant information may include, depending on the research: possible risks, benefits, funding organizations, use of results, contact information for researchers, how confidentiality is maintained and who should be contacted with any concerns about the research.

2. Understanding.

Informed consent is not simply providing the information to the subject. The principles of informed consent require researchers to ensure that research subjects understand the information. Ensuring understanding requires consent information to be provided in a language and medium (written, oral) that the subject can understand. Obtaining understanding does not mean that a human subject must understand in depth the research methodology and outcomes, but rather this element seeks to capture information in a way that allows the participants to make a knowledgeable decision to participate or not.

3. Voluntariness.

Informed consent is voluntary. In no way, should research participants be coerced, persuaded, manipulated or forced to participate. To do so would not only be unethical, but would remove the research participant's ability to make an independent, knowledgeable decision, free from outside influence. Researchers should not "convince" subjects to participate, to do so is considered unethical. However, giving potential subjects information, answering questions and providing additional sources of information are all components of ensuring informed consent.

4. Decision Making Capacity.

In addition to complete, relevant information, comprehension of the research, and voluntary participation, informed consent requires that human subjects have the capacity to make the decision. This requires participants to have the ability to weigh risks and benefits and be in an environment that allows for individual choice. For this reason, many ethical review boards, research organizations, governments and individual researchers have identified populations that require special consideration, and sometimes special consent, review and protective structures, when considered for research. This does not mean that these groups are not eligible for participation in research, but rather that before any research begins, researchers and ethical review boards work to ensure that these groups are protected.

Protected or vulnerable populations include:

- **Children:** Children, particularly young children, may not have matured developmentally enough to make an informed choice. Children may be highly vulnerable to coercion and manipulation (even when unintended). For this reason, parental or guardian consent is required before children can be approached for participation in any research. If parental or guardian consent is obtained, the child (if mature enough to understand) is also asked for consent. An ethics review board is often responsible for deciding when child consent should be sought.
- **Pregnant Women:** Pregnant women are considered vulnerable populations because their unborn children may also suffer any negative consequences of research participation.
- **Prisoners:** Prisoners are in an environment in which they are not free to make decisions. Therefore by the very definition of informed consent, they may be unable to consent and should be approached with care for any research.
- **People with Mental Disabilities:** People with mental disabilities may lack the cognitive development to make a knowledgeable decision. An ethics review board is often responsible for deciding who can agree to participation on the person's behalf. This may be a legal guardian or parent who acts on the person's behalf.

- **People with Limited Education/Illiterate:** Special care and consideration are required when working with those with limited education and the illiterate, as they are unable to provide written consent. Ethical review boards may require additional modes of consent and will often determine what documentation is required for informed consent.
- **People with Limited access to Health Services:** Those with limited access to health services may be more vulnerable to outweigh the benefits of research than the risks in hopes of receiving treatment. The need for health services may impede the subject's ability to make a voluntary decision, as they may feel they have no choice.
- **Poor:** The poor may have limited options for services and may participate in the research as a mechanism for obtaining services or remuneration. Ethical review boards often review any proposed remuneration and/or language to ensure that there is no implicit coercion in the consent.
- **Employees:** Any research project in a workplace that could affect the status of one's employment requires special consideration.

Informed consent is most often required in written format. However, in the cases described with several of the above vulnerable populations, written consent is not an option. In these cases, oral consent can be substituted for written consent, but should be witnessed by a third, objective party. Most ethical review boards will require a clearly detailed plan for how the informed consent will be obtained. Signed consent forms are not the same as informed consent; consent forms merely document that informed consent has occurred.

CRS Guidance Regarding Informed Consent

Informed consent is always required when conducting any HIV operations research. This consent should be obtained from all participants (regardless of research design and inclusive of both control and experimental groups).

Whenever possible, the informed consent should include written informed consent. The informed consent document should be in a language understandable to the participants. When the participants are non-English speaking, a translated document in the local language should be used, and a copy of the consent document should be given to the participants. While a translator may be helpful in local contexts, ad hoc translation of the consent documents should not be used in place of a written translation (as ad hoc translations can very greatly). In addition, the language level used in the informed consent should be at a level easily understood by participants.

Participants who do not read or write can provide consent by ticking (often marking an "X" or providing a thumbprint) the consent document, as long as this is acceptable in the research setting. In addition, all CRS research must provide opportunity for the prospective participants to ask questions and receive answers.

All CRS research must inform participants about (1) the purpose of the research, expected duration, and process; (2) their right to decline to participate and to withdraw from the research once participation has begun; (3) the foreseeable consequences of declining or withdrawing; (4) reasonably foreseeable factors that may be expected to influence their willingness to participate such as potential risks, discomfort, or adverse effects; (5) any prospective research benefits; (6) limits of confidentiality; (7) incentives and/or remuneration for participation; and (8) whom to contact for questions about the research and research participants' rights.

As most participants with whom CRS works are marginalized and/or disadvantaged, often economically, CRS should attempt to avoid remuneration for participation in the research whenever possible. While some basic costs may be covered (i.e. lunch for participants, travel costs as appropriate, etc.), excessive remuneration could be coercive in nature, as participants may not be able to decline participation due to their economic situations.

For all children, parental or guardian informed consent is required before approaching the child for participation in the research. The research should also be explained to all minors involved in the research, and additional assent from the children should be obtained when the children are cognitively mature enough to understand the basic research.
Ethical review boards normally require review of informed consent documents. CRS research projects should have these documents ready for submission to the ethics review board when submitting the study or research protocols.

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CONFIDENTIALITY

The World Medical Association's Declaration of Helsinki 1964/2004 declares: "The right of research subjects to safeguard their integrity must always be respected. Every precaution should be taken to respect the privacy of the subject, the confidentiality of the patient's information and to minimize the impact of the study on the subject's physical and mental integrity and on the personality of the subject."

Data: Data, including demographic, medical and status information, must be kept confidential. Maintaining confidentiality is not only ethical, but in fact may serve as a major motivating factor to increase confidence in participation in the research. Examples of steps to maintain confidentiality include: storage of information in secure files, electronic or paper, that restrict access to those who need to know to do their jobs. Other strategies include, coding data and removing all other identifiable information from accessible data sources.

Recordings: Verbal and written consent should be obtained prior to start of research. For instance, in the case of focus groups, before focus groups begin to discuss the subject matter, researchers should obtain recorded verbal consent from all participants before beginning to record the discussion.

Photographs: There is no *overarching* legal requirement to obtain someone's authorization to take his or her photograph. However, there are ethical considerations when photography can infringe on people's privacy and dignity. Photographs of people may amount to exploiting the persons concerned or misrepresenting the truth (Verbauwhede, 2006). Often, you may be free to take a photograph of a person, but the way the image is used may infringe on the photograph subject's privacy or dignity. This is especially true in medical settings, where nearly all photographs require a signed release by photography subjects before use.

CRS Guidance Regarding Confidentiality

All CRS operations research, evaluations and learning projects should respect confidentiality whenever possible. Some general guidelines include:

- Keep all identifiable information under lock and key and destroy appropriately when the information is no longer valuable.
- Do not disclose any participant's identity during the research beyond the agreed upon parameters. If your research will occur in a participant's workplace, be sure that these parameters are clear both with the employer and the employee.
- Informed consent must be obtained from anyone being recorded.
- Verbal consent should be obtained for all photographs of people. This consent should include not only the consent to take pictures, but also to use the pictures in future CRS work.
- Written consent should be obtained for all photographs of people if there is a delicate situation (i.e. taking pictures of hospital clients, children, or clients in health care settings such as an HIV Clinic counseling session). In health care settings, the policy of the facility must be honored since many will require written consent. CRS contracts (i.e. with an independent photographer) should honor the terms of this consent.
- Photographs should not be used in a misrepresentative manner. If you have taken pictures of children playing in Shu Phen, these children should not be used to depict OVC in general. While the photos may be used in an OVC publication, a clear caption should be included that details that these children are not necessarily OVC.
- If a contractor is used for photography and has contractual rights to use photos taken for CRS, be sure that the contract protects the confidentiality of any patient or client in a medical or health setting as to the use the contractor may make of the photos.

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CONCLUSION

These guidelines are meant to be a tool to assist country programs to conduct HIV-related operations research in an ethical way. While some of the guidelines may seem heavy, they exist to protect program participants, CRS and partners. These are not meant to be a deterrent to conducting operations research. Many of these guidelines are easily followed.

The information presented here only begins to scratch the surface of ethics and is not meant to be all inclusive. However, these are some of the issues that CPs have already begun facing. As more issues emerge, updates to these guidelines will be made available.

If you are interested in conducting HIV-related operations research, but are unsure how to follow the guidelines presented here, please contact Shannon Senefeld **(ssenefel@crs.org)** or Sr. Phyllis Hughes **(phughes@crs.org)**. Other country programs have experience in this type of work, and these examples can be provided to you to facilitate your walk through this new territory.

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