# Casebook on Ethical Issues in International Health Research

Editors:

Richard Cash
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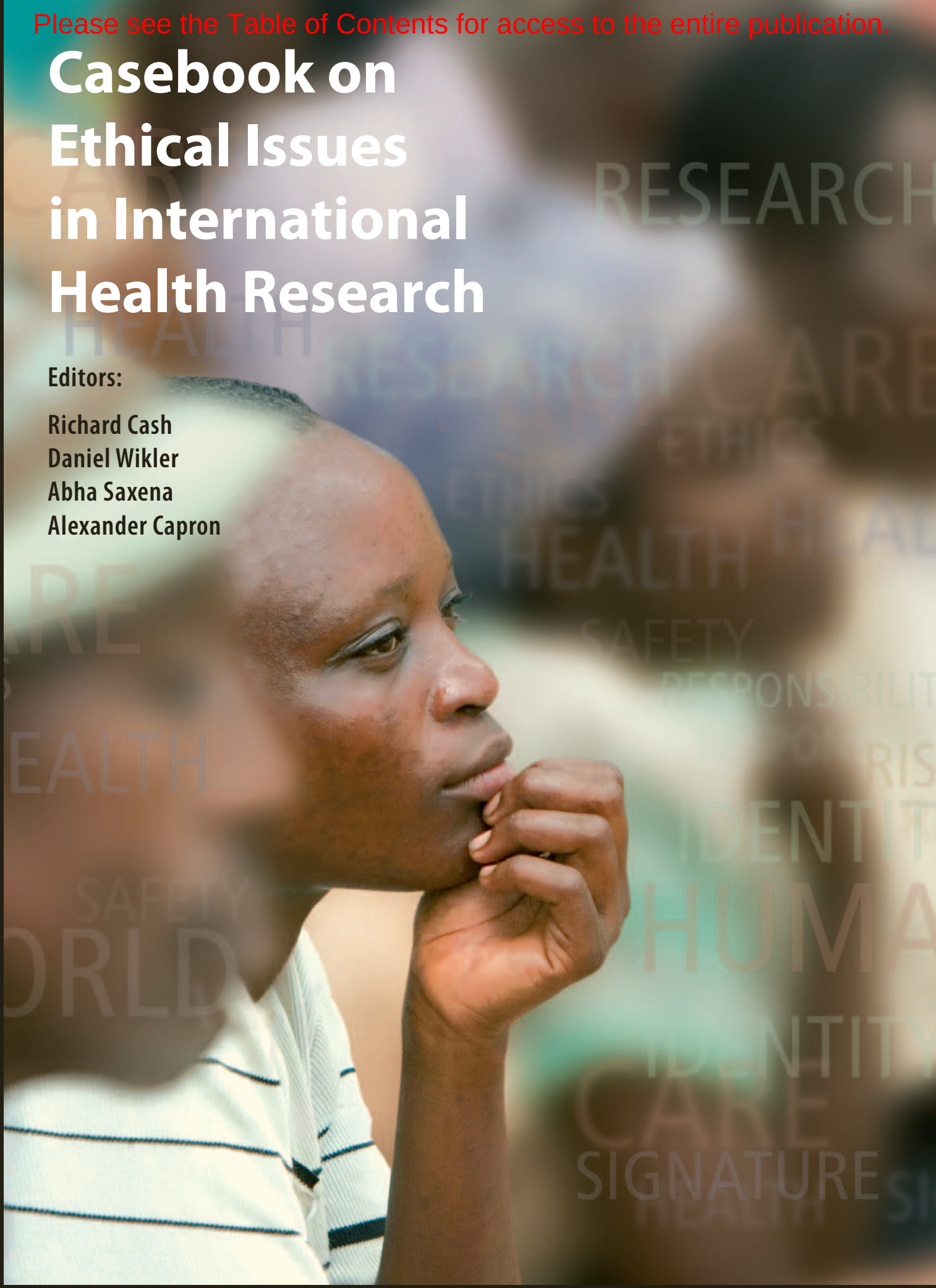
Abha Saxena
Alexander Capron




World Health Organization

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**Using this casebook**

This casebook has been developed as a teaching tool for instructors and workshop leaders rather than as a textbook for students or workshop participants. There is no need for participants to have copies of the casebook: facilitators can provide participants with individual case studies and chapter introductions relevant to the research ethics topic being addressed. Individual case studies and chapter introductions relevant to the research ethics topic being addressed can be photocopied from the print version or downloaded from the WHO web site without additional permission from WHO, unless the planned use is in conjunction with commercial purposes. Please ensure that the WHO source is appropriately acknowledged. If you plan to publish, adapt or translate the materials, please contact WHO directly at the following email: pubrights@who.int

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# Acknowledgements

This casebook is the result of a collaborative effort titled "the Research Ethics Training Project" between the World Health Organization and the University of Geneva undertaken with the generous financial support of Réseau universitaire international de Genève/Geneva International Academic Network (RUIG/GIAN).

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March 2009

Boston, Massachusetts — Richard Cash
Dan Wikler
Geneva, Switzerland — Abha Saxena
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# Foreword

For the World Health Organization, research is a vital ingredient for improved global health. Our dedication to producing and using knowledge to improve human health is itself grounded on an ethical commitment: that such research is carried out ethically and offers the prospect of raising the standard of health for everyone.

One of the essential components of health research is a strong set of ethical standards, well understood and applied by research teams and sponsors. Examination of, and education about, the ethical issues raised by health research has been an important part of WHO's work for many years. As we step up our involvement with health research, it is thus important that we also increase our efforts within the Organization and with our collaborating centres and other groups at country and regional levels to ensure that ethical standards are met in all fields of health research – from initial trials of new technologies to epidemiologic studies to research on health systems.

These efforts are especially important in resource poor settings, where the need for locally applicable research findings is a foremost concern. As sponsors increase their funding of such research, it is crucial that local researchers who initiate or collaborate on such studies be able to identify and respond appropriately to the ethical issues they raise. Likewise, research ethics committees must be prepared to provide appropriate oversight to make sure that research projects are well designed and executed. Helping those who fund, carry out and review health research to deal with the ethical aspects is a matter of particular importance to WHO's departments of Research Policy and Cooperation and Ethics, Equity, Trade and Human Rights and to our in-house Ethics Review Committee, which has taken the lead in the development of the present casebook.

This book aims to help investigators, ethics review committee members, health authorities, and others to play their respective roles in the ethical conduct of research. Rather than take a didactic approach, the book is set up to provide cases – based on actual research studies – which can be read by individuals or discussed in group settings. Thinking one's way through the problems raised by such case studies has been shown both to be an extremely effective means of learning to understand and apply general ethical principles and to provide good preparation for dealing with the real world of health research.

Timothy Evans, D.Phil., M.D.
Assistant Director General
Information, Evidence and Research

# The editors

**Richard A. Cash MD, MPH,** is a Senior Lecturer in the Department of Global Health and Population at the Harvard School of Public Health (HSPH). He is the Director of the Program on Ethical Issues in Global Health Research at HSPH. Dr Cash has been involved in international health for over 40 years as a researcher, a funder and developer of health research projects, and as a visiting faculty at a number of schools of public health around the world. He has conducted numerous research ethics workshops throughout Latin America, Africa, and Asia. Dr Cash began his research career in what is now Bangladesh where he and his colleagues conducted the first clinical trials of Oral Rehydration Therapy (ORT) for the treatment of diarrhoea. In 2006 he was awarded the prestigious Prince Mahidol Award in Thailand for his work on ORT.

**Daniel Wikler, PhD,** is Mary B. Saltonstall Professor of Population Ethics in the Department of Global Health and Population at the Harvard School of Public Health. Together with colleagues across the campus, he created the Harvard Program in Ethics and Health, addressing ethical issues involving health arising at the population and global levels. His research addresses ethical issues in global health, including health resource allocation, health measurement, and public health policy. Among numerous other publications, he is author, along with three fellow philosophers, of *From Chance to Choice: Genes and Justice*, published by Cambridge University Press. Prof. Wikler was co-founder and second president of the International Association of Bioethics. He served as the first "staff ethicist" at the World Health Organization in Geneva.

**Abha Saxena MD** has been managing the Research Ethics Review Committee of the World Health Organization in Geneva, Switzerland since 2002. Trained as an anaesthesiologist, she was a faculty member and Professor at the All India Institute of Medical Sciences, New Delhi, India, before joining WHO in 2001. As a medical practitioner, she was actively engaged for 20 years in hospital and community-based research. At WHO, in addition to running a dynamic research ethics committee, she conducts short training programmes in research ethics not only for WHO staff, but also in several African and Asian countries, using many of the case studies that are included in this casebook.

**Alex Capron** holds the Scott H. Bice Chair in Healthcare Law, Policy and Ethics in the Gould School of Law at the University of Southern California where he is also Professor of Law and Medicine at the Keck School of Medicine, and Co-Director of the Pacific Center for Health Policy and Ethics. Prof. Capron served as the first Director of Ethics, Trade, Human Rights and Health Law at the World Health Organization in Geneva. He was the Executive Director of the President's Commission for the Study of Ethical Problems in Medicine and Biomedical and Behavioral Research, and subsequently served as Chair of the Biomedical Ethics Advisory Committee of the U.S. Congress and as a member of the National Bioethics Advisory Commission. Prof. Capron has been President of the International Association of Bioethics, President of the American Society of Law, Medicine and Ethics, and Vice President of the Council for International Organizations of Medical Sciences (CIOMS). He has published widely on ethical, legal and social issues in biomedical research, health care and public health.

# Introduction

# Introduction

This casebook collects 64 case studies, each of which raises an important and difficult ethical issue connected with planning, reviewing, or conducting health-related research. The book's purpose is to contribute to thoughtful analysis of these issues by researchers and members of research ethics committees (RECs, known in some places as ethical review committees or institutional review boards), particularly those involved with studies that are conducted or sponsored internationally.

This collection is envisioned principally as a tool to aid educational programmes, from short workshops on research ethics to in-service learning for scientists and REC members, to formal degree or certificate courses. In such settings, instructors will typically select a number of case studies that will be distributed to the participants to provoke and focus discussion. (To assist those using these case studies in their classrooms and workshops, a teaching guide has been included.) Individuals who want to stimulate their own thinking about research ethics or to become more familiar with a range of real-world dilemmas in international health research, especially in developing countries, may also benefit from perusing this book, either on topics of special interest to them or as a whole.

## The Case Studies

The case studies have been kept short (generally no more than two pages) and include only those descriptive background details that are relevant to the issue under discussion. While careful analysis will often reveal that more than one issue is raised by a case, each study is centred on one or two ethical problems. Cases are grouped in chapters based on the principal ethical questions that they address, but the table of contents suggests secondary categories under which the cases may also be fruitfully studied. In turn, as readers or course organizers become familiar with particular cases, they might want to re-assign them under further headings to take account of the additional issues that seem important to them. The arrangement of the cases (including the list of principal issues as delineated by the topical chapter headings) is intended to facilitate, not restrict, creative use of these materials.

The cases in this collection were not invented. Rather, each was drawn from one or more actual research projects. Some might seem familiar because they were controversial enough to prompt ethical debate in the news media or scientific journals, while others concern issues that have received less attention – but are not therefore less important. The names in the case studies and other topical information (such as dates and locations) have been changed so readers can focus on the ethical dilemmas. Some cases that were set in specific geographical contexts have been moved elsewhere by changing details to make them more useful in a particular educational setting. The descriptions are usually generic enough that readers can imagine what they would do if the research were proposed in their own locale. In some other cases, however, a specific disease being discussed is only found in a particular country or region, so that fact can't be changed, though such cases have also been edited to remove superfluous identifying details.

## The Background

The publication of these materials by the World Health Organization (WHO) reflects its long-standing leadership in public health and biomedical research, especially on vaccines and drugs for the so-called "neglected diseases". In these activities, WHO works in partnership with its 193 Member States, other intergovernmental bodies, and nongovernmental organizations such as groups that deliver health care, foundations that sponsor research, research centres, and pharmaceutical companies. The growing complexity of such research – which can involve public-private partnerships, coordination of collaborators from diverse institutions and multiple countries, sponsors located far from the communities that host the research, growing commercial sponsorship of research, and the collection (and possible removal to distant repositories) of biological samples – has been accompanied by increased international attention to ethical problems. At the heart of this increased concern is the recognition that health-related studies have the potential to benefit the communities and populations involved – but can also harm them. The possibility of harm is especially

great in settings where research participants are socially and economically vulnerable, poor and illiterate, and where they lack other access to health care.

All research projects supported by WHO are scrutinized by the WHO Research Ethics Review Committee (ERC) or by one of the WHO regional or country-level research ethics committees. In addition to its activities in developing guidance on research ethics and in reviewing research protocols, the ERC Secretariat organizes educational programmes for WHO staff at headquarters, and for WHO regional and country offices who are responsible for developing and overseeing research, and for members of the ERC itself. In reviewing research projects, the ERC Secretariat has also become aware of settings (especially but not exclusively in low-resource countries) where more education on research ethics would be helpful for researchers and the committees that provide ethical and scientific review of projects.

In its own educational programmes on research ethics, the ERC Secretariat has made extensive use of case studies, with case-based discussions guided by WHO's own staff and by external experts, especially colleagues from the Harvard School of Public Health (HSPH). The HSPH Program on Ethical Issues in International Health Research began holding an annual one-week workshop on research ethics in 1999. From the beginning, participants have been equally divided between developed and developing country scientists, researchers, administrators, and members of RECs and have been from governments, universities, and nongovernmental organizations. The workshops introduce participants to important (and sometimes controversial) concepts in research ethics through a mix of lectures and case study discussions. Although both methods are necessary, the HSPH organizers found that the case studies, which encourage participants to draw on – and then examine and defend – their own understanding of ethically acceptable actions, provided a safeguard against the imposition of cultural biases that may colour lecture-based sessions. Although people are sometimes reticent to question a lecturer, they are more likely to be willing to share their views about practical situations with which they are familiar. Moreover, analyzing case studies helps participants to move beyond generalities and to formulate concrete responses to dilemmas, just as researchers and REC members must do in practice. This collection of teaching cases has emerged from the HSPH and WHO workshops held around the world over nearly a decade, supplemented with ideas and cases suggested by many colleagues.

# Teaching Guide

# Teaching Guide

## Introduction

This brief teaching guide is intended as an aide to those using these case studies in their teaching or training workshops.

The guide first addresses the ***process*** of teaching case studies. Case-based teaching differs significantly from traditional lectures and, therefore, requires a different approach and additional skills. Because case-based teaching is typically used to enrich a learning experience by actively engaging students or workshop participants in structured discussions, one of the most important skills needed is the ability to lead a case study discussion. This guide offers some suggestions on how to do this well.

Second, the teaching guide addresses the ***content*** of the case studies by identifying some of the main issues in the case studies that the facilitator[1] should be aware of. The guide also suggests some questions that the facilitator can raise in order to encourage a thoughtful discussion of the issues. In some situations, the facilitator may have experience in using case studies to teach research ethics and can readily draw upon examples and counter-examples, guidelines and regulations to stimulate debate and discussion. More typically perhaps, the facilitator will have some background in research ethics and would like a little guidance on how to incorporate case studies in teaching the subject.

This guide also includes a list of additional resources for case-based teaching focused on articles dealing specifically with how to use case studies. In addition, the casebook itself includes a suggested reading list with links to international research ethics guidelines and numerous review articles. Finally, a glossary of medical, health and research terms is provided.

### Using this casebook

This casebook has been developed as a teaching tool for instructors and workshop leaders rather than as a textbook for students or workshop participants. There is no need for participants to have copies of the casebook: facilitators can provide participants with individual case studies and chapter introductions relevant to the research ethics topic being addressed. Individual case studies and chapter introductions relevant to the research ethics topic being addressed can be photocopied from the print version or downloaded from the WHO web site without additional permission from WHO, unless the planned use is in conjunction with commercial purposes. Please ensure that the WHO source is appropriately acknowledged. If you plan to publish, adapt or translate the materials, please contact WHO directly at the following email: pubrights@who.int

[1] The term 'facilitator' is used here – instead of the term 'professor', 'teacher', 'instructor' or 'leader' – to emphasize that the faculty's role in case-based classes and workshops centres on enabling participants to utilize the case studies in an educationally enriching fashion. By using the term 'facilitator' we do not mean to introduce an additional person besides the professor or other leader of the course or training session, but merely to stress the difference in teaching method from a typical class.

# Teaching Guide

## Leading case-based discussions: the process

### The role of the facilitator: helping participants learn through active engagement

In a typical lecture-based learning environment the focus is on the lecturer and the material he or she presents. Case-based teaching shifts the focus to the participants. The goal is for participants to *learn through actively engaging with the case studies*. Participants are encouraged to apply knowledge, reasoning, and their experiences and contexts to a real-life situation (the case study) and to learn from each others' responses. The role of the instructor or lecturer changes from being the expert who provides answers to that of a facilitator who encourages structured discussion among participants. In this section, we offer some suggestions for doing this.

At the outset, it is important to acknowledge that some teachers may feel that in facilitating a discussion, rather than delivering a lecture, they are not fulfilling their professional responsibility. This may be particularly true when there is a personal, professional or cultural expectation that a teacher's role is to provide "the answers". Case-based teaching, while less reliant on an obvious display of facilitators' expertise, actually places greater demands on their skills and knowledge than does straightforward lecturing. First, a thorough understanding of the subject matter is required so that the facilitator will be able to spot important points raised in a discussion even when they emerge in an unfamiliar fashion or in terms that may differ from those used by other experts. Second, special skills are needed to provide a supportive environment for students to develop their own analyses of the cases in a manner that is thorough and well-focused. You will, in short, be using your expertise, but sharing it in a less direct way as you encourage participants to address a range of ideas and to add to these by bringing in their own ethical reasoning and perspectives.

### Being comfortable with cases that permit debate and disagreement

The case studies included here do not have easy or ready answers. They were chosen precisely because situations in which reasonable people can disagree about the right course of action are better suited for stimulating thinking than those about which everyone would agree. But teaching with these "open-ended" cases requires practice and skill. For example, there is no single correct answer regarding the extent of researchers' or sponsors' responsibility to provide tuberculosis care to participants in an HIV vaccine trial when screening of potential trial participants reveals that some are suffering from TB. You may have reached your own conclusion on the level and type of treatment that is owed, but the answer to this question is neither obvious nor self-evident, and it is important not to take sides by dismissing alternatives. Leading the participants towards your own conclusion or taking sides risks shutting down the discussion as participants may seek to please you by searching for what they think you regard as the 'right' answer. Meanwhile, they will not benefit from the potential of case-based discussion to motivate careful thinking and problem-solving, including articulating justifications for their conclusions.

Being comfortable with cases that permit debate and disagreement will allow you to both recognize that the ethical issues in the cases often pose dilemmas without easy answers and to help participants to recognize this as well. In addition to the questions at the end of each case study, there are a number of others that encourage the type of analytical discussion that the case studies are designed to elicit. Again, using the example of tuberculosis treatment in an HIV vaccine trial:

- Which points in the international guidance documents such as the CIOMS *International Ethical Guidelines*[1] or the *Declaration of Helsinki*[2] address the question of researchers' responsibility to treat conditions other than those that are the object of the study?

[1] Council for International Organizations of Medical Sciences (CIOMS). International Ethical Guidelines for Biomedical Research Involving Human Subjects. Geneva, Switzerland: Council for International Organizations of Medical Sciences (CIOMS), 2002. http://www.cioms.ch (accessed 9 May 2008)

[2] World Medical Association. Declaration of Helsinki: Ethical Principles for Medical Research Involving Human Subjects. Helsinki, Finland: World Medical Association, 1964. Most recent revised and updated version 2008. http://www.wma.net/e/ethicsunit/helsinki.htm (accessed 5 June 2009)

- Are there different ways that the guidelines can be interpreted and, if so, which ethical principles will help to resolve the question of responsibility?
- Does the context where the trial is taking place matter? More specifically, would people in your own community expect or need more from research and the researchers than those in more developed countries?
- Do, or should, participants in clinical trials have a right to benefit from their participation by obtaining much-needed medical care?

## Preparing to use a case study

A facilitator should aim to select case studies that allow participants to concretely apply their understanding to the topic of the course module or workshop. Such cases offer an excellent opportunity for sharing and debating perspectives of immediate relevance across

- cultures (e.g. various approaches to individual signed consent),
- disciplines (e.g. a lawyer's analytic approach may raise significantly different issues than an anthropologist's),
- interests (e.g. a sponsor may raise different concerns than a ministry of health policy-maker or a community representative).

In choosing a case study, consideration should be given to the cultural context in which the case study will be used. Some case studies will be more difficult to teach in certain contexts than others and may even be inappropriate. Sensitivity to community norms (cultural, religious, gender) may rule out the use of particular cases either because the cases may seem irrelevant or because they may be considered too sensitive.

It is always a good idea to provide participants with a copy of the case study in advance of the session when it will be discussed and to ask them to read and think about it beforehand. In some circumstances, it may also be appropriate to give participants an additional assignment (such as preparing an informed consent form for the clinical trial discussed in a case study, or a memorandum listing the relevant issues and proposing how to resolve them) that can be used as a starting point for discussion when the case is presented.

Case studies can be discussed either before or after the participants have been introduced (through a lecture or a discussion) to the substantive issues being addressed in the workshop or class session.

- When a case study is used before a lecture or seminar discussion introducing the topic or issue, participants will draw on their existing knowledge to examine the case study and identify areas where they need more background both to fully understand the issues and to make informed suggestions on how to address them. Participants can then be provided with additional resources (theory, relevant current debates, existing guidelines which may be applicable, examples of various practices), or when circumstances permit, participants may be encouraged to seek out appropriate resources for themselves. To aid participants, the material covered in such additional resources may be reviewed in a lecture given by the facilitator or another expert who has been invited to address the class or workshop on the issues raised by the case study.
- When a case study is used after the participants have obtained some relevant background through advanced reading, a lecture, or a seminar discussion of the general issues that will be raised by the case, the participants would generally be expected to apply or relate the material to the case study.

Each approach has its advantages. Starting with a case study is likely to engage the participants more than starting with a lecture; it may also cause them to be more receptive to ethical concepts and guidelines which they will then recognize as potentially helpful in resolving the issues that arose in their discussion of the alternatives presented by the case study. On the other hand, starting with a lecture and/or a review of background materials is likely to improve the quality of the discussion and to give the students a more immediate sense of mastery.

Whatever the timing of the case study, an important part of the facilitator's preparation is devising a good starting point for the case discussion. If the group is large (i.e. 20 or more participants), the discussion will probably be enhanced by dividing into small groups of 6 to 8 people and allowing 20-30 minutes for small group discussion before assembling into the large group. (For example, in a workshop setting, the small group discussion could take place over breakfast.) The facilitator should remind the small groups that everyone should express themselves and be respectful of other participants' comments; the facilitator can also walk among the groups to keep an eye on their progress and add a question or comment if the group seems to need additional input. Some participants may be reluctant to express their ideas or to argue a point in a large group but feel more comfortable speaking in a more intimate setting; after exploring their ideas in the small group, they may feel emboldened to speak in a larger audience.

The introduction you provide to a case study – such as the first question you ask or the exercise you assign – will serve to guide the subsequent discussion. For example, if you would like workshop participants to explore the obligations owed to trial participants such as the type, level and duration of care before approaching issues of study design and informed consent, then your opening should be crafted to elicit responses about obligations. You may want to begin by initially asking questions specifically about obligations to those accepted into the trial before asking about obligations to those who contract the study disease, those who contract a different disease, or the ethics of treating a participant for the target disease but not her infant child. If there is immediate agreement on all the answers, gently probe a little further to determine where individual participants would draw the limits of these obligations; you can also explore the different ethical as well as human rights principles on which they are based. Only after a topic has reached an analytical depth you are satisfied with should you move onto the other issues in the case study. If participants raise other issues (such as study design or informed consent) in the course of the discussion on obligations, thank them and write these issues on a flip chart or whiteboard (so that the idea does not get lost) but indicate that these issues will be discussed later in the session.

One way to encourage discussion is to ensure that the initial question you raise is one that permits more than one single appropriate response. Continuing with the previous example, ask whether sponsors should provide treatment for tuberculosis in the HIV vaccine trial and if so, why? Rather than agreeing or disagreeing with any statements, follow up with a question such as: if 50% of trial participants are anticipated to be in need of the treatment, in addition to those who get treatment for HIV/AIDS, might sponsors find these obligations too onerous? Based on expense and a possibility of conflict, what if the sponsor would therefore likely decide to abandon the vaccine trial, or to take it to another setting where the added requirements wouldn't be imposed? And if this might happen, should there be no demand for such treatment? Try to anticipate what the responses might be; thinking about follow-up questions in advance will help you to guide the participants to a deeper analysis and awareness. Anticipating the flow of the discussion will also allow you to seek out pertinent examples, topical debates, and relevant articles in advance. These can be used to stimulate the discussion or take it in another direction when it is timely to do so.

Be prepared to stimulate discussion by *posing challenges to viewpoints and positions that you agree with* in addition to questioning those with which you disagree. You will encounter participants who share your views but whose reasons for holding these views do not offer logical support for them.

If you challenge them to re-think their arguments, they will gain knowledge and skills that can serve them well when faced with other ethical dilemmas in their future work.

## Guidelines for facilitating a group discussion

While each facilitator will bring his or her own skills to the role, we offer a few brief suggestions here.

1. Provide affirming and encouraging comments as these will promote a safe and supportive environment that will help to overcome any initial reluctance of some participants to speak. Encourage everyone to be supportive rather than competitive with each other as this will promote a full and lively discussion.

2. Try to get many different people to speak when the case is discussed; move the discussion around from left to right and front to back so that all feel that they are active participants. When a speaker's voice is too soft, repeat the comment or question.

3. In order to discourage "in-groups" and "out-groups", treat all participants fairly and equally even if some are known to you. When speaking, address the entire group, not just the speaker or questioner as everyone is part of the audience.

4. The language used in the classroom or workshop may be the second or third language of some of the participants. Some participants may be struggling to communicate and may be abrupt in their communication as a result of language and not intent. When that occurs, you can reiterate the heart of the participant's comment; such rephrasing will not only allow others to comprehend the point and provide them with a model of how to make a point but will also allow you to confirm that the original speaker's idea has been correctly understood.

5. Discourage participants from bringing in private debates; rather, encourage them to open the discussion to everyone.

6. Avoid and deflect any personal attacks.

7. Assist participants in looking at the same issue from a number of different perspectives.

8. Feel free to modify the case study by adding more information or changing certain details when that will help the discussion move forward.

9. Encourage participants to move back and forth between the case studies and the research guidelines and other material they may have read or been presented in order to build the most comprehensive knowledge. Use phrases like, "What about if…", "That's a good point but how does it fit with…", "Here's an example of a drug trial where the opposite was done and …", "Can you think of a local example or an example from your own experience…?"

10. Encourage participants to speak succinctly and directly.

11. Discussions can take unexpected turns – both for the better and for the worse. Try to determine which is which, and be flexible enough to follow the good leads and astute enough to gently re-direct the discussion if the diversion is not useful.

12. As the discussion progresses, from time to time summarize what has been covered in order to assure participants that learning is indeed happening. Case studies, which can be full of dilemmas and don't have ready answers, can leave participants feeling frustrated that nothing has been resolved even though there has been much talk. A summary in which attention is drawn to the key insights can reassure participants, move discussion forward to the next points to be addressed, and provide a useful wrap-up for the session. A group discussion of a case can, at its best, impart insights as effectively as an expert "Socratic" lecture, i.e. one in which the lecturer draws the insights out of the participants rather than offering them as part of a prepared talk.

# Teaching Guide

## Exploring the content of each chapter

This section is intended for discussion facilitators or leaders while the chapter introductions in the casebook itself are suitable for copying and sharing with students and workshop participants.

The case studies are organized into chapters based on the principal ethical issue raised in each study. Most raise additional dilemmas and can easily be used to raise more than one issue; the table of contents suggests ways for reassigning some cases among the existing categories. Facilitators may choose to identify cases that deal with a particular topic of interest, such as studies involving reproductive health or a phase II clinical trial or studies conducted in a particular geographical location.

While the chapter introductions provide important background material for participants in the workshop or class, the material provided here in this teaching guide is intended to help facilitators identify some of the main ethical issues chapter by chapter. The questions provided are intended to suggest how the ethical issues in the case studies can be approached in a discussion and some areas that the facilitator may wish to prepare for in advance of the discussion. Although there are many more questions, readings and examples than are provided here, we hope that these prove to be a useful starting point.

### Chapter I: What is research?

This chapter encourages workshop or classroom participants to consider two distinctions: first, research with human participants as distinct from medical treatment and, second, the differences between research and other activities involving some sort of investigation with human beings (e.g. evaluation, surveillance or audit). What is it that distinguishes each of these activities and leads only some (i.e. health research) to require approval by a research ethics committee? For example, does the level of risk to participants play a role in the decision to require ethical oversight? An exploration of these questions can lead quite naturally into a discussion of the mandate and authority of research ethics committees. The points below expand on these questions and can be used to encourage participants to consider the following:

- Why lines might need to be drawn between research, on the one hand, and medical treatment or public health activities, on the other.
  - Are such lines primarily useful for analytic purposes, or as a means of determining which activities need which types of ethical standards and oversight?
  - Is research inherently more risky than medical treatment or public health activities, and hence in need of oversight by people other than researchers, or can non-research activities pose equal or greater risks, and if so, are oversight mechanisms used for research relevant or irrelevant to reducing the risks of non-research activities?
- The differences in objectives, and hence of obligations, between medical treatment (the therapeutic or humanitarian mission) and health research (the knowledge generation mission). Awareness of such differences (or 'conflict of missions') is relevant for a number of reasons, prime among them is whether the trust of patients in the medical profession is endangered when a physician recruits a patient into a research study.
  - How should a physician engaged in health research ensure that a patient who is a 'potential research participant' is aware that a medical intervention is being undertaken to generate knowledge and not necessarily (or, at least, not solely) to advance the patient's individual health interests? What does a patient need to know before becoming a participant and how and by whom should this information be relayed?

- What is the role of informed consent? That is, what purpose is it supposed to serve? Why would (most) research be unethical without informed consent?
- Are there circumstances when it would be inappropriate – even wrong – to enrol patients as research participants? Is this true even when the patients would be willing to participate, if asked?
- If potential participants are vulnerable – perhaps because they have limited or no access to appropriate health care, as is often the case in developing countries – are there additional considerations that need to be taken into account? Does it make sense to describe patients from ethnic minorities or women and children as 'vulnerable', a term that is often used for people who are poor (or, more generally, residents of developing countries)?
- Some patients join research studies because they have no other way to get the care they need. Is their participation "voluntary"? Even if they understand the terms of the invitation to participate, should their consent be regarded as valid? Should the recruitment of these patients be carried out any differently? Do the various guidelines have anything to say on this? How would the ethical principle of 'respect for persons' be applied in this case?

- What role-confusion may researchers experience when working with patient-participants?
  - If a medical practitioner begins with the role of treating patients using the best known methods, then how is research, which uses unproven and possibly risky new interventions, justifiable?
  - Is it an ethical problem, or even a conflict of interest, for a physician to be paid for recruiting patients into a research study?
  - Does the determination of which body or committee should be charged with providing ethical review and oversight depend upon the objective of a particular activity? What considerations does a research ethics committee need to take into account in its review as opposed to considerations which ought to concern bodies that oversee medical practice?
- Compare research activities (including epidemiological research, operations research, formative research) with activities that also aim to produce information, such as public health surveillance, audit, and programme evaluation.
  - The common definition of research, which focuses on the production of 'generalizable knowledge', is intended to exclude the practice of medicine even though therapeutic and diagnostic interventions sometimes produce new information (especially about a particular patient) or amount to 'innovative treatment'. Does the same distinction hold between research and the practice of public health when activities such as public health surveys and disease surveillance may involve large numbers of observations and produce scientifically valid findings?
  - Advance review and approval were instituted for clinical trials and other biomedical studies because of the numerous instances where physicians and other scientists had overstepped ethical lines in carrying out research. Are the same requirements appropriate for public health research that is carried out by publicly accountable officials? What sorts of authorization, in terms of statutes or regulations, should be regarded as substitutes for the prior ethical review and individual informed consent mandated for clinical trials and comparable types of health research?

This chapter on defining research can also:

- Provide a starting point for examining research guidance documents such as the World Medical Association's *Declaration of Helsinki* (DoH),[1] the CIOMS *International Ethical Guidelines for Biomedical Research Involving Human Subjects*,[2] and the CIOMS *International Ethical Guidelines for Epidemiological Studies*,[3] since all address the tension between health research with human beings and medical treatment. The DoH was developed by the World Medical Association to address the ethical responsibilities of physicians when conducting research; both of the CIOMS international ethical guidelines documents are intended to elaborate the *Declaration* especially for use in developing country settings.

- Be used to explore the evolution of research ethics guidelines and the importance of separating research from medical practice; the preamble in each of the CIOMS guidance documents provides a good introduction for understanding what constitutes research.

- Provide concrete examples for exploring the mandate of a research ethics committee (REC) and therefore a good place to begin an initial training workshop for REC members. Facilitators may wish to provide additional examples of situations where it was either not clear whether the information being gathered was research or, for example, public health surveillance, and examples where research must be stopped and medical treatment provided.

## Chapter II: Issues in Study Design

The proper design of research studies presents numerous scientific and management questions, such as the appropriateness of a study design to answer the hypothesis, whether it has adequate statistical power to produce valid results, and the ability to achieve the sample size in a timely fashion. But the scientific design of a study can also raise significant ethical issues. For example, research in social psychology often relies on deception. In one famous series of experiments, research participants were placed in a group and were tested to see if their judgments were influenced by the opinions of other group members. However, unknown to the research participants, the group members were actually confederates of the research team whose statements were set by the experimental script.[4] According to the investigators, the study would have been impossible if they were required to disclose this deception in order to obtain informed consent. Instead, they argued, it would be ethical to wait to tell the research participants these facts as part of a 'debriefing' after they had participated in the experiment. A different kind of ethics-related design issue arises when research designs appear to be chosen specifically to ensure an outcome favourable to the study's sponsor. For example, to increase the chance that an investigative drug will prove superior to a rival treatment a clinical trial might use the latter at a subclinical dosage, or the endpoints chosen might be those known through preliminary trials to be particularly affected by the investigative drug rather than those of greater clinical importance.

International research carried out in developing or resource-poor countries requires that the research be sensitive to the social, cultural, political and economic context of the country and community in which the research will take place. The design of these studies should avoid exploiting the population; furthermore, there is growing consensus that research should contribute to expanding the capacities of the health systems in such countries and to reducing health disparities.

[1] WMA, op.cit., p.13.

[2] CIOMS, op.cit., p.13.

[3] Council for International Organizations of Medical Sciences (CIOMS). International Ethical Guidelines for Epidemiological Studies. Geneva, Switzerland: Council for International Organizations of Medical Sciences (CIOMS), 2009. http://www.cioms.ch (accessed 19 May 2009)

[4] Asch, S. E., Opinions and Social Pressure, *Scientific American*, 193: 31-35 (1955); Korn, J.H., Illusions of Reality: A History of Deception in Social Psychology, Albany, NY: State University of New York Press (1997), esp. pp. 76-80.

A recent monograph by Dr Patricia Marshall, *Ethical Challenges in Study Design and Informed Consent for Health Research in Resource-poor Settings*,[1] provides excellent background preparation for facilitating a discussion based on this chapter and is useful also for chapters 3 to 6. Her work draws attention to the centrality in designing ethical research, of paying attention to cultural contexts, health disparities, collaborative partnerships and capacity building, standards of care, and access to benefits derived from research. In addition, the case studies and commentaries in *Ethical Issues in International Biomedical Research: A Casebook*,[2] provide very useful background and real life examples that can be used to illustrate ideas raised in the classroom or workshop.

A number of issues are raised by the case studies in this chapter, including:

- The relationship between questionable science and ethics, and how an ethics committee should respond when asked to review a protocol that appears to be scientifically unsound, naïve, or inappropriate to the task. One viewpoint is that research ethics committees should be concerned primarily with ethical questions, referring questions of scientific soundness to others responsible for (and expert in) the particular field of scientific research. An alternative view is that 'bad science is bad ethics', even in studies that pose little or no risk to subjects, and that research ethics committees must therefore be concerned with scientific as well as ethical questions. A complicating factor is that in resource-poor settings it may be impractical to divide these responsibilities among multiple committees.
- Whether individual rights and protections are compromised by the research design when, for example, the risk-benefit ratio appears too high, when the research is conducted with an identifiable population or group which may be stigmatised or otherwise harmed by the results, or when the participants are not fully informed such as in a study design which uses deception or observation. The "Tearoom Trade" study, conducted by Laud Humphreys, is one of the most well-known studies in which an investigator disguised the purpose of the research from his subjects.[3] It may provide a useful example for a discussion concerning the trade-off between gaining scientific knowledge and respecting research participants. The article in the reading list by F. Van den Borne, entitled Using Mystery Clients to Assess Condom Negotiation in Malawi, is an excellent resource for understanding deception design and the rationale for 'mystery clients'.[4]
- Whether there are research designs which could yield quality results but are less risky for subjects or impose a smaller burden on them.

[1] Marshall PA. Ethical Challenges in Study Design and Informed Consent for Health Research in Resource-poor Settings. Geneva, Switzerland: WHO/TDR, 2007. https://www.who.int/tdr/publications/tdr-research-publications/ethical-challenges-study-design/pdf/ethical_challenges.pdf (accessed 30 August 2008)

[2] Lavery JV, Grady C, Wahl ER, Emanuel E (eds.). Ethical Issues in International Biomedical Research: a casebook. Oxford, UK: Oxford University Press, 2007.

[3] Humphreys L. Tearoom Trade: Impersonal Sex in Public Places. Chicago: Aldine Publishing Co., 1970.

[4] Van den Borne F. Using Mystery Clients to Assess Condom Negotiation in Malawi: Some Ethical Concerns. *Studies in Family Planning* 2007;38[4]. http://dx.doi.org/10.1111/j.1728-4465.2007.00144.x (accessed 25 August 2008)

- The question of justice when certain populations are excluded because of age, gender or an existing disease. These people may be spared the burden (if any) of the research, but the information obtained through the study may then not be as useful in treating people in these populations. Conversely, when participation in research would be likely to confer a net benefit for research participants, is it unfair to exclude members of these populations in order to strengthen the study design (e.g. when the inclusion of older patients, who are more likely to die of other causes, might obscure a modest but real extension of life among research participants who receive the experimental intervention)?

- What provision must be made for treatment and care of participants, their families and communities? Given that ethical guidelines generally operate at the level of broad principles, rather than specifying practical applications, how would one go about negotiating or determining the exact obligations regarding treatment for research subjects in light of the principles stated in the guidelines? Do the guidelines themselves provide adequate ethical justification for such obligations?

- Whether it is ethical to give the participants assigned to the control arm of a clinical trial a placebo, and if so, under what circumstances and contexts? Two important features of research design, equipoise and randomisation, can be explored through the case studies in this chapter. In addition to the articles in the suggested reading list for this chapter, and the basic ethics guidelines (such as the DoH and the CIOMS *International Ethical Guidelines*), both the previously cited *Ethical Issues in International Biomedical Research: A Casebook*,[1] and the *Ethical Challenges in Study Design and Informed Consent for Health Research in Resource-poor Settings*[2] monograph address the topic of using placebos in clinical trials.

- Whether traditional medicine can and should be tested and measured using western scientific research methodologies (as in Case Study 14, titled *Evaluating the Use of Traditional Medicines for Diarrhoea*). If not, then how can they be effectively researched? Is it ethical to test a traditional treatment when an effective allopathic alternative exists? Do the same standards apply – and if not, why not? Are the international guidelines in conflict with the testing and promotion of traditional and alternative treatments?

- Whether, to win approval from a research ethics committee, a study must be in line with the country's national priorities in health care and research. If the disease under study is not a high priority, or if citizens of that country will not be able to afford the treatment being tested, should the research be carried out there?

## Chapter III: Harm and Benefit

Risk of harm to research participants is one of the most difficult issues that all stakeholders in the research process (researchers, sponsors, research institutions, host countries, research ethics committees and participants) must consider and weigh. What risks are acceptable to achieve the anticipated benefits? Who should be asked to accept these risks and why? Who should decide what level of risk is acceptable? In the context of research in developing countries, resolving the issues raised by such questions is crucial in ensuring ethical research.

[1] Lavery, op.cit., p. 21.

[2] Marshall, op.cit., p.20.

With research increasingly being conducted in developing countries, there has been a greater focus on the broad range of potential harms and benefits, and the special allocation issues that arise in contexts where many factors – poverty, a lack of access to healthcare, gender inequality and other vulnerabilities – need to be taken into consideration in weighing the harm-benefit ratio. How can one achieve the "optimal synergy between the development of new health technologies, on the one hand, and the promotion and protection of ethical and human rights principles, on the other ".[1] Recent clinical trials of microbicides for HIV prevention (such as those described in *Ethical Issues in International Biomedical Research: A Casebook*[2]) bring these issues to the forefront. The National Bioethics Advisory Commission report, *Ethical and Policy Issues in International Research: Clinical Trials in Developing Countries*,[3] can also be a useful resource for this chapter. Recent ethical guidance strongly suggests that the question of benefits is not only about benefits to individuals – although this remains important – but also benefits to families, communities and countries (for example, providing post-trial access to a successful intervention broadly rather than solely to the people who took part in the research). There is, as yet, little consensus on the extent of such obligations, and research ethics committees have to reach their own judgments.

When working with each of the case studies in this chapter, students or workshop participants will need to consider the following:

- The risk of participants being harmed either during the research process or once the results are disseminated. The risks to participants in social science research ought not be overlooked as, for example, the literature on research on violence against women aptly demonstrates.
- Whether any aspects of the research design generate unnecessary risks and, if so, what can be changed to provide subjects with greater protection?
- Whether the benefits to the participants, or to other future beneficiaries, warrant the risk of harm to this particular group of participants, their families and communities. What contextual factors or specificities need to be considered in each case study in order to make a decision as to whether the harm/benefit ratio is acceptable?
- If participants are informed of, understand, and accept the risks of a research study, does this release the research ethics committee of responsibility for approving what may be a risky trial? How should responsibility for adverse outcomes be apportioned among the scientists, the research subjects, and the research ethics committee? What do international guidelines and norms have to say on the just allocation of potential harms and benefits, particularly in research conducted in developing countries?
- Whether certain potential harms are ethically acceptable… What safeguards are in place – e.g. a data safety monitoring board (DSMB) – to monitor and stop trials should problematic results occur in each of the phases? What are the ethical responsibilities of a DSMB?

[1] Tarantola D, et al. Ethical considerations related to the provision of care and treatment in vaccine trials. Vaccine, 2007, 25:4863-4874. http://dx.doi.org/10.1016/j.vaccine.2007.03.022 (accessed 25 August 2008)

[2] Lavery, op.cit. p. 21.

[3] National Bioethics Advisory Commission. Ethical and Policy Issues in International Research: Clinical Trials in Developing Countries, Volumes I and II. Bethesda, MD, USA: National Bioethics Advisory Commission, 2001. http://bioethics.georgetown.edu/nbac/pubs.html (accessed 9 May 2008)

- What benefits are anticipated and do these outweigh the risks? What factors would you consider in determining the right balance? How are the risks and benefits allocated? Are there obligations which come with asking people to take risks and what are these? Are they to participants alone or to broader groups of people? In a country where participants may have little access to health care, are the obligations to provide benefits higher than they would be in a developed country?

- Can a potential trial benefit become an 'undue inducement' to participate? Is this a universal standard or contextual? If a potential participant who is aware that a trial entails high risk is given substantial amounts of money – or other goods or services – to "compensate" for the risk and then agrees to take part in the trial, is this unethical? Conversely, would it be unethical to seek out subjects willing to participate for a more modest reward? What ethical principles might one use to help reach a decision?

## Chapter IV: Voluntary Informed Consent

The case studies in this chapter are intended not only to draw attention to the importance of informed consent, but to explore informed consent processes in the context of international health research. Numerous studies have shown that participants in research too often do not have an adequate understanding of the purpose of the research they are being asked to consent to, nor of its potential harms and benefits and the alternatives to participation. Because informed consent is mandatory in most research contexts, an important question becomes how to ensure that information about the research, and the participant's agreement to participate, is appropriately communicated. The case studies in this chapter encourage discussion of a range of alternatives.

- Contextual factors in countries and communities where international research is conducted make it highly inappropriate to try to export a standardized consent form from one country and context to another, especially from a developed to a developing country. But is it appropriate to export the requirement for individual informed consent itself? (As a facilitator teaching Case 24, you may wish to be familiar with the work of Love et.al., whose work is relevant to this case.[1])

- "Informed consent" is an ambiguous term: it could mean either that a potential subject has been informed about a clinical trial or that the subject has understood what he or she has been told, or both. In the context of treatment, the former seems to have been the original meaning, whereas in the context of research, the people introducing the term apparently had the latter meaning in mind. Should we therefore abandon the term and look instead for "consent based on adequate disclosure" and "comprehending consent," respectively? Should we call the process "understood consent" as a way of determining whether the participant can answer specific questions, either verbally or in writing, regarding the specifics of the study?

[1] Love RR., et al. Oophorectomy and Tamoxifen Adjuvant Therapy in Premenopausal Vietnamese and Chinese Women with Operable Breast Cancer. *Journal of Clinical Oncology*. 2002 May 15;20(10):2559-66. http://jco.ascopubs.org/cgi/content/full/20/10/2559 (accessed 30 August 2008)

- Informed consent as an underlying principle of ethical research implies (and depends on) each research participant's ability to make a decision autonomously. However, culture, custom, or other factors having to do with safety or trust for example, may place a higher value on the prerogative of a community leader or a male head of household to make decisions for others. Individual autonomy may hold a much lower value and may even be seen as challenging an established structure. Students or workshop participants should be encouraged to think about the application of international guidelines and human rights principles – all of which require individual informed consent by competent persons – in local contexts. This may involve both looking at the concept of individual consent, as well as the process by which it can be negotiated in order to ensure that the research is possible.

- A signed informed consent form is generally seen as adequate assurance that the participant has understood and agreed to the research. However, rather than looking at informed consent as merely a signature that signals a person's agreement to participate, students or workshop participants can consider what it would mean, in theory and practice, to treat informed consent as a process that is sensitive to contextual specificities. Culturally appropriate ways of disclosing information about the research should be found, as should an appropriate way of manifesting true consent and assent. Marshall's *Ethical Challenges in Study Design and Informed Consent for Health Research in Resource-poor Settings*[1] draws attention to, and provides examples of, a wide range of issues relevant for informed consent, including comprehension of information, communication of risks, decisional authority to consent to research, community consultation, and awareness of, and sensitivity to, social position and power inequities.

- Informed consent challenges researchers to take the time necessary to learn about the community where they are planning to conduct research, for example:

  - how are concepts of health and disease explained in this community, and how are illnesses traditionally treated? Is there a concept of research, and if so, who is trusted to conduct research?

  - what role does the community leadership play in decision-making in areas such as this? Is it clear who the leaders are, and who represents the best interests of the community and of the individuals who are part of that community?

  - could perceived or actual dangers result from signing a consent form or having a signed copy in one's home? In some places, people have (naively or under duress) signed forms that led to the loss of their homes or land; to ask potential subjects in such a locale to sign an informed consent form may therefore be inappropriate. A different sort of example arises in research on violence against women; investigators must exercise a high degree of sensitivity, since anything that links subjects to such a study risks exposing them to further violence.

  - is the potential participant literate and able to read the information provided or is it important to provide the information in a more accessible manner?

  - who is, and who isn't, competent to sign on their own behalf and why? If people are found to be incompetent (on account, for example, of being a minor or having a mental handicap), do provisions exist to allow for their wishes to be taken into account?

[1] Marshall, op.cit., p.20.

## Chapter V: Standard of Care

This chapter focuses on the heated debate in research ethics over whether a single, universal standard of care should be applied (i.e. participants in a clinical trial conducted in multiple locations would all receive the same care, even when care for non-participants differs greatly among the locations), or whether, taking socio-economic differences among locales into account, the standard of care changes as well. (Chapter VI on obligations to participants and communities raises additional related issues.)

The Nuffield Council on Bioethics report titled *The Ethics of Research Related to Healthcare in Developing Countries*[1] provides a good discussion of standards of care in developing country contexts and is suitable background for students and workshop participants. The report draws attention to the many ways that the research context adds complexities to what may initially seem like a fairly straightforward proposition – that equity requires that care for patients in health research should meet the 'highest possible standard' or care.

Some of the issues raised by the case studies in this chapter are as follows:

- What do international ethics documents say on the subject of placebos and what ethical reasoning do they provide? When an effective therapy exists, can the use of a placebo control ever be consistent with such documents' requirement that researchers and sponsors must provide the highest possible standard of care to all research participants?
- How is the "highest standard of care" defined? Compare these circumstances in which the treatment deemed best in wealthy countries:
  - is simply not feasible in a developing country context, e.g. because there are not adequate refrigeration or storage facilities, or because the drug supply chain does not operate well in a consistent fashion.
  - has not yet been approved for sale in the developing country, though it probably would be if it were submitted for approval.
  - is available in the developing country but only at high prices, or to a small elite, and though it could in practice be provided to all who need it, the cost (in money and/or in medical resources) would make this an unwise use of resources
  - has not be designated as the treatment of choice by the local ministry of health (whether for sound reasons or otherwise)
- If the prevailing standard of care is noticeably higher in a developed country (from where the investigator and/or sponsor come from) than in a developing country (where the research will be carried out),
  - is it ethical to provide the highest standard of care available anywhere in the world to the control arm *knowing* that others in the country with the same medical condition are not able to access that care? Might care at such a high level amount to an unfair inducement to participate in the research?
  - is it ethically preferable to provide – or not to provide – the highest standard of care to participants in the trial if there is no commitment (on the part of the research sponsor or the local health authorities) to continue to provide that level of care after the trial is finished?

[1] Nuffield Council on Bioethics. The Ethics of Research Related to Healthcare in Developing Countries. London, UK: Nuffield Foundation, 2002. http://www.nuffieldbioethics.org/go/ourwork/developingcountries/introduction (accessed 24 August 2008)

- would it ever be justified not to provide the highest standard of care to the control arm and instead to give them the local standard because that is what they would be getting if they weren't in the trial? Would doing so exploit an already vulnerable population and indicate that this population is of lesser value because its members live in a developing rather than a developed country where the highest standard is available to people like themselves?

- would it ever be justified not to provide the highest standard of care to the study participants when that standard would be so expensive or logistically difficult that requiring it would preclude testing a new therapy that would probably be very effective – albeit not as effective as the best therapy – when the new therapy would (if proven effective) be affordable for people in the test country, whereas the best therapy will not become available to the population for many years?

- is it ethical to test an intervention that is less than the highest standard against the highest standard, knowing that the intervention being tested is not likely to be as efficacious? How much less efficacious is acceptable? Would it be wrong to test such an intervention against the current best standard because the new intervention is likely to "fail" in such a trial, which would cause it to be rejected (even if it would "succeed" compared to a placebo and would offer the local population a better alternative than any now actually available to them)?

- if conducting such a trial would not be acceptable in a developed country, under what circumstances, if any, should it be approved by a research ethics committee in a developing country? What ethical principles or other factors should be considered?

## Chapter VI: Obligations to Participants and to the Community

There is little consensus on exactly what obligations researchers, sponsors, research institutions, governments and other stakeholders in the research process owe to participants and their communities. The authors of an article titled *Ethical Considerations Related to the Provision of Care and Treatment in Vaccine Trials*, point out that "[e]thical principles of beneficence and justice combined with international human rights norms and standards create certain obligations on researchers, sponsors and public health authorities…However, these obligations are poorly defined in practical terms; inconsistently understood or inadequately applied."[1] The case studies in this chapter are intended to stimulate thoughtful discussion of obligations in research, identifying who is responsible for providing those obligations and the process by which those obligations are discussed and negotiated. Although this discussion of obligations is pertinent to all research, the case studies here focus on international research in developing countries.

In addition to the article just cited – which provides a very good table of considerations regarding obligations relevant to good research governance – two recent guidance documents provide useful frameworks for thinking about these issues both in broad theoretical terms and in a very practical manner. Although they focus on HIV prevention trials, they may prove useful in other research contexts as well.

- Ethical Considerations in Biomedical HIV Prevention Trials. Geneva: UNAIDS and WHO, 2007. http://whqlibdoc.who.int/unaids/2007/9789291736256_eng.pdf (accessed 25 August 2008)

- Good Participatory Practices in the Conduct of Biomedical HIV Prevention Trials. Geneva: UNAIDS/AVAC, 2007. http://whqlibdoc.who.int/unaids/2007/9789291736348_eng.pdf (accessed 25 August 2008)

[1] Tarantola, op.cit., p. 23.

The topic of 'obligations in health research' is extremely broad and may contain too many wide-ranging issues for a short classroom or workshop discussion. As a facilitator, you may find that the discussion is of a higher quality with more analytical depth if very specific issues are examined systematically. You may, for example, wish to separate out a discussion of what participants and other stakeholders believe should be the obligations to participants and their families, from a discussion of the process by which those obligations are negotiated and who is charged with fulfilling them. The article by L. Belsky and H.S. Richardson titled *Medical Researchers' Ancillary Clinical Care Responsibilities*[1] provides an interesting framework which may be helpful for facilitating a discussion on obligations. The *Good Participatory Practices* document cited above addresses the process of discussing obligations. Facilitators may also want to be aware of the range of non-negotiable obligations placed on research by some national bodies, as well as by international guidelines.

The case studies in this chapter address questions of who is obligated and what their obligations are. This list is not exhaustive but should be seen as providing some initial ideas. Examples include obligations to research participants

- who are harmed as the result of research. Does it make a difference whether or not the healthcare system is accessible to the people who are research participants when determining the obligation to treat the harm?
- who experience a serious adverse event (and how is this defined?) Is pregnancy during a contraceptive trial a SAE?
- who are discovered by the researchers during enrolment screening to have a condition (HIV for example) other than the target disease Do researchers or sponsors have any obligation to provide care for such a condition or other benefits such as general health care, counselling, nutritional supplements, follow up care for short term or chronic conditions? What about for conditions that arise during the research? Does it matter whether they are related or unrelated to the intervention or disease being studied?

There may also be obligations to people who are not research participants, e.g. those who

- are directly negatively affected by any earnings loss or other harm to the participant
- live in close proximity to a participant receiving benefits and who may also be in need of those benefits (such as an older child in a poor household whose younger sibling is taking part in a study on the effects of nutritional supplements on young children's learning).
- need to be protected, based on information gained during research, such as when a researcher learns of abusive behaviour by a parent or drug abuse by a child. This also raises privacy and confidentiality issues that are examined in the next chapter.
- require someone to advocate for, or to give them, broad access to successful interventions.

Finally, is there an obligation to increase research and health literacy (knowledge and skill building)?

## Chapter VII: Privacy and Confidentiality

The case studies in this chapter are designed to encourage students and workshop participants to explore the many dilemmas that confront researchers in their attempts to uphold confidentiality and to protect privacy. Facilitators may want to begin by introducing the idea that the value placed on confidentiality and privacy is not universal but varies by culture. Some cultures or communities are suspicious of the emphasis on privacy and confidentiality or would understand a completely different set of actions as manifestations of privacy and confidentiality. Recognizing that there are various understandings of what is meant by those terms, as well as the different cultural value placed on them, can help the student or workshop participant to think through the purposes, and the limitations, of confidentiality and privacy in the research context.

[1] Belsky L, Richardson HS. Medical Researchers' Ancillary Clinical Care Responsibilities. *British Medical Journal*, 2004;328:1494-1496. http://dx.doi.org/10.1136/bmj.328.7454.1494 (accessed 25 August 2008)

Duties of privacy and confidentiality also have consequences for data protection, for who controls access to information, and for public health. This issue is explored in the article in the chapter reading list titled *Public Health and Data Protection: An Inevitable Collision or a Meeting of Minds?*[1] (The many issues raised by genomic research and data banks are not explored in the case studies but increasingly are becoming issues for researchers in international health research.) Issues related to the principles of confidentiality and privacy that facilitators may want to explore include:

- Whether there are there any limits to the expectation of confidentiality. If, in the course of research, a researcher learns of illegal, unethical or dangerous behaviour, should this be reported? Are there national or local laws which are applicable? What should happen if a consent form stating that all information will be kept confidential has been signed but it becomes clear that the participant poses a danger to him or herself, or to others? Should the informed consent form indicate that there are limits? What if reporting the illegal behaviour will likely result in the authorities (police or parents, for example) responding in a manner that the researcher thinks will be overly harsh? Some situations where the limits of confidentiality can be explored include:
  - researcher knowledge of child abuse
  - diagnosis of a contagious disease which could pose a public health threat
  - observational studies of dangerous or life-threatening behaviour to self or others involving a vulnerable person (an infant being fed with dirty water, a needle being reused in a health centre, a teenager who expresses a suicide plan)
  - illegal abortions resulting in post-abortion complications
  - focus group participants sharing information from the FG despite having been asked not to do so.
- How are confidentiality and privacy best achieved and maintained? What measures are in place and are these adequate?
  - When conducting research with a population who has disease that creates stigma, as is often the case with tuberculosis or HIV/AIDS, what extra precautions, if any, should be taken to ensure confidentiality (e.g. study data kept in a locked filing cabinet)?
  - Has adequate anonymisation (or other de-linking process) occurred for all data including samples stored for future use? Are all stakeholders aware of the need for confidentiality and how to maintain it? Who has legal rights to the data and for how long? When can the data be destroyed? How safe are electronic records?

## Chapter VIII: Professional Ethics

The case studies in this chapter focus on two aspects of professional ethics: conflicts of interest and scientific misconduct.

A discussion of conflicts of interest – which arises when an investigator can obtain money or comparable personal benefits through behaviour that is not consistent with his or her professional obligations as a physician and/or scientist – can encompass a number of important topics:

- In some countries, a majority of faculty in medical schools have financial links to industries in their field.[2] What effect would this be expected to have on rules about conflicts of interest?

[1] Lawlor DA, Stone T. Public Health and Data Protection: An Inevitable Collision or Potential for a Meeting of Minds? *International Journal of Epidemiology*, 2001; 30:1221-1225. http://ije.oxfordjournals.org/cgi/content/full/30/6/1221 (accessed 9 May 2008)

[2] Campbell EG et al., Institutional Academic-Industry Relationships. JAMA 2007; 298:15: 1779-1786.

- The trend toward commercially funded research and testing has been accompanied by a variety of financial incentives for investigators to recruit patients rapidly and to allow other ethically questionable practices such as "ghostwriting" (i.e. a scientist's agreement, that a paper actually written by a company employee can be published under the scientist's name). Some argue that these incentives stimulate innovation and the rapid translation of laboratory advances into therapeutic products. Critics argue that such arrangements threaten the integrity of scientists and of medical science.

- Are all conflicts of interest inherently wrong, or is it only wrong when someone who has a conflict of interest behaves wrongly?

- Which conflicts of interest are inconsistent with a professional being responsible for patient care? With being responsible for research design and conduct?

- What about conflicts that arise not from financial rewards but from an investigator's commitment to a particular set of ideas or theories? How do such conflicts differ from financial conflicts, for example, in the risks they raise for research participants, for the integrity of research, and in the means available to uncover and mitigate the conflicting interest?

- What evidence of conflict of interest should be routinely collected by research ethics committees? Is it their responsibility to ensure that the reports of conflicts of interest are complete and accurate, or should they rely on the investigator's integrity?

- What constitutes conflict of interest for a member of a research ethics committee? What precautions or remedies should be undertaken?

"Scientific misconduct" is the deliberate falsification of scientific data, or a distortion in the reporting of scientific data; it also encompasses similar violations of the internal norms of scientific investigation. While once regarded as unusual, these offences now appear to be more widespread and have been the target of investigations by governments, funding sources, universities, and journalists. Among the issues to explore in case-based discussions are:

- Are norms of scientific conduct – and, therefore, criteria for judging scientific misconduct – variable across regions and national boundaries? Or is science a single, global profession with common standards?

- What forms of scientific misconduct are the most serious? Which are the proper concern of research ethics committees?

- Who is responsible for identifying scientific misconduct (e.g. peers, staff, employers, journal editors, sponsors, government regulators)? If those deemed responsible do not take action, what are the responsibilities of others who learn of the misconduct, including research ethics committee members?

## Additional resources for case based teaching

*Fourtner, A.W., Fourtner CR. and Herreid CF.* **"Case Teaching Notes for "Bad Blood:" A Case Study of the Tuskegee Syphilis Project"** University at Buffalo, state University of New York

http://ublib.buffalo.edu/libraries/projects/cases/blood_notes.html (accessed 2 May 2009)

*Herriod CF.* **Return to Mars – How Not to Teach a Case Study**

http://ublib.buffalo.edu/libraries/projects/cases/teaching/mars.html (accessed 2 May 2009)

*Husock, H.* **"Using a Teaching Case"**, Kennedy School of Government Case Program. Harvard University: 2000

http://www.ksgcase.harvard.edu/ (accessed 7 April 2009)

*Pimple KD.* **Using Case Studies in Teaching Research Ethics**

http://poynter.indiana.edu/tre/kdp-cases.pdf
(accessed 2 June 2009)

*Waterman, MA., Stanley, EDA.* **"Assessing Case Learning"**
Case Based Learning in Your Classes. Author copyright 2004

http://cstl-csm.semo.edu/waterman/CBL/
(accessed 2 June 2009)