

MODULE FIVE: IMPLEMENTATION OF ETHICS REVIEW

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ABSTRACT

The objective of this module is to inform you on issues of concern for Research Ethics Committee members and investigators during the review process. The many guidelines on research ethics, including those from the South African Department of Health and the World Health Organisation, will be referred to extensively to educate you on the requirements of Research Ethics Committees. The evolution of the review process in South Africa will be detailed.

INTRODUCTION

South Africa is endowed with a rich, unique environment for qualitative and quantitative research, providing researchers from a range of clinical, medical, and allied disciplines with fertile grounds for the evaluation and testing of hypotheses, new treatments, and medicines. Concurrently, South Africa runs the risk of unethical research conduct, as it is home to a large number of vulnerable groups of poor populations that have limited or no access to education and health services, and who accept authority without question. Hence, it is not surprising that many researchers are drawn to South Africa.¹ The clinical trial industry in South Africa is reported to have increased by 40% between 1997 and 1998.² The total budget during 2000 for the industry

¹ South African Department of Health. 2000. *Guidelines for Good Practice in the Conduct of Clinical Trials in Human Participants in South Africa*. South African Department of Health. 2003. *Ethics in Health Research: Principles, Structures and Processes*. Draft.

² H.M. Christley. Conducting Clinical Trials in South Africa. *Applied Clinical Trials* 1998; 9: 56–59.

was estimated to be R826 million.³ Accordingly, the promotion of high ethical standards in research is imperative. Ethical review requires the appraisal of research proposals to objectively assess their effects on the potential participants and the general day-to-day functioning of the health systems.⁴

REVIEW METHODS

Currently, three methods requiring three different committee structures are used for review:

1. Research Ethics Committees – this chapter focuses on these committees;
2. Data and Safety Monitoring Committees – these oversee ongoing clinical trials with respect to treatment, efficacy, and safety. Where efficacy or harm is clearly evidenced, premature termination can be recommended on ethical grounds prior to the end of the trial; and
3. The Regulatory Authority (i.e. the Medicine Control Council) – responsible for reviewing the study design and in doing so, reviewing important ethical questions.⁵

To ensure a proper understanding of the implementation of an ethics review, it is necessary to comprehend what the requirements are that makes research ethical.

ETHICAL RESEARCH – REQUISITES

Purpose of research

The object of research in the medical and allied fields is to develop generalisable knowledge that leads to an improvement of health and/or increases the understanding of human biology.⁶ According to the *Declaration of Helsinki*, the ‘... primary purpose of medical research involving human subjects is to improve prophylactic, diagnostic, and therapeutic procedures and the understanding of the aetiology and pathogenesis of disease. Even the best proven prophylactic, diagnostic, and therapeutic methods

³ M. Joffe. Unpublished Research. *Informal Survey of Pharmaceutical Industry Performed in September 2000*. Wits Health Consortium (Pty) Ltd. (A wholly owned subsidiary of the University of the Witwatersrand.)

⁴ South African Department of Health, *op. cit.* note 1.

⁵ *Ibid.*

⁶ E.J. Emanuel, D. Wendler & G. Christine. What makes Clinical Research Ethical? *JAMA* 2000; 283: 2701–2711.

must continuously be challenged through research for their effectiveness, efficiency, accessibility, and quality.⁷ Research participants, who are placed at risk of harm for the good of others, are the means of securing this knowledge albeit at the expense of possible exploitation. For research to be considered to be ethical, this possibility for exploitation has to be safeguarded against. This can be achieved by ensuring that research participants are ‘... not merely used but are treated with respect while they contribute to the social good.’⁸

Codes and Declarations for the Ethical Conduct of Research – Difficulties

While there are various codes and declarations that guide the ethical practice of research, most of them lack a systematic and coherent framework for evaluating research studies that incorporate all requisite ethical considerations. This is because these documents were, in the main, responses to specific incidents and tools to avoid future scandals. Hence, by focusing on specific instigating events, particular ethical requirements are accentuated while others are suppressed or even omitted. The Nuremberg Code, for example, while focusing on the need for consent and a favourable risk-benefit ratio, makes no mention of fair subject selection or independent review. In addition, tensions and even contradictions exist among the provisions of various guidelines.⁹

Systematic and Coherent Evaluation – A Framework

In view of this absence of a universally applicable ethical framework to give guidance to researchers and reviewers alike, Emanuel et al.¹⁰ have proposed seven requirements that provide a systematic and coherent framework for determining whether research is ethical. These requirements have to be fulfilled in chronological order, from the conception of the research, to its formulation, to its implementation. Their purpose is to guide the ethical

⁷ World Medical Association. 2000. *Declaration of Helsinki: Ethical Principles for Medical Research Involving Human Subjects*. Adopted by the 18th WMA General Assembly, Helsinki, Finland, June 1964. Amended by the 29th WMA General Assembly, Tokyo, Japan, October 1975; 35th WMA General Assembly, Venice, Italy, October 1983; 41st WMA General Assembly, Hong Kong, September 1989; 48th WMA General Assembly, Somerset West, Republic of South Africa, October 1996; and the 52nd WMA General Assembly, Edinburgh, Scotland, October 2000.

⁸ Emanuel et al., *op. cit.* note 6.

⁹ *Ibid.*

¹⁰ *Ibid.*

development, implementation and review of individual protocols. They elucidate the ethical standards specific to medical and allied research, and assume general ethical obligations such as intellectual honesty and responsibility. While these requirements are meant to be universal, and not limited to particular tragedies, scandals or countries, their application will require adaptation to particular cultures, health conditions, and economic settings. Additionally, they elucidate the fundamental protections embedded in the basic philosophy of all the declarations and codes. As reviewers need to know what to enforce, the systematic delineation of the seven requirements is an important requisite to the review process.

The Seven Requirements in Chronological Order

- (a) **Value:** To be ethical, research must have a social or scientific value or both, i.e., it will lead to improved health and well-being and/or increased knowledge. Additionally, research where results are unlikely to be disseminated or in which the intervention could never be practically implemented, even if effective, is not valuable. The fundamental reasons for social, scientific, or clinical values to be ethical requirements are:
1. Avoidance of exploitation – research participants should not be exposed to harms without some possible social or scientific benefit; and
 2. Responsible use of finite resources – research resources are limited despite funding received from major funding agencies. It is unethical to waste resources and divert funding from other worthy social/scientific pursuits.
- (b) **Scientific Validity:** Unless research is conducted in a methodologically rigorous manner, the consequence would be scientifically unreliable or invalid, even where the research seeks to test socially valuable questions. Hence, not only is a valid research design necessary, but the research itself has to be carried out carefully and accurately in accordance with a sound design. The development and approval of a well-founded method is of little use if the research is conducted carelessly, without regard for accuracy – it results not only in data that cannot be interpreted, but is also a waste of time and scarce resources.

It is important to note that a valid hypothesis can be approached by poor research techniques. Hence, substandard research methods do not necessarily render the

research question valueless. The significance of the question should be assessed prior to, and independently of, the specific research method. Reviewers should not dismiss research proposals where the scientific validity is flawed without prior considerations being given to adjustments that could make the proposal scientifically valid.

Hence, poor science can be equated with poor ethics because:

1. Participants would be exploited and exposed to unnecessary risks; and
 2. Limited resources would be wasted on research that produces results that are questionable.
- (c) Fair Subject Selection: Participants must be selected fairly with respect to decisions regarding who will be included, both through the development of inclusion/exclusion criteria and strategies adopted for the recruitment of communities and potential groups. The scientific goals of the study, must be the primary basis for determining who is recruited and not vulnerability, privilege, or other factors unrelated to the purpose of the research. In addition, individuals, groups, or communities should not be excluded from the opportunity to participate without adequate scientific basis, or a demonstration of susceptibility-to-risk that justifies their exclusion. Research results must be generalisable to the populations researched, and hence these populations must have access to the proven interventions, e.g. women should be included in research unless a good reason, such as excessive risk, requires their exclusion. Consistent with the scientific goals of the research, participants should be selected in a way that minimises risks and maximises benefits to individuals and society. It is important that the stigmatisation of communities or groups is avoided at all costs. It is an ethical requirement that those who bear the risks and burdens of research should be able to enjoy the benefits. Fair selection is guided by the principle of justice:
1. Equals should be treated similarly; hence
 2. The benefits and burdens generated by social co-operation and activities such as research should be distributed equally.
- (d) Favourable Risk-Benefit Ratio: Research consistent with the scientific aims of the study will only be justified if three conditions are satisfied:
1. The potential risks to the individual participants are minimised;

2. The potential benefits to individual participants are heightened; and
3. The potential benefits to individuals and society are proportional to, or outweigh the risks.

The assessment of risks and benefits by reviewers and researchers will involve multiple steps. Firstly, the risks are identified, and within the context of good clinical practice minimised by the adoption of procedures with sound research design. It is important to remember that while participants in clinical research may receive some health services and benefits, the purpose of research is not the provision of health services. Researchers and reviewers are reminded that services directly related to research are necessary to ensure scientific validity and to protect the well-being of the individual participants. In the final analysis, if the potential benefits to subjects are proportional to the risks of participation, the additional benefits of the socially valuable and scientifically valid research will imply that the cumulative benefits outweigh the risks.

Requiring a favourable risk-benefit ratio embodies the long recognised fundamental values of research – the principles of non-maleficence and beneficence. In addition, ensuring that the benefits outweigh the risks is necessary in order to avoid the exploitation of the participants.

- (e) Independent Review: Investigators may have multiple competing interests that may generate conflicts, e.g. the need to complete a study quickly may result in using questionable scientific methods, or readily available research participants, rather than the most appropriate methods or participants. In order to minimise the potential impact of such conflicts of interests, reviews should be conducted by independent reviewers unaffiliated with the research. Independent review is also a requisite in order to ensure social accountability. Society will be assured that research participants will be treated ethically and that some segments of society will not benefit from the misuse of other human beings.
- (f) Informed Consent: This has two aims:
 1. To ensure that individuals control whether or not they enrol in research; and
 2. To ensure that individuals participate only when the research is consistent with their interests, values, and preferences.

Individuals must make rational and free decisions as to whether the research trials are compatible with their

interests. If not, enrolling them into trials would be treating them as a means to an end that they may not endorse.

- (g) Respect for Potential and Enrolled Subjects: Individuals must continue to be treated with respect from the time they are approached, throughout their participation, and after the completion of the research. This respect would entail:
1. Respecting privacy by managing all their information in accordance with confidentiality rules;
 2. Permitting participants to change their minds and withdraw from the trial without being penalised;
 3. Providing participants with new information gained during the trial;
 4. Monitoring their welfare throughout their participation; and
 5. Informing participants of what was learned from the research.

Respect is justified by the principles of beneficence, non-maleficence, and autonomy (see module 1 for details on the principle-based approach).

The above seven requirements should be treated as essential for the planning and reviewing of research. The fulfilment of each requirement in chronological order ensures that research has value, there is no exploitation, participants are treated fairly and with respect, and that their interests are protected. While these requirements are probably sufficient to ensure that, in the main, research will be ethical, additional requirements may be necessary in rare cases.

THE ROLE OF A RESEARCH ETHICS COMMITTEE (REC)

RECs provide ethical advice to researchers so as to assist decision-making on the adequacy of proposed research projects, with respect to the protection of potential and actual human research participants. RECs are constituted, and perform, according to four principles for ethical review: independence, competence, pluralism, and transparency.¹¹ In promoting its objectives, RECs should remember that research benefits society – hence research should not be hindered without good reason. RECs also serve to protect investigators from unjust criticism.¹²

¹¹ World Health Organization. February 2002. *Surveying and Evaluating Ethical Review Practices*. TDR/PRD/ETHICS/2002.1. Geneva.

¹² Medical Research Council of South Africa. 2002. *Guidelines on Ethics for Medical Research: General Principles*. Book I. Fourth edition.

HISTORY OF ETHICS REVIEW IN SOUTH AFRICA

In 1974, the Tuskegee Syphilis Study (1932–1972) scandal resulted in the United States Congress passing the National Research Act, which required the establishment of Institutional Review Boards (IRBs) to review all state-funded research. The basis for Congress' decision was the Belmont Report, which is a statement of the basic ethical principles and guidelines that should assist in resolving the ethical problems that surround the conduct of human subject research.¹³ In South Africa, despite there being no statutory requirement for ethics review of research at that time, individual institutions had already constituted review bodies to look at the ethical aspects of research. For instance, in October 1966 the University of the Witwatersrand formed a Committee for Research on Human Subjects (Medical), which has continued to function since its establishment, using the South African Medical Research Council Guidelines to assist REC members during the review process.¹⁴ The University has a clear policy on research on humans – any research, including record reviews, must be approved in advance by the ethics committee. In 1998, a process to develop guidelines to promote good practice and standards in the conduct of clinical trials in South Africa was started by the National Department of Health. This resulted in the production of a conceptual framework by the end of 1998, and a final document in 2000, 'The Clinical Trials Guidelines',¹⁵ which has been guided by and based extensively on the following documents:

- *Declaration of Helsinki*, October 2000;
- *International Guidelines for Ethical Review of Epidemiological Studies*, Council for International Organisations of Medical Sciences (CIOMS), 1991;
- World Health Organisation, WHO Technical Report series, No 850, *Guidelines for Good Clinical Practice (GCP) for Trials on Pharmaceutical Products*, 1995;
- World Health Organisation, *Operational Guidelines for Ethics Committees that Review Biomedical Research*. Geneva. TDR/PRD/Ethics 2000.1;

¹³ The National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research. April 18, 1979. *The Belmont Report: Ethical Principles and Guidelines for the Protection of Human Subjects of Research*.

¹⁴ P. Cleaton-Jones. Scientific Misconduct in a Breast-Cancer Chemotherapy Trial: Response of University of the Witwatersrand. *Lancet* 2000; 255: 1011–1012.

¹⁵ South African Department of Health, *op. cit.* note 1.

- MEDSAFE, New Zealand Regulatory Guidelines for Medicine, *Volume 3: Interim Good Clinical Research Practice Guideline*, August 1998;
- *ICH Guidelines for Good Clinical Practice*, ICH Harmonised Tripartite Guideline, May 1997;
- *Association of the British Pharmaceutical Industry Clinical Trial Compensation Guidelines*, Issued January 1991, Reprinted March 1994; and
- *Institutional Review Board (IRB) Guidebook*. Office for the Protection from Research Risk – National Institute of Health, USA, 1993.

Hence, it can be stated that the South African guidelines are informed by, and drawn from, the basic philosophies underlying major international codes, declarations, and other documents relevant to research with human participants. These guidelines, by incorporating all relevant ethical considerations, satisfy the criteria as advanced by Emanuel et al. in making available a systematic and coherent framework for evaluating studies.

In 2000, the Interim Ministerial Committee on Health Research Ethics was appointed, and has since functioned to review the guideline documents of 2000 and to act in an advisory capacity to local RECs. Once the National Health Bill is promulgated in Parliament, the National Health Research Ethics Council (NHREC) will be established, its functions being to:

- a) 'determine guidelines for the functioning of health research ethics committees;
- b) register and audit health research ethics committees;
- c) set norms and standards for conducting research on humans and animals, including norms and standards for conducting clinical trials;
- d) adjudicate complaints about the functioning of health research ethics committees;
- e) hear any complaint by a researcher who believes that he or she has been discriminated against;
- f) institute disciplinary action against any person found to be in violation of any norms and standards, or guidelines, set for the conducting of research; and
- g) advise the national department and provincial departments on any ethical issues concerning research.'¹⁶

¹⁶ National Health Bill. Government Gazette No. 23696 of 8 August, 2002.

The Bill further affirms that every institution, health agency, and health establishment at which health research is conducted must either establish or have access to a health research ethics committee, which is registered with the NHREC. To ensure uniformity in ethics review processes, the NHREC will accredit all RECs that review research. Hence, it is evident that the ethical practice of research will soon be a statutory requirement in South Africa.

COMPOSITION OF RECS

The REC should consist of a reasonable number of members who collectively have the qualifications, experience, and a citizen's understanding of the social priorities of the communities being researched. Hence, membership should include academics together with lay people to ensure that reviewers are not limited to individuals socially and culturally removed from the societies being researched. RECs need to be independent, multi-disciplinary, multi-sectoral, and pluralistic. To this end the South African guidelines¹⁷ recommend that the REC must:

- be representative and reflective of the communities served and the demographic profile of the country;
- have a membership of at least 9 with a quorum of at least 60% of members;
- be inclusive of members of both genders with not more than 70% being from one gender;
- have at least two lay persons who are not affiliated with the institution and who are not currently involved in medical, scientific, and legal work, and are preferably from the community;
- have at least one member who should have knowledge of, and current experience in, research areas regularly considered for review;
- have at least one member with professional training in both qualitative and quantitative research methodologies;
- have a member with knowledge of and current experience in the professional care, counselling and treatment of people (e.g. general practitioner, psychologist, social worker, nurse); and
- have a member with legal training.

¹⁷ Christley, *op. cit.* note 2.

RESPONSIBILITIES OF RECS

The core responsibility of RECs is to safeguard the dignity, rights, safety, and well-being of all participants in human subject research, with special attention allowed to studies including vulnerable individuals and populations. The REC must ensure that it is adequately informed of all the relevant aspects of a research protocol, including its scientific and statistical validity, in order to decide acceptability on ethical grounds. The following documents must be made available to the REC by the Principal Investigator of a study for review:

- trial protocol, any protocol amendments, scientific, and other literature validating research need and design, together with questionnaires where appropriate;
- written informed consent forms, participant information forms and updates of these forms with progress of the study, together with translated versions where appropriate;
- information on payments and compensation available to participants;
- declaration of conflict of interest of the researcher where appropriate;
- participant recruitment procedures e.g. advertisements;
- investigator's Brochure and available safety information where indicated;
- all reports from the Data and Safety Monitoring Board;
- reports on adverse events and serious adverse events;
- the investigator/s current curriculum vitae and/or other documentation evidencing qualifications;
- 6 monthly to yearly reports on the research (dependent on the complexity of the study) for continuous review; and
- any other document that the REC may require to fulfil its responsibilities.

The REC must review a research protocol within a reasonable period of time and document its views in writing. A review may result in an approval, a request for modifications before approval, disapproval, or termination/suspension of any prior approval.

Where research is to be conducted in vulnerable populations, the REC should determine that the proposed protocol and/or other documents adequately address the relevant ethical concerns, including a valid justification for the research not being conducted in less vulnerable groups. In addition, the protocol should meet applicable regulatory requirements, e.g. research with children, or in emergency situations.

Both the amount and method of payment to participants must be reviewed by RECs to ensure that the problem of coercion and undue influence on participants is avoided. Payment to participants should not be contingent on the completion of the trial and should be prorated. This information, including the methods, amounts, schedule of payments, and how payment will be prorated must be specified to participants in the written information form. (To be discussed in detail under inducements.)

REC members also have a responsibility to ensure that they possess research ethics capacity when reviewing research. To this end, it is necessary for the institution to ensure that members attend regular updates or courses in research ethics. Presently, most, if not all, RECs are constituted of members who have full-time jobs in academia and carry a heavy service commitment. Protocol review is voluntary and in most institutions individuals are not paid for services rendered as REC members. As the number of studies in South Africa has been increasing steadily, the REC chairpersons should regulate the number of protocols for monthly review to avoid members reviewing too many studies too quickly and incompletely.

To ensure the research participants' safety, the REC is responsible for the continuous review and monitoring of risk-prone studies, to make certain that emerging information has not altered the original risk-benefit analysis. Monitoring is also necessary to ascertain that the ethical aspects of the study, especially that of respect for persons, are upheld. At present, most RECs will do a continuous review of studies, but do not have the infrastructure or finances for active ethics monitoring of protocols approved by them. This is a failing of the participant protection ethic and needs to be addressed urgently.

MULTI-CENTRE STUDIES

Some research is designed so as to be conducted in different centres in differing communities or countries. As a general rule, to ensure the validity of the results, the studies need to be identical and must be conducted in an identical way at each centre.¹⁸ The number of multi-centre trials being undertaken in South

¹⁸ The Council for International Organizations of Medical Sciences (CIOMS). 2002. *International Ethical Guidelines for Biomedical Research Involving Human Subjects*. Available at: http://www.cioms.ch/guidelines_nov_2002_blurb.htm

Africa has increased substantially in recent years.¹⁹ It must be ensured that designs are appropriate for our local settings. Particular modifications may be necessary to the local study, e.g. inclusion/exclusion criteria. Hence, the research must undergo local review processes even though the sponsor country/site would have approved the protocol. Local RECs are empowered to prevent a study that they believe to be unethical. Where South Africa is chosen for research that is not being undertaken in a sponsor country, an explanation must be submitted to the REC explaining why this is the case. Special attention is paid to sampling strategies (regarding study design) and the appropriateness of incentive packages to trial participants.

INDUCEMENTS

The participation in research may affect the subjects financially, as they may have to take time off work and may incur costs due to travel to the research site. Participation in research could also have a positive benefit, in that free medical treatments may be received especially where healthcare is not readily available or at times non-existent. There is a fine line between acceptable recompense and undue inducement – hence the need for scrutiny and approval by the REC of all payments, reimbursements, and medical services provided by researchers to the participant.

Guideline 7 of CIOMS²⁰ describes the different situations where recompense may or may not be acceptable:

Acceptable recompense includes reimbursement for transport and other expenses, including lost earnings, inconvenience, and time spent as a result of their participation in research. Free medical services either related or unrelated to research participation would also be viewed as acceptable recompense. Large payments in money or kind and very extensive medical services would have the effect of persuading participants to take undue risks or volunteer against their better judgement, thereby undermining their capacity for free choice and manipulating the consent process, which would be rendered invalid. Recompense must be estimated taking into consideration the traditions and values of the populations being researched in order to avoid the situation of undue influence arising. Some cultures may have a tradition of gifts and exchanges, which will make some forms of

¹⁹ South African Department of Health, *op. cit.* note 1.

²⁰ CIOMS, *op. cit.* note 18.

recompense more appropriate than others.²¹ The REC will be the best judge of what constitutes material recompense in particular circumstances. RECs should safeguard incompetent persons against exploitation for financial gain by guardians. The only recompense offered to guardians should be a refund of travel and related expenses. Where a participant withdraws from a study due to study-related reasons (e.g. unacceptable side effects of the trial drug or on health grounds) he/she should be compensated as though full participation had taken place. Where withdrawal is for any other reason, compensation should be in proportion to the amount of participation. Where a subject has to be removed from the trial because of wilful non-compliance, the investigator is entitled to withhold part or all of the payment.²²

RISK/BENEFIT ANALYSIS

All the codes and declarations in research ethics clearly state that the risk to research subjects posed by participation in research should be justified by the anticipated benefits to the subjects and society. The term 'risk' refers to a possibility that harm may occur. The term 'benefit' refers to something of positive value related to health or welfare. Hence, risk/benefit assessments are concerned with the probabilities and magnitude of possible harm and anticipated benefits.²³ The research method should be designed so that the investigator ensures that the potential benefits and risks are reasonably balanced, and risks are minimised. The assessment of risks and benefits requires a careful appraisal of all available relevant data, including in some cases, alternative ways of obtaining the benefits sought in the research. This is borne out in several paragraphs in the *Declaration of Helsinki* – October 2000.²⁴ Considerations related to the well-being of the human subject should take precedence over the interests of science and society (Paragraph 5). Adequate laboratory testing and/or animal experimentation must precede clinical testing to demonstrate a reasonable probability of success without undue risk (Paragraph 11). Every project should be preceded by careful assessment of

²¹ Nuffield Council on Bioethics. 2002. *The Ethics of Research Related to Health Care in Developing Countries*.

²² CIOMS, *op. cit.* note 18.

²³ The National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research, *op. cit.* note 13.

²⁴ World Medical Association, *op. cit.* note 7

predictable risks and burdens in comparison with foreseeable benefits to the subject or others (Paragraph 16). Physician-researchers need to ensure that the risks involved have been adequately assessed and can be satisfactorily managed (Paragraph 17). Risks and burdens to the subjects must be minimised and reasonable in relation to the importance of the hypothesis being tested (Paragraph 18).

Minimal risk is defined as a risk 'where the probability and magnitude of harm or discomfort anticipated in the proposed research are not greater, in and of themselves, than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests.'²⁵ Many types of possible harms or benefits may result as a consequence of being enrolled in a study. There are, for example, risks of psychological, physical, legal, social, and economic harms, and the corresponding benefits. Risks and benefits may affect individual participants, their families, and society at large. Communities, as identifiable cohorts, run the risk of stigmatisation or even social and commercial victimisation as a result of the outcome of research in certain fields, e.g. epidemiology, genetics, or sociology. The research plan should be sensitive to such considerations, including the need to maintain confidentiality during and after the study, and the need to publish results in a manner that is respectful of the interests of all concerned, and perhaps in certain situations not to publish at all. The REC review includes ensuring that the interests of all concerned are given due consideration; often it is advisable to have individual consent supplemented by community consultation.²⁶

When research involves children, it should only be approved if the research places the child at no greater than minimal risk; if more than minimal risk is involved but this is justified by possible benefit for the child; or if there is greater than minimal risk with no prospect of possible benefit but there is a high probability that the research will provide generalisable knowledge about the child's disorder that is vitally important for the understanding or the amelioration of the condition.²⁷ (Risk/benefit favourability

²⁵ International Review Board. *Institutional Review Board Guidebook*. Chapter 3: Basic IRB Review. Available at: http://ohrp.osophs.dhhs.gov/irb/irb_chapter3.htm

²⁶ CIOMS, *op. cit.* note 18.

²⁷ South African Department of Health, *op. cit.* note 1.

analysis for children and other vulnerable groups have been discussed in detail in the previous chapter.)

CONFIDENTIALITY

Respect for research participants includes ensuring that their confidentiality and privacy is maintained. When research participants enrol in a trial they do so from a position of trusting that their confidences will be respected. If this were not the case, they would be deterred from participating or making complete disclosures where required. Accordingly, recruitment into, or retention in, the study may be compromised. In addition, results obtained from the study could possibly be inaccurate due to incomplete disclosures. It is imperative that investigators develop strategies to ensure that the confidentiality of the participants throughout the trial and after its completion is maintained. This will have to be discussed with participants during the informed consent process and written into the information document. Focus group discussions should be conducted where only absolutely necessary to the research design. Discussions should be facilitated in ways that steer away from individual personal, private, and sensitive disclosures. Strategies to protect the privacy of groups and communities will also have to be addressed where applicable. Harms to identifiable cohorts have been discussed above. RECs have to ensure during the review process that the investigator has paid adequate and appropriate attention to privacy protection in the research design.

Some research may require the use of hospital, school or employment records. The researcher must protect the confidentiality of that information. A breach of confidentiality may result in psychological harm, e.g. embarrassment, guilt or stress, or in social harms. Social harms may result in embarrassment within one's business or social group, loss of employment, or criminal prosecution. Particularly sensitive information that should be safeguarded against breaches in confidentiality is that concerning alcohol or drug abuse, mental illness, illegal activities, and sexual behaviour. Any plans that researchers may have to contact these individuals for follow-up studies should be reviewed with care.²⁸

Where databases are to be used to store raw data and results, confidentiality must be secured by use of appropriate standard

²⁸ International Review Board, *op. cit.* note 25.

operating procedures, including passwords for all staff involved in data capture and analysis in the case of a computer database. The use of a computer system that logs who has had access to the information and logs and dates all changes to the information is recommended. Satisfactory maintenance and back-up procedures for computer databases must be provided.²⁹

CONFLICTS OF INTEREST

Conflicts of interest involving RECs can occur at multiple levels. It has been suggested that RECs in academic institutions, by virtue of their constitution and location, are remarkably close to the scientific community whose research they review. This could possibly result in institutional and investigator protection at the expense of subject protection.³⁰ RECs should protect and maintain their independence within organisational structures so as to reduce the risk of compromising participant protections by institutional interests.³¹

Conflict of interest can also occur at the individual REC member level. Individual members may have ties to the researchers whose proposals they are reviewing. There may be concerns for the institution's financial welfare and reputation. REC members, at an individual level, may have excess faith in science and this could be harmful to human participants if potential consequences are overlooked. Increasing the number of members on the REC that are unaffiliated to the institution may be a way to overcome these conflicts at the individual and structural levels. In addition, where potential does exist for a conflict of interest, the REC member should disclose this and recuse him/herself from the review, discussion and voting processes. Where RECs are paid for review, these payments should be made prior to review and not be dependent on review outcome. Business management functions should be separate from the review function.

²⁹ South African Department of Health, *op. cit.* note 1.

³⁰ G.J. Annas. Ethics Committees: From Ethical Comfort to Ethical Cover. *Hastings Center Report* 1991; 21: 18–21. L. Francis. IRBs and Conflict of Interest. In *Conflicts of Interests in Clinical Practice and Research*. R.G. Spece, D.S. Shim & A.E. Buchanan, eds. New York. Oxford University Press: 418–436.

³¹ D.D. Federman, E.H. Kathi & L.L. Rodriguez, eds. 2002. *Responsible Research. A Systems Approach to Protecting Research Participants*. Washington. The National Academies Press.

CASE STUDIES

Case scenario I

A postgraduate psychology student at the University of Clinton, California, has obtained funding from her institution to do a study investigating and comparing attitudes towards safe sex among students at a tertiary institution in California and a developing world country. She has obtained REC approval to do the research from the University of Clinton. She has completed the study in her institution and arrived at the University of the Witwatersrand Medical School last week to commence the study here. She contacts Professor Fisher, head of Psychology, to make arrangements to commence the study. Her time is limited in South Africa and she has to return to California after two weeks. How should Professor Fisher advise her?

Model Answer

Despite having obtained approval for the study at her home institution, the study will still have to undergo formal local review by our local REC. It would be difficult for her to get approval and complete the study in the short time she has to spend in South Africa. She should have attempted to obtain local approval for the research before coming down to South Africa.

Case scenario II

The Department of Public Health at the University of the Kingdom of the Zulus has submitted a study protocol for review by the institutional REC. The aim of the research is to examine the attitudes of labour ward staff towards the patient in labour in a local state hospital. The research will have public health benefits because if it is demonstrated that women are poorly treated in labour, the Provincial Department of Health will be approached to institute remedial measures. Despite the research having social value, the reviewers find that the research methodology is very poor and have decided to reject the protocol. Has the REC acted correctly? Discuss.

Model Answer

In view of this research having important social value, the REC acted incorrectly by turning down the protocol. The correct line of action would have been to inform the investigator of the flaws

in the research design, to recommend changes and request that the protocol is resubmitted for review once these queries have been addressed.

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