GOVERNMENT OF BERMUDA
Ministry of Health
Department of Health

DEPARTMENT OF HEALTH

RESEARCH GOVERNANCE FRAMEWORK

GOVERNMENT OF BERMUDA

Ministry of Health

Department of Health

DEPARTMENT OF HEALTH
RESEARCH GOVERNANCE FRAMEWORK

April 2008

Published by:
Government of Bermuda, Department of Health
P.O. Box HM 1195, Hamilton HM EX, Bermuda
Phone: (+1 441) 278-6500 ● Fax: (+1 441) 296-3221 ● E-mail: healthpromotion@gov.bm

Author:
Jennifer Attride-Stirling, PhD
Health Promotion Coordinator, Department of Health

Kindly reference as:
Department of Health (2008) Research Governance Framework. First Edition. Government of Bermuda.

Contents

Introduction

1. The Department of Health is committed to the value of research in all health fields. Research is essential to the successful promotion and protection of health and well-being, and to the assurance of quality health care provision. However, some research can involve risk for individuals, families or communities, so it is imperative to ensure that there is proper governance of research practice. Patients and the public have a right to expect high quality scientific investigation and adherence to core ethical standards.

2. The purpose of this document is to set out a framework for the governance of research involving human subjects. The framework applies to research conducted in Bermuda or by Bermudian researchers, sponsors or funders. It applies to research involving the active participation of human subjects, or the collection of information about or tissue from human subjects. The framework applies equally to medical, behavioural and epidemiological studies pertaining to human health.

3. A Research Governance Framework is needed to establish standards for ethical research practice in the local context. Bermuda currently has no legal instruments to regulate research practice. Nevertheless, in the interest of the public, patients and vulnerable populations an explicit set of standards for ethical research practice is needed, to assure that the rights and integrity of human research subjects, their families and communities are protected.

4. Governance can be understood as the collection of processes that enable an organisation to make effective decisions in an efficient manner. This research governance framework has been established to set out the local standards for ethical practice in research involving human subjects.

International & Legal Framework

5. The Department of Health Research Governance Framework has adopted the World Health Organisation's International Ethical Guidelines for Biomedical Research Involving Human Subjects[1], and the International Guidelines for Ethical Review of Epidemiological Studies[2].

6. These international guidelines were developed by the Council for International Organisations of Medical Sciences (CIOMS), in collaboration with the World Health Organisation (WHO). Their purpose was "to indicate how the ethical principles that should guide the conduct of biomedical research involving human subjects, as set forth in the Declaration of Helsinki, could be effectively applied"[3]. The guidelines were intended, in particular, to support countries where socioeconomic circumstances, laws, regulation, or executive or administrative arrangements may render populations at risk of exposure to inadequate ethical research practices.

7. The CIOMS/WHO guidelines take the position, adopted herewith by the Bermuda Department of Health, that research involving human subjects must not violate any universally applicable ethical standards. It is acknowledged that the application of ethical principles has to take into account the socio-cultural context and local values, while respecting and adhering to the core ethical standards.

8. Internationally, biomedical research is generally guided by recognised and accepted principles of human rights, as stated in documents such as the Nuremberg Code, the World Medical Association's Declaration of Helsinki, and the Universal Declaration of Human Rights. These form the basis of the CIOMS/WHO guidelines.

9. The Nuremberg Code is a set of principles for human experimentation established in 1947 as a result of the trial of physicians at the end of the Second World War. The "Doctors' Trial" dealt with physicians who had conducted inhumane experiments on unconsenting prisoners and detainees during the Second World War. The trial verdict established ten points that constituted the "Nuremberg Code", which was designed to protect the integrity of research subjects and set out the conditions for the ethical conduct of research involving human subjects. The Code includes such principles as informed consent and absence of coercion, properly formulated scientific experimentation, and beneficence towards experiment participants. The Nuremberg code has been incorporated into law in many countries.

10. The Declaration of Helsinki was developed by the World Medical Association (WMA) in 1964, as a set of ethical principles for the medical community regarding

[1] CIOMS, 2002
[2] CIOMS, 1991
[3] Quoted in CIOMS, 2002

research on human subjects. The Declaration is broadly regarded as the fundamental document for biomedical research ethics. It has influenced the formulation of international, regional and national legislation and codes of conduct. The Declaration developed the ten principles of the Nuremberg Code; it is a comprehensive international statement of the ethics of research involving human subjects, setting out ethical guidelines for physicians involved in biomedical research.

11. The Universal Declaration of Human Rights is an advisory declaration adopted by the United Nations General Assembly in 1948. It was enshrined in international law in 1976 in the form of two covenants that comprise the International Bill of Human Rights. One of the covenants, the International Covenant on Civil and Political Rights (ICCPR) states in Article 7 that, "No one shall be subjected to torture or to cruel, inhuman or degrading treatment or punishment. In particular, no one shall be subjected without his free consent to medical or scientific experimentation". The ICCPR was extended to Bermuda by the UK on 5th May 1976. The Constitution of Bermuda enshrines the majority of articles of the ICCPR into domestic law.

12. The Bermuda Department of Health subscribes to the Principles of the Ethical Practice of Public Health[4], which includes two standards with immediate relevance to biomedical research ethics. Principle 2 states that "Public health should achieve community health in a way that respects the rights of individuals in the community", and Principle 10 states that "Public health institutions should protect the confidentiality of information that can bring harm to an individual or community if made public". These are in line with the CIOMS/WHO guidelines and support the general principles of confidentiality and respect for autonomy enshrined therewith.

[4] Public Health Leadership Society, 2002

Ethical Principles

13. The integrity, dignity, rights, safety and well-being of research participants must be the principal concern of any study, in order to be ethically sound. There are three fundamental ethical principles that govern appropriate practice in research involving human subjects: respect for persons, beneficence and justice. These principles are stated as foundational in the CIOMS/WHO guidelines, and in specific countries' regulations, such as the U.S. Belmont Report, which states them as the core ethical principles for the protection of human subjects.

14. It is broadly agreed that these principles underlie ethical treatment of individuals and communities in conducting research studies. Although other important principles often apply to research, and the application of these principles can vary according to circumstances, they remain the accepted foundations for ethical decision-making in research involving human subjects.

15. **Respect for Persons:** This principle concerns the autonomy of individuals, the dignity that must be afforded in all cases, and the additional protection necessary for individuals with diminished autonomy. Specifically, it demands:
    - That the autonomy of persons always be respected: people who are capable of making personal choices must always have this capacity respected and be enabled to exercise it by giving informed consent to participation in research; and
    - That persons with impaired or diminished autonomy be respected and protected: that is, people who are dependent or vulnerable, with less capacity to make personal choices, have their human condition respected equally to others' with full capacity, and that additional protections be in place to safeguard them against harm or abuse; these include children, prisoners, people with cognitive disabilities, and people with severe illnesses.

16. **Beneficence:** This principle refers to the requirement that research should always maximise benefits and minimise harm. The principle requires that possible risks of research are reasonable in light of the expected benefits; that the design of a research study is sound; and that those conducting the research and handling patients and data be competent and able to protect the well-being of the participants involved. By the same token, the principle of non-maleficence ("do no harm") must always be applied to guard against avoidable harm to research participants. Research risks must always be justified by the expected benefits of the study.

17. **Justice:** This principle concerns the fair treatment of research participants. It is based on the tenet of *distributive justice*, which demands the equitable distribution of burdens and benefits. In research terms, it refers to the relative influence and power of researchers and participants, a balance that must always be in favour of participants' interests. This includes the need to make special arrangements where research involves vulnerable populations, i.e. those with less capacity to protect

their own interests. Research participants must always be the least vulnerable necessary to accomplish the purposes of the research. Therefore, risk to vulnerable populations may be justified when research is intended to develop knowledge with the prospect of delivering health-related benefits for that particular population. However, research should not involve populations unlikely to benefit from subsequent findings; careful ethical consideration must be given to justify exceptions. Sponsors of research have an ethical obligation to refrain from practices that contribute to unjust conditions or inequalities in a given setting or population, or that avoid complex regulatory systems by conducting research in less regulated or disadvantaged communities.

Ethical Review of Research Studies

18. The purpose of ethical review by an approved ethics committee is to consider a proposed research study in light of ethical principles, in order to ensure that all aspects of the study satisfy the established ethical standards. Ethics committees have a responsibility to ensure that possible ethical objections are identified, that potential risks and benefits are taken into consideration, and to consider proposals in the context of the time and place where the research is to be conducted. Researchers must demonstrate that ethical objections are satisfactorily resolved before a study begins.

19. Research is understood as any systematic investigation designed to develop or contribute to generalisable or new knowledge by addressing clearly defined questions using rigorous methods. In this context, research includes medical and behavioural studies pertaining to human health. Any research involving human subjects, or any information or tissue from them, must secure ethical approval before it begins.

20. Programme evaluation and audit are excluded from the definition of research if the knowledge derived is intended exclusively to inform investigators on the performance of that particular programme. This refers to the collection and analysis of data about a particular programme in order to ascertain its efficacy and assure quality. Such activity cannot be used to derive or publicly report generalisable knowledge about a population or intervention. Where generalisable knowledge is sought, it must be regarded as research and be subjected to ethical approval processes.

21. The Department of Health requires that the Ethics Committee of the Bermuda Hospitals Board (BHB) approve any research study involving human subjects' participation, information or tissue that is to be conducted in Bermuda or by a Bermudian agency, sponsor or funder. Specific requirements for ethics approval application can be obtained from the BHB Ethics Committee. Ethics approval must be obtained before the study begins.

22. If key sponsors or primary researchers are based in another jurisdiction, the Department of Health requires that ethical approval be secured from the relevant authorities in the country of origin (e.g. hospitals, universities, government) before seeking Bermuda approval.

23. The Department of Health requires that the final research protocol, the BHB Ethics Committee's letter of approval, and written approval from participating centres confirming acceptance of final protocol be submitted to the Chief Medical Officer.

24. The final research protocol must include all relevant elements described in Appendix 1, including a clear statement of the aim of the research, the nature and degree of any known risks, the sources from which subjects will be recruited, justification for any use of vulnerable populations, and the means by which the obtaining of participants' informed and voluntary consent will be ensured.

Consequences of Non-compliance

25. Researchers are required to demonstrate that ethical objections are resolved, to the satisfaction of the BHB Ethics Committee, before a study begins. This responsibility is given by the aforementioned international codes of practice and laws including the Nurenberg Code, the Declaration of Helsinki and the International Bill of Human Rights.

26. If the BHB Ethics Committee identifies that a study is not being conducted in accordance with the approved protocol and/or is violating ethical standards, it may withdraw ethical approval of a research project. Failure to submit a protocol to the committee is considered a violation of ethical standards.

27. The BHB Ethics Committee is required to inform the Department of Health of any serious or continuous non-compliance with ethical standards, and to recommend appropriate sanctions. Where sanctions are deemed necessary, they may include recommendation to governmental, institutional, professional or other authorities possessing disciplinary power over the research sponsors or funders to issue fines, or suspend from eligibility to practice medicine, use medical facilities or receive funding.

28. It is recommended that sanctions be used as a last resort. Preferred methods of control are dialogue, development of mutual trust, and education to enable ethical practice.

Ethical Standards

29. The CIOMS/WHO International Ethical Guidance for Biomedical Research Involving Human Subjects sets out 21 guidelines for ethical practice. A separate supporting document sets out guidelines for epidemiological research specifically[5]. It is understood that the WHO issued these as guidelines to facilitate their applicability in an international context. However, the Bermuda Department of Health has adopted these in their entirety as the standards for determining the ethical propriety of any research involving human subjects.

30. Therefore any research involving human subjects conducted in Bermuda or by a Bermudian sponsor or funder is expected to satisfy all of these standards in order to be eligible for ethics approval.

31. The CIOMS/WHO International Ethical Guidance for Biomedical Research Involving Human Subjects is stated herewith in its brief form (without amendment). For additional detail and commentary on each standard, the reader may refer to the original CIOMS International Ethical Guidance for Biomedical Research Involving Human Subjects of 2002[6].

Standard 1: Ethical justification and scientific validity of biomedical research involving human beings

The ethical justification of biomedical research involving human subjects is the prospect of discovering new ways of benefiting people's health. Such research can be ethically justifiable only if it is carried out in ways that respect and protect, and are fair to, the subjects of that research and are morally acceptable within the communities in which the research is carried out. Moreover, because scientifically invalid research is unethical in that it exposes research subjects to risks without possible benefit, investigators and sponsors must ensure that proposed studies involving human subjects conform to generally accepted scientific principles and are based on adequate knowledge of the pertinent scientific literature.

Standard 2: Ethical review committees

All proposals to conduct research involving human subjects must be submitted for review of their scientific merit and ethical acceptability to one or more scientific review and ethical review committees. The review committees must be independent of the research team, and any direct financial or other material benefit they may derive from the research should not be contingent on the outcome of their review. The investigator must obtain their approval or clearance before undertaking the research. The ethical

[5] Can be found at: www.who.int/ethics/research/en
[6] Can be found at: www.cioms.ch/frame_guidelines_nov.2002.htm

review committee should conduct further reviews as necessary in the course of the research, including monitoring of the progress of the study.

Standard 3: Ethical review of externally sponsored research

An external sponsoring organization and individual investigators should submit the research protocol for ethical and scientific review in the country of the sponsoring organization, and the ethical standards applied should be no less stringent than they would be for research carried out in that country. The health authorities of the host country, as well as a national or local ethical review committee, should ensure that the proposed research is responsive to the health needs and priorities of the host country and meets the requisite ethical standards.

Standard 4: Individual informed consent

For all biomedical research involving humans the investigator must obtain the voluntary informed consent of the prospective subject or, in the case of an individual who is not capable of giving informed consent, the permission of a legally authorized representative in accordance with applicable law. Waiver of informed consent is to be regarded as uncommon and exceptional, and must in all cases be approved by an ethical review committee.

Standard 5: Obtaining informed consent: Essential information for prospective research subjects

Before requesting an individual's consent to participate in research, the investigator must provide the information detailed in Appendix 2, in language or another form of communication that the individual can understand.

Standard 6: Obtaining informed consent: Obligations of sponsors and investigators

Sponsors and investigators have a duty to:

- refrain from unjustified deception, undue influence, or intimidation;
- seek consent only after ascertaining that the prospective subject has adequate understanding of the relevant facts and of the consequences of participation and has had sufficient opportunity to consider whether to participate;
- as a general rule, obtain from each prospective subject a signed form as evidence of informed consent – investigators should justify any exceptions to this general rule and obtain the approval of the ethical review committee (See Guideline 4 Commentary, Documentation of consent);
- renew the informed consent of each subject if there are significant changes in the conditions or procedures of the research or if new information becomes available that could affect the willingness of subjects to continue to participate; and,
- renew the informed consent of each subject in long-term studies at pre-determined intervals, even if there are no changes in the design or objectives of the research.

Standard 7: Inducement to participate

Subjects may be reimbursed for lost earnings, travel costs and other expenses incurred in taking part in a study; they may also receive free medical services. Subjects, particularly those who receive no direct benefit from research, may also be paid or otherwise compensated for inconvenience and time spent. The payments should not be so large, however, or the medical services so extensive as to induce prospective subjects to consent to participate in the research against their better judgment ("undue inducement"). All payments, reimbursements and medical services provided to research subjects must have been approved by an ethical review committee.

Standard 8: Benefits and risks of study participation

For all biomedical research involving human subjects, the investigator must ensure that potential benefits and risks are reasonably balanced and risks are minimized.

- Interventions or procedures that hold out the prospect of direct diagnostic, therapeutic or preventive benefit for the individual subject must be justified by the expectation that they will be at least as advantageous to the individual subject, in the light of foreseeable risks and benefits, as any available alternative. Risks of such 'beneficial' interventions or procedures must be justified in relation to expected benefits to the individual subject.
- Risks of interventions that do not hold out the prospect of direct diagnostic, therapeutic or preventive benefit for the individual must be justified in relation to the expected benefits to society (generalisable knowledge). The risks presented by such interventions must be reasonable in relation to the importance of the knowledge to be gained.

Standard 9: Special limitations on risk when research involves individuals who are not capable of giving informed consent

When there is ethical and scientific justification to conduct research with individuals incapable of giving informed consent, the risk from research interventions that do not hold out the prospect of direct benefit for the individual subject should be no more likely and not greater than the risk attached to routine medical or psychological examination of such persons. Slight or minor increases above such risk may be permitted when there is an overriding scientific or medical rationale for such increases and when an ethical review committee has approved them.

Standard 10: Research in populations and communities with limited resources

Before undertaking research in a population or community with limited resources, the sponsor and the investigator must make every effort to ensure that:

- the research is responsive to the health needs and the priorities of the population or community in which it is to be carried out; and
- any intervention or product developed, or knowledge generated, will be made reasonably available for the benefit of that population or community.

Standard 11: Choice of control in clinical trials

As a general rule, research subjects in the control group of a trial of a diagnostic, therapeutic, or preventive intervention should receive an established effective intervention. In some circumstances it may be ethically acceptable to use an alternative comparator, such as placebo or "no treatment".
Placebo may be used:

- when there is no established effective intervention;
- when withholding an established effective intervention would expose subjects to, at most, temporary discomfort or delay in relief of symptoms;
- when use of an established effective intervention as comparator would not yield scientifically reliable results and use of placebo would not add any risk of serious or irreversible harm to the subjects.

Standard 12: Equitable distribution of burdens and benefits in the selection of groups of subjects in research

Groups or communities to be invited to be subjects of research should be selected in such a way that the burdens and benefits of the research will be equitably distributed. The exclusion of groups or communities that might benefit from study participation must be justified.

Standard 13: Research involving vulnerable persons

Special justification is required for inviting vulnerable individuals to serve as research subjects and, if they are selected, the means of protecting their rights and welfare must be strictly applied.

Standard 14: Research involving children

Before undertaking research involving children, the investigator must ensure that:

- the research might not equally well be carried out with adults;
- the purpose of the research is to obtain knowledge relevant to the health needs of children;
- a parent or legal representative of each child has given permission;
- the agreement (assent) of each child has been obtained to the extent of the child's capabilities; and,
- a child's refusal to participate or continue in the research will be respected.

Standard 15: Research involving individuals who by reason of mental or behavioural disorders are not capable of giving adequately informed consent

Before undertaking research involving individuals who by reason of mental or behavioural disorders are not capable of giving adequately informed consent, the investigator must ensure that:

- such persons will not be subjects of research that might equally well be carried out on persons whose capacity to give adequately informed consent is not impaired;
- the purpose of the research is to obtain knowledge relevant to the particular health needs of persons with mental or behavioural disorders;

- the consent of each subject has been obtained to the extent of that person's capabilities, and a prospective subject's refusal to participate in research is always respected, unless, in exceptional circumstances, there is no reasonable medical alternative and local law permits overriding the objection; and,
- in cases where prospective subjects lack capacity to consent, permission is obtained from a responsible family member or a legally authorized representative in accordance with applicable law.

Standard 16: Women as research subjects

Investigators, sponsors or ethical review committees should not exclude women of reproductive age from biomedical research. The potential for becoming pregnant during a study should not, in itself, be used as a reason for precluding or limiting participation. However, a thorough discussion of risks to the pregnant woman and to her fetus is a prerequisite for the woman's ability to make a rational decision to enrol in a clinical study. In this discussion, if participation in the research might be hazardous to a fetus or a woman if she becomes pregnant, the sponsors/ investigators should guarantee the prospective subject a pregnancy test and access to effective contraceptive methods before the research commences. Where such access is not possible, for legal or religious reasons, investigators should not recruit for such possibly hazardous research women who might become pregnant.

Standard 17: Pregnant women as research participants

Pregnant women should be presumed to be eligible for participation in biomedical research. Investigators and ethical review committees should ensure that prospective subjects who are pregnant are adequately informed about the risks and benefits to themselves, their pregnancies, the foetus and their subsequent offspring, and to their fertility.

Research in this population should be performed only if it is relevant to the particular health needs of a pregnant woman or her foetus, or to the health needs of pregnant women in general, and, when appropriate, if it is supported by reliable evidence from animal experiments, particularly as to risks of teratogenicity and mutagenicity .

Standard 18: Safeguarding confidentiality

The investigator must establish secure safeguards of the confidentiality of subjects' research data. Subjects should be told the limits, legal or other, to the investigators' ability to safeguard confidentiality and the possible consequences of breaches of confidentiality.

Standard 19: Right of injured subjects to treatment and compensation

Investigators should ensure that research subjects who suffer injury as a result of their participation are entitled to free medical treatment for such injury and to such financial or other assistance as would compensate them equitably for any resultant impairment, disability or handicap. In the case of death as a result of their participation, their

dependants are entitled to compensation. Subjects must not be asked to waive the right to compensation.

Standard 20: Strengthening capacity for ethical and scientific review and biomedical research

Many countries lack the capacity to assess or ensure the scientific quality or ethical acceptability of biomedical research proposed or carried out in their jurisdictions. In externally sponsored collaborative research, sponsors and investigators have an ethical obligation to ensure that biomedical research projects for which they are responsible in such countries contribute effectively to national or local capacity to design and conduct biomedical research, and to provide scientific and ethical review and monitoring of such research.

Capacity-building may include, but is not limited to, the following activities:

- establishing and strengthening independent and competent ethical review processes/ committees
- strengthening research capacity
- developing technologies appropriate to health-care and biomedical research
- training of research and health-care staff
- educating the community from which research subjects will be drawn

Standard 21: Ethical obligation of external sponsors to provide health-care services

External sponsors are ethically obliged to ensure the availability of:

- health-care services that are essential to the safe conduct of the research;
- treatment for subjects who suffer injury as a consequence of research interventions; and,
- services that are a necessary part of the commitment of a sponsor to make a beneficial intervention or product developed as a result of the research reasonably available to the population or community concerned.

References

CIOMS (1991) *International Guidelines for Ethical Review of Epidemiological Studies.* Council for International Organisations of Medical Sciences (CIOMS) & World Health Organisation (WHO): Geneva, Switzerland.

CIOMS (2002) *International Ethical Guidelines for Biomedical Research Involving Human Subjects.* Council for International Organisations of Medical Sciences (CIOMS) & World Health Organisation (WHO): Geneva, Switzerland.

Department of Health (2006) *Research Governance Framework for Health and Social Care, Second Edition.* Department of Health: England.

Department of Health, Education and Welfare (1979) *The Belmont Report: Ethical Principles and Guidelines for the Protection of Human Subjects for Research.* U.S. Department of Health and Human Services: USA.

Medical Research Council (2005) *Medical Research Council Ethics Series: Good Research Practice.* Medical Research Council: London.

Nuremberg Code (1949) *Trials of War Criminals before the Nuremberg Military Tribunals under Control Council Law No. 10,* Vol. 2, pp. 181-182. Washington, D.C.: U.S. Government Printing Office.

Public Health Leadership Society (2002) *Principles of the Ethical Practice of Public Health.* Version 2.2. Public Health Leadership Society: USA.

United Nations General Assembly (1948) *Universal Declaration of Human Rights.* http://www.un.org/rights

U.S. Department of Health and Human Services (2004) *Guidelines for the Conduct of Research Involving Human Subjects at the National Institutes of Health.* Department of Health and Human Services: USA.

WHO (2000) *Operational Guidelines for Ethics Committees that Review Biomedical Research.* WHO: Geneva, Switzerland.

Declaration of Helsinki (1989) Recommendations Guiding Medical Doctors in Biomedical Research Involving Human Subjects. In *British Medical Journal,* 1996; 313:1448-1449 (7 December).

Appendix 1: The Research Protocol

A research protocol must be submitted to the BHB Ethics Committee to apply for ethical review. The final, approved protocol must be submitted to the Department of Health with supporting documentation, on approval from BHB.

The research protocol should be adhered to fully in conducting the study and any amendments must be submitted for ethical approval following the same process.

The research protocol must include all of the relevant sections from this list. Sections marked "Essential" represent the minimum requirement for all protocols, and must be completed for all research studies.

This list has been adapted from the CIOMS/WHO International Ethical Guidance for Biomedical Research Involving Human Subjects. It pertains specifically to Ethical Standard 2 of the Department of Health Research Governance Framework:

Ethical review committees: All proposals to conduct research involving human subjects must be submitted for review of their scientific merit and ethical acceptability to one or more scientific review and ethical review committees. The review committees must be independent of the research team, and any direct financial or other material benefit they may derive from the research should not be contingent on the outcome of their review. The investigator must obtain their approval or clearance before undertaking the research. The ethical review committee should conduct further reviews as necessary in the course of the research, including monitoring of the progress of the study.

1. **Title:** (Essential) Title of the study; include a short and a long title, if necessary
2. **Contact details:** (Essential) Name and address of the sponsor
3. **Research team:** (Essential) Names, addresses, institutional affiliations, qualifications and experience of the principal investigator and other investigators
4. **Summary:** (Essential) A summary of the proposed research in lay/non-technical language
5. **Purpose:** (Essential) A clear statement of the justification for the study, its significance in development and in meeting the needs of the country /population in which the research is carried out
6. **Ethical issues:** (Essential) The investigators' views of the ethical issues and considerations raised by the study and, if appropriate, how it is proposed to deal with them

7. **Literature review:** (Essential) Summary of all previous studies on the topic, including unpublished studies known to the investigators and sponsors, and information on previously published research on the topic, including the nature, extent and relevance of animal studies and other preclinical and clinical studies

8. **Statement of ethical intent:** (Essential) A statement that the principles set out in these Guidelines will be implemented

9. **Study's history:** (Essential) An account of previous submissions of the protocol for ethical review and their outcome

10. **Research sites:** (Essential) A brief description of the site(s) where the research is to be conducted, including information about the adequacy of facilities for the safe and appropriate conduct of the research, and *relevant* demographic and epidemiological information about the country or region concerned

11. **Objectives:** (Essential) The objectives of the trial or study, its hypotheses or research questions, its assumptions, and its variables

12. **Methodology:** (Essential) A detailed description of the design of the trial or study. In the case of controlled clinical trials the description should include, but not be limited to, whether assignment to treatment groups will be randomized (including the method of randomization), and whether the study will be blinded (single blind, double blind), or open

13. **Vulnerable populations (sub-section of Methodology):** (Essential) Whether such populations are included in the study and the justification for involving as research subjects any persons with limited capacity to consent or members of vulnerable social groups, and a description of special measures to minimize risks and discomfort to such subjects

14. **Sampling (sub-section of Methodology):** (Essential) The number of research subjects needed to achieve the study objective, and how this was statistically determined

15. **Sample criteria (sub-section of Methodology):** (Essential) The criteria for inclusion or exclusion of potential subjects, and justification for the exclusion of any groups on the basis of age, sex, social or economic factors, or for other reasons

16. **Sample recruitment (sub-section of Methodology):** (Essential) The process of recruitment, e.g., advertisements, and the steps to be taken to protect privacy and confidentiality during recruitment

17. **Procedure (sub-section of Methodology):** (Essential) Description and explanation of all interventions (the method of treatment administration, including route of administration, dose, dose interval and treatment period for investigational and comparator products used)

18. **Therapy withholding (sub-section of Methodology):** Plans and justification for withdrawing or withholding standard therapies in the course of the research, including any resulting risks to subjects

19. **Other treatments (sub-section of Methodology):** Any other treatment that may be given or permitted, or contraindicated, during the study

20. **Clinical tests (sub-section of Methodology):** Clinical and laboratory tests and other tests that are to be carried out

21. **Case report forms (sub-section of Methodology):** Samples of the standardized case-report forms to be used, the methods of recording therapeutic response (description and evaluation of methods and frequency of measurement), the follow-up procedures, and, if applicable, the measures proposed to determine the extent of compliance of subjects with the treatment

22. **Removal from study (sub-section of Methodology):** (Essential) Rules or criteria according to which subjects may be removed from the study or clinical trial, or (in a multi-centre study) a centre may be discontinued, or the study may be terminated

23. **Adverse events (sub-section of Methodology):** (Essential) Methods of recording and reporting adverse events or reactions, and provisions for dealing with complications

24. **Risks:** (Essential) The known or foreseen risks of adverse reactions, including the risks attached to each proposed intervention and to any drug, vaccine or procedure to be tested

25. **Insurance:** For research carrying more than minimal risk of physical injury, details of plans, including insurance coverage, to provide treatment for such injury, including the funding of treatment, and to provide compensation for research-related disability or death

26. **Investigational treatment after study:** Provision for continuing access of subjects to the investigational treatment after the study, indicating its modalities, the individual or organization responsible for paying for it, and for how long it will continue

27. **Pregnant women:** For research on pregnant women, a plan, if appropriate, for monitoring the outcome of the pregnancy with regard to both the health of the woman and the short-term and long-term health of the child

28. **Benefits to participants:** (Essential) The potential benefits of the research to subjects and to others

29. **Benefits to population:** (Essential) The expected benefits of the research to the population, including new knowledge that the study might generate

30. **Informed consent:** (Essential) The means proposed to obtain individual informed consent and the procedure planned to communicate information to prospective subjects, including the name and position of the person responsible for obtaining consent. See Appendices 2 and 3 for guidance

31. **Informed consent of vulnerable populations:** When a prospective subject is not capable of informed consent, satisfactory assurance that permission will be obtained from a duly authorized person, or, in the case of a child who is sufficiently mature to understand the implications of informed consent but has not reached the legal age of consent, that knowing agreement, or assent, will be obtained, as well as the permission of a parent, or a legal guardian or other duly authorized representative. See Appendices 2 and 3 for guidance

32. **Incentives:** (Essential) An account of any economic or other inducements or incentives to prospective subjects to participate, such as offers of cash payments, gifts, or free services or facilities, and of any financial obligations assumed by the subjects, such as payment for medical services

33. **Communication with participants:** Plans and procedures, and the persons responsible, for communicating to subjects information arising from the study (on harm or benefit, for example), or from other research on the same topic, that could affect subjects' willingness to continue in the study

34. **Results to participants:** (Essential) Plans to inform subjects about the results of the study

35. **Confidentiality:** (Essential) The provisions for protecting the confidentiality of personal data, and respecting the privacy of subjects, including the precautions that are in place to prevent disclosure of the results of a subject's genetic tests to immediate family relatives without the consent of the subject

36. **Confidentiality procedures:** (Essential) Information about how the code, if any, for the subjects' identity is established, where it will be kept and when, how and by whom it can be broken in the event of an emergency

37. **Data use:** (Essential) Any foreseen further uses of personal data or biological materials

38. **Analysis:** (Essential) A description of the plans for analysis of the study, whether qualitative or statistical, including plans for interim analyses, if any, and criteria for prematurely terminating the study as a whole if necessary

39. **Drug safety:** Plans for monitoring the continuing safety of drugs or other interventions administered for purposes of the study or trial and, if appropriate, the appointment for this purpose of an independent data-monitoring (data and safety monitoring) committee

40. **References:** (Essential) A list of the references cited in the protocol

41. **Budget and funding:** (Essential) The source and amount of funding of the research: the organization that is sponsoring the research and a detailed account of the sponsor's financial commitments to the research institution, the investigators, the research subjects, and, when relevant, the community

42. **Conflict of interest:** (Essential) The arrangements for dealing with financial or other conflicts of interest that might affect the judgement of investigators or other research personnel: informing the institutional conflict-of-interest committee of such conflicts of interest; the communication by that committee of the pertinent details of the information to the ethical review committee; and the transmission by that committee to the research subjects of the parts of the information that it decides should be passed on to them

43. **Timescale:** (Essential) The time schedule for completion of the study

44. **Capacity-building assurance:** For research that is to be carried out in a developing country or community, the contribution that the sponsor will make to capacity-building for scientific and ethical review and for biomedical research in the host country, and an assurance that the capacity-building objectives are in keeping with the values and expectations of the subjects and their communities

45. **Publication of results:** (Essential) Particularly in the case of an industrial sponsor, a contract stipulating who possesses the right to publish the results of the study, and a mandatory obligation to prepare with, and submit to, the principal investigators the draft of the text reporting the results

46. **Results publication assurance:** (Essential) In the case of a negative outcome, an assurance that the results will be made available, as appropriate, through publication or by reporting to the drug registration authority

47. **Publication exceptions:** Circumstances in which it might be considered inappropriate to publish findings, such as when the findings of an epidemiological, sociological or genetics study may present risks to the interests of a community or population or of a racially or ethnically defined group of people

48. **Falsification of data:** (Essential) A statement that any proven evidence of falsification of data will be dealt with in accordance with the policy of the sponsor to take appropriate action against such unacceptable procedures

Appendix 2: Information for Participants - Guidelines

Research participants must be provided with sufficient information, in a language and manner that they can easily understand, before they can give informed consent. Prospective participants must be given adequate time to consider participation and must be given the opportunity to have any questions clarified.

The research protocol submitted for ethical review must include the proposed information sheet for participants.

The information sheet must include all of the relevant sections from the following list. Sections with a question title (e.g. 'do I have to take part?") must be completed for all research studies. Those with a statement title (e.g. "reimbursement") need to be completed if relevant to the study.

This list has been adapted from the CIOMS/WHO International Ethical Guidance for Biomedical Research Involving Human Subjects. It pertains specifically to Ethical Standard 5 of the Department of Health Research Governance Framework:

Obtaining informed consent: Essential information for prospective research subjects - Before requesting an individual's consent to participate in research, the investigator must provide the following information, in language or another form of communication that the individual can understand.

1. Statement that the individual is invited to participate in research, the reasons for considering the individual suitable for the research, and that participation is voluntary
2. **Do I have to take part?:** statement that the individual is free to refuse to participate and will be free to withdraw from the research at any time without penalty or loss of benefits to which he or she would otherwise be entitled
3. **What is this about?:** the purpose of the research, the procedures to be carried out by the investigator and the subject, and an explanation of how the research differs from routine medical care
4. **How will people be selected?:** for controlled trials, an explanation of features of the research design (e.g., randomization, double-blinding), and that the subject will not be told of the assigned treatment until the study has been completed and the blind has been broken
5. **How long will I be involved?:** the expected duration of the individual's participation (including number and duration of visits to the research centre and the total time involved) and the possibility of early termination of the trial or of the individual's participation in it

6. **Reimbursement:** whether money or other forms of material goods will be provided in return for the individual's participation and, if so, the kind and amount
7. **Will I be told the results?:** that, after the completion of the study, subjects will be informed of the findings of the research in general, and individual subjects will be informed of any finding that relates to their particular health status
8. **Can I access the data about me?:** that subjects have the right of access to their data on demand, even if these data lack immediate clinical utility (unless the ethical review committee has approved temporary or permanent non-disclosure of data, in which case the subject should be informed of, and given, the reasons for such non-disclosure)
9. **What risks are involved?:** any foreseeable risks, pain or discomfort, or inconvenience to the individual (or others) associated with participation in the research, including risks to the health or well-being of a subject's spouse or partner
10. **Will I benefit from taking part:** the direct benefits, if any, expected to result to subjects from participating in the research
11. **What are the benefits of the study?:** the expected benefits of the research to the community or to society at large, or contributions to scientific knowledge
12. **Resulting products or interventions:** whether, when and how any products or interventions proven by the research to be safe and effective will be made available to subjects after they have completed their participation in the research, and whether they will be expected to pay for them
13. **Alternative treatments:** any currently available alternative interventions or courses of treatment
14. **Will my data be confidential?:** the provisions that will be made to ensure respect for the privacy of subjects and for the confidentiality of records in which subjects are identified
15. **What would happen if my data became known outside the research team?:** the limits, legal or other, to the investigators' ability to safeguard confidentiality, and the possible consequences of breaches of confidentiality
16. **Genetic information:** policy with regard to the use of results of genetic tests and familial genetic information, and the precautions in place to prevent disclosure of the results of a subject's genetic tests to immediate family relatives or to others (e.g., insurance companies or employers) without the consent of the subject
17. **Who is doing this study?:** the sponsors of the research, the institutional affiliation of the investigators, and the nature and sources of funding for the research
18. **Medical records:** the possible research uses, direct or secondary, of the subject's medical records and of biological specimens taken in the course of clinical care (See also Guidelines 4 and 18 Commentaries)

19. **Biological specimens:** whether it is planned that biological specimens collected in the research will be destroyed at its conclusion, and, if not, details about their storage (where, how, for how long, and final disposition) and possible future use, and that subjects have the right to decide about such future use, to refuse storage, and to have the material destroyed (See Guideline 4 Commentary)

20. **Remuneration for product development:** whether commercial products may be developed from biological specimens, and whether the participant will receive monetary or other benefits from the development of such products

21. **Physician investigator:** whether the investigator is serving only as an investigator or as both investigator and the subject's physician

22. **Access to health care:** the extent of the investigator's responsibility to provide medical services to the participant

23. **Injury or complications:** that treatment will be provided free of charge for specified types of research-related injury or for complications associated with the research, the nature and duration of such care, the name of the organization or individual that will provide the treatment, and whether there is any uncertainty regarding funding of such treatment

24. **Compensation:** in what way, and by what organization, the subject or the subject's family or dependants will be compensated for disability or death resulting from such injury (or, when indicated, that there are no plans to provide such compensation)

25. **Right to compensation:** whether or not, in the country in which the prospective subject is invited to participate in research, the right to compensation is legally guaranteed

26. **Is this study ethical?:** that an ethical review committee has approved or cleared the research protocol

Appendix 3: Consent Form Guidelines

A signed consent form is the preferred method for obtaining informed consent. The research protocol submitted for ethical review must include the sample consent form intended for use and the process for obtaining consent; or detailed justification if it is not to be used.

The requirement for informed consent is in accordance with the CIOMS/WHO International Ethical Guidance for Biomedical Research Involving Human Subjects. It pertains specifically to Ethical Standard 4 of the Department of Health Research Governance Framework:

Individual informed consent: For all biomedical research involving humans the investigator must obtain the voluntary informed consent of the prospective subject or, in the case of an individual who is not capable of giving informed consent, the permission of a legally authorized representative in accordance with applicable law. Waiver of informed consent is to be regarded as uncommon and exceptional, and must in all cases be approved by an ethical review committee.

The sample Consent Form overleaf is the minimum requirement. It is suitable for many studies involving adults, but may need alterations in accordance with the study. The participant is consenting to everything described in the text of the information sheet (Appendix 2).

Some studies may require a more detailed, itemised consent form to cover other important issues, e.g.:

1. invasive tests or samples required for the study
2. consent to use audio-visual recording, indicating any potential use of verbatim quotes, photographs or video material
3. transfer of data or samples to countries outside Bermuda
4. agreement to receive individual results / comment from testing, etc.

The consent form should be signed by those who are involved in the consent process; that is: the study participant and the researcher or a representative of the researcher delegated to take consent.

An alternative and appropriate consent process and form must be implemented if vulnerable populations are involved; that is, participants who are not deemed to have the mental capacity to consent due to disability or age. For persons aged 17 years or less, parental consent is always required.

(Form to be on headed paper)

CONSENT FORM

Title of Project:

Name of Researcher:

Please initial box

1. I have read and understand the information sheet [*insert title*] for the above study. I have had the opportunity to think about the information, ask questions and have had these answered to my satisfaction. ☐
2. I understand that my participation is voluntary and that I can withdraw at any time, without giving any reason, without my medical care or legal rights being affected. ☐
3. I understand that relevant sections of any of my medical notes and data collected during the study may be looked at by responsible individuals from the research team, where it is relevant to this study. I give permission for these individuals to have access to my records. ☐
4. I agree to my doctor being informed of my participation in the study. ☐
5. I agree to take part in the above study. ☐

Name of Patient	Date	Signature
Researcher Name	Date	Signature
Name of Person taking consent (if different from researcher	Date	Signature

When completed: one copy for patient, and original to be kept in research file