PNHRS | Philippine National Health Research System

NATIONAL ETHICAL GUIDELINES FOR HEALTH RESEARCH 2011

NATIONAL ETHICAL GUIDELINES FOR HEALTH RESEARCH

2011

Prepared by the Philippine Health Research Ethics Board
Ad Hoc Committee for the Revision of the Ethical Guidelines

TABLE OF CONTENTS

LIST OF ACRONYMS

ABS	access and benefit sharing
ADAP	Alzheimer's Disease Association of the Philippines
AIDS	acquired immune deficiency syndrome
AO	Administrative Order
ART	assisted reproductive technology
ASEAN	Association of South East Asian Nations
CAM	complementary and alternative medicine
CERC	Cluster Ethics Review Committee
CIOMS	Council of International Organizations of Medical Sciences
CBD	Convention on Biological Diversity
CRO	Clinical Research Organization / Contract Research Organization
DA	Department of Agriculture
DMC	Data Monitoring Committee
DNA	deoxyribonucleic acid
DOH	Department of Health
DOST	Department of Science and Technology
ERB	Ethics Review Board
ERC	Ethics Review Committee
FDA	Food and Drugs Administration
FERCAP	Forum for Ethical Review Committees in the Asia and the Pacific Region
GCP	Good Clinical Practice
GMP	Good Manufacturing Practice
HIV	human immunodeficiency virus
ICD	informed consent document
ICF	Informed consent form
ICH	International Conference on Harmonization
ICU	intensive care unit
IDE	investigational device exemption
IERC	Institutional Ethics Review Committee
IP	indigenous peoples
IPRA	Indigenous Peoples' Rights Act
IRB	Institutional Review Board
LUA	limited use agreement
MMSE	mini-mental state examination
MOA	memorandum of agreement
MTA	material transfer agreement

NCBP	National Committee on Biosafety of the Philippines
NCCAM	National Center for Complementary and Alternative Medicine
NCIP	National Commission on Indigenous Peoples
NEC	National Ethics Committee
NIH	National Institutes of Health
NUHRA	National Unified Health Research Agenda
PALAS	Philippine Association for Laboratory Animal Science
PCHRD	Philippine Council for Health Research and Development
PHREB	Philippine Health Research Ethics Board
PNHRS	Philippine National Health Research System
POGS	Philippine Obstetrical and Gynecological Society
PSREI	Philippine Society of Reproductive Endocrinology and Infertility
RERC	Research Ethics Review Committee
RITM	Research Institute for Tropical Medicine
RNA	ribonucleic acid
SAE	serious adverse event
SIDCER	Strategic Initiative for Developing Capacity in Ethical Review
SOP	standard operating procedure
SUSAR	suspected unexpected serious adverse reactions
TM	traditional medicine
TWG	technical working group
UNDRIP	United Nations Declaration on the Rights of Indigenous Peoples
UP	University of the Philippines
WHO	World Health Organization

FOREWORD

The years following the publication of the 2006 edition of the **National Ethical Guidelines for Health Research** were marked by significant developments in Philippine health research. The 2008 version of the Declaration of Helsinki was released. The number of identified ethics review committees doubled from approximately a hundred committees to more than two hundred by January 2010. Three institutional review committees, namely, the University of the Philippines (UP) College of Medicine Ethics Review Board, the UP Manila—National Institutes of Health Institutional Review Board and the Research Institute for Tropical Medicine Ethics Review Committee, were internationally recognized by the *Strategic Initiative for Developing Capacity in Ethical Review*—Forum for Ethical Review Committees in the Asian and Western Pacific Region (SIDCER-FERCAP). The Philippine National Health Research System Bill was certified urgent by the Office of the President. There was an observed increase in the conduct of clinical trials in medical centers and private clinics. The Philippine Genome Center was proposed for development**.** Significantly, regulatory authorities of Southeast Asian countries have been meeting to harmonize regulations and procedures for drug registration. It is in this very stimulating research environment that the revision of the 2006 National Ethical Guidelines for Health Research was conceived.

The 2011 edition of the National Guidelines was put together by people who had actively used the earlier editions as members of ethics review committees, as trainers, as researchers and as members of the faculty in various teaching institutions. The group was a mix of social scientists, philosophers, medical practitioners, health educators and representatives of both the private and public sectors; all of whom wholeheartedly accepted the responsibilities of the task. A few were contributors in the 2006 edition but many were involved for the first time. Majority said that they found the earlier edition wanting and saw an opportunity to put in black and white their ideas on ethics review. The first meeting was held on 25 May 2010. The group agreed that the revision shall include health research areas and activities that were not part of the previous edition and, when appropriate, update or improve provisions in the 2006 guidelines.

All meetings were full of interesting exchanges that reflected personal advocacies and passionate convictions, while being mindful of institutional constraints. There was openness to ideas and grace in conceding to opposite opinions. Often – when clarity was given time and space – there was realization in the sameness of perceived opposites.

The highlights of the first draft were presented to a large audience of health researchers on 13 August 2010 during the celebration of the PNHRS week. The consultation with the end-users brought forth several suggestions to make the final form of the guidelines more user-friendly. Issues were raised concerning health research in the military, among the elderly and the ethnic groups. The problem of conflict of interest in clinical trials and the practice of forum-shopping underlined the need for quality assurance in ethics review.

The Ad Hoc Committee on the Revision of the Guidelines met for the last time on 9 November 2010 to harmonize the proposed revisions and prepare the draft for the review of content and language. The whole draft was then submitted to the members of the Philippine Health Research Ethics Board on 1 June 2011 for approval.

The seriousness of purpose and the challenges of the issues (especially when human rights, laws and guidelines clashed) were made lighter by the wit and humor that could only be generated by people of wisdom and good will.

Marita V. T. Reyes, M.D.
Chair, Ad Hoc Committee 2010—2011

MESSAGE

The Philippine National Health Research System (PNHRS) recognizes the importance of ethics in promoting a robust and responsible health research system. This is evident in the inclusion of ethics in PNHRS's program roster and the creation of the Philippine Health Research Ethics Board (PHREB) to plan and implement activities that would promote ethical research involving human participants.

Responding to the needs of an evolving and growing national health research system, the PHREB revised the 2006 guidelines and came up with this updated 2011 National Ethical Guidelines for Health Research. The updated version includes special guidelines on clinical trials, herbal medicine research, complementary and alternative medicine, epidemiological studies, social research, investigations involving traumatized populations, HIV and AIDS research, studies on assisted reproductive technology, genetic research, studies on emerging technologies, and international/collaborative research.

With its continuous updating of the National Ethical Guidelines, PHREB remains true to its mandate, "to ensure that all phases of health research adhere to universal ethical principles that value the protection and promotion of the dignity of health research participants."

We, in the Philippine Council for Health Research and Development of the Department of Science and Technology (PCHRD-DOST), laud the efforts of the PHREB and members of the Ad Hoc Committee which spearheaded the updating/revision of the guidelines.

Mabuhay!

Jaime C. Montoya, M.D., M.Sc., CESO III
Executive Director
Philippine Council for Health Research and Development
Department of Science and Technology

MESSAGE

Part of my vision as new University of the Philippines (UP) Manila Chancellor is making the University a Center for Excellence in translational research, producing not only published works but also innovative patents. In order to realize this, however, an enabling environment for research should be provided and sustained.

Ethics review forms an essential part of a stimulating research environment. UP Manila is honored to be one of the first two institutions in the Philippines to be accredited in 2007 by the Forum for Ethical Review Committees in Asia and the Pacific (FERCAP). The accreditation has been renewed after three years following our researchers' strict compliance with ethics review principles and guidelines.

We attribute a great part of this recognition to the efforts of the Philippine Council for Health Research and Development (PCHRD) and the Philippine National Health Research System to ensure the protection of the rights of human participants in research.

Thus, I commend PHREB for coming up with an updated version of the National Ethical Guidelines for Health Research. We are grateful to the editors and writers of the 2006 and the 2011 versions for their painstaking efforts to assist our researchers in the pursuit of relevant health research that address many of our health problems. We are thankful for the inclusion of new guiding principles for researches involving minors, elderly, military, indigenous peoples, as well as new topics, such as nanotechnology, among others.

As far as UP Manila is concerned, the establishment of the UP Manila Research Ethics Board that integrates the existing ethics review boards is a step in the right direction as far as streamlining and harmonizing the process of ethics review in the University is concerned.

This manual will certainly serve well my administration's goal of transforming UP Manila into a leader in translational research. The updated guidelines reflect the changing landscape in health research and confirm the essential role of ethics in securing the University's research status.

Manuel B. Agulto, M.D.
Chancellor
University of the Philippines Manila

MESSAGE

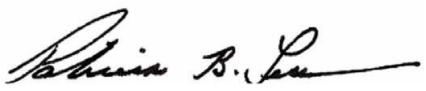
Greetings to the Philippine Health Research Ethics Board (PHREB) for spearheading the revision of the National Ethical Guidelines for Health Research! These updated Guidelines seek to accommodate the numerous changes in the landscape of health research and in the various ethical considerations after 2006 when the latest version of the Guidelines was released.

The health of a nation's population is one of society's important pillars. Health research that takes into account the specific needs of the different sectors—the minors, the elderly, the indigenous peoples, among others—is an imperative in nation-building. The principles provided by the guidelines will ensure better protection of the rights and the dignity of the human participants involved in research.

The Board's role has become more significant in light of the tremendous scientific and technological advances, both locally and globally. The task to process the data and structure them into a coherent system of guidelines should be an essential tool that various sectors in our society, both public and private, can utilize to further promote healthcare in the Philippines.

Congratulations to the Philippine Health Research Ethics Board for the leadership it has provided for health and research development in the country.

Mabuhay!



Patricia B. Licuanan, Ph. D.
Chair
Commission on Higher Education

MESSAGE

Meeting the health needs of all Filipinos, especially those of our vulnerable populations, is the ultimate goal of the health sector. This is precisely what *Kalusugan Pangkalahatan* is for. As our poorest families have limited, if any, access to clinic or hospital services, they are more likely to give up seeking medical attention. The fundamental rights to life and to health, guaranteed by the basic laws of the land, have yet to be realized in a universal scale. Through *Kalusugan Pangkalahatan* we are ensuring that access to medical care and health services will be available to everyone, most especially the poor. The success of this program depends largely on various support structures, which of course include research.

Through researches we are able to find ways and means to improve our programs and make them more effective. The same is true for testing new drugs, therapies, medical interventions and modalities for alleviating suffering and illness; they help us explore possibilities for enhancements. However, there are unnecessary risks brought about by participation in clinical researches, and they are borne mostly by the poor and the sick who stand helpless against them. We must therefore step up to protect them from exploitation and make sure that they reap the benefits of their participation.

As early as 2003, the Department of Health has institutionalized a research ethics review in researches involving human participants through Administrative Order No. 46-A, series of 2003. This issuance established a research ethics system in the DOH and the DOH Research Ethics Committee (DREC). The DREC adopted international guidelines, such as the Helsinki Declaration of 1964 and its amendments, the WHO Council of International Organizations of Medical Sciences (CIOMS) and the International Conference of Harmonization Good Clinical Practice Guidelines of 1996, and other international laws prescribing safety standards of research participants. The National Ethical Guidelines for Health Research (NEGHR), published by the Philippine National Health Research System (PNHRS) in 2006, was the first local guideline relating to different types of research involving human participants. We lauded PNHRS then for providing us guidelines suited to the best interest of the Filipinos and in sync with Philippine culture and traditions.

The 2011 edition of the National Ethical Guidelines for Health Research promises updated and more nuanced guidelines on research. It encompasses more special sectors in society such as the indigenous people, elderly, minors, military, and includes new topics such as research in emergency situations and ICU settings, and other new modalities of treatment. These supplements more than reflect the hard work that has been put into this undertaking. The updated guideline is a marker of the passionate service of the men and women who make up the Philippine Health Research Ethics Board (PHREB), which untiringly prodded for its revision. The periodic update of the NEGHR assures us that we will be able to continuously safeguard the rights of those participating in researches in the light of incessant technological advances.

Congratulations and more power!

Enrique T. Ona, MD
Secretary
Department of Health

The Ad Hoc Committee for the revision of the National Ethical Guidelines for Health Research patiently and carefully reviewed and revised the old guidelines, and formulated new ones in order to provide researchers and ethics review committees a new set of guidelines that is responsive to the needs of an evolving and growing national health research system. The committee is composed of the following:

Marita V. T. Reyes, M.D. *(Chair)*	Chair National Ethics Committee Co-Chair Philippine Health Research Ethics Board
Sonny Matias E. Habacon, M.D. *(Co-Chair)*	Chair Department of Pharmacology School of Medicine Far Eastern University Nicanor Reyes Medical Foundation
Fatima Alvarez Castillo	Professor Politics and Qualitative Research College of Arts and Sciences University of the Philippines Manila
Leonardo D. de Castro, Ph.D.	Chair Philippine Health Research Ethics Board Member UNESCO Advisory Expert Committee for the Teaching of Ethics
Edlyn B. Jimenez	Research Faculty National Institutes of Health Secretariat Coordinator University of the Philippines Manila Research Ethics Board
Jaime C. Montoya, M.D.	Executive Director Philippine Council for Health Research and Development Department of Science and Technology Professor Department of Medicine College of Medicine

Filipinas F. Natividad, Ph.D.	Vice President Research and Biotechnology Division St. Luke's Medical Center
Elizabeth Aguiling-Pangalangan, Li.B.	Professor College of Law University of the Philippines Diliman
Evangeline O. Santos, M.D.	Clinical Associate Professor Department of Ophthalmology and Visual Sciences College of Medicine University of the Philippines Manila
Cecilia V. Tomas, M.D.	Member Philippine Health Research Ethics Board Chair Sub-Committee on Standards and Accreditation Philippine Health Research Ethics Board
Crispinita A. Valdez	Director Information Management Service Department of Health Chair Research Ethics Board Department of Health
Ma. Salome Nicdao-Vios, M.D.	Fellow Philippine Neurological Association Diplomate Philippine Board of Pain Medicine Chair University of the Philippines Manila Research Ethics Board

CONTRIBUTORS	
Alvin B. Caballes, M.D.	Chief Social Medicine Unit College of Medicine University of the Philippines Manila
Eva Maria Cutiongco-dela Paz, M.D.	Director Institute of Human Genetics National Institutes of Health University of the Philippines Manila Chair Technical Review Board National Institutes of Health University of the Philippines Manila
Shelley F. de la Vega, M.D.	Associate Professor College of Medicine University of the Philippines Manila Director Institute of Health Policy and Development Studies University of the Philippines Manila-National Institutes of Health President Philippine College of Geriatric Medicine
Godofreda V. Dalmacion, M.D.	Professor Department of Pharmacology and Toxicology cross appointed: Department of Clinical Epidemiology College of Medicine University of the Philippines Manila

Jacinto Blas V. Mantaring III, M.D.	Associate Professor Department of Clinical Epidemiology College of Medicine University of the Philippines Manila Clinical Associate Professor Department of Pediatrics College of Medicine University of the Philippines Manila
Ricardo M. Manalastas, Jr., M.D.	Professor Department of Obstetrics & Gynecology College of Medicine & Philippine General Hospital University of the Philippines Manila
Isidro C. Sia, M.D.	Professor Department of Pharmacology College of Medicine University of the Philippines Manila
Elizabeth R. Ventura	Professor Department of Psychology College of Social Sciences and Philosophy University of the Philippines Diliman
CONTENT EDITOR	
Peter A. Sy	Professor Department of Philosophy College of Social Sciences and Philosophy University of the Philippines Diliman

PHREB Secretariat / PCHRD Staff	
Ms. Carina L. Rebulanan	Chief, Institution Development Division
Ms. Marie Jeanne B. Berroya	Senior Science Research Specialist
Ms. Charisma C. Cruz	Science Research Specialist I
Ms. Anthea Maliz V. Cortes	Science Research Specialist I
Mr. Nico Angelo C. Parungao	Science Research Specialist I

HOW TO USE THE GUIDELINES

This set of Guidelines is divided into two major topics: 1) the General Guidelines on ethical review of health research, and 2) the Special Guidelines on specific research areas, namely: a) clinical trials on drugs, devices, and diagnostics; b) herbal medicine research; c) complementary and alternative medicine research; d) research on assisted reproductive technology; e) emerging technology research; f) genetic research that includes a section on stem cell research; g) epidemiological research; h) social research; i) conduct of research (in emergencies and disasters, in indigenous peoples, in pediatric population, and in elderly); and j) HIV and AIDS research. Guidelines on international collaborations and authorship and publications complete this new set of ethical guidelines.

Nine appendices are provided in these Guidelines. Appendix A1 and A2 are templates that list the essential information that should be reflected in the patient information and informed consent forms. By answering each question under each heading, the proponent(s) would be able to make the potential study participant understand the nature, risks, and benefits of his/her participation in the study, and thus be able to decide to participate or not. Appendix B is the standard application form for ethical evaluation of proposal that must be submitted to the Ethics Review Committees (ERCs) together with the proposal. Appendix C lists the documents that the proponent(s) should provide the ERC. Appendix D and E show the composition of the National Ethics Committee (NEC) and of the Philippine Health Research Ethics Board (PHREB), respectively. And lastly, Appendix F, G, and H provide the guidelines for recognition/accreditation, and the Standard Operating Procedures (SOPs) of ethical review committees.

A glossary of technical terms is available as a quick reference (see pages 122-169).

It is important for the readers to familiarize themselves with the general ethical guidelines for health research (see pages 29-42) which contain the general provisions of the various elements of and considerations in research ethics. Some elements of research ethics (e.g. informed consent) as operationally applied in specific types of research, for instance, genetic studies, are discussed in great detail in the guidelines for that particular type of research.

These specific provisions complement those in the General Ethical Guidelines. They should not be considered as separate from the general guidelines. The subject index (see pages 174-180) should be able to direct the readers to all the sections where a particular item appears.

Much effort was exerted to make this guidebook easy to use by researchers, members of ERCs and funding agencies, research policy makers including young students in health research.

For questions, please contact:

The Secretariat, Philippine Health Research Ethics Board (PHREB)
Philippine Council for Health Research and Development
Department of Science and Technology
General Santos Avenue, Bicutan, Taguig City
Telephone Number(s): (632) 837-7535 to 37
Fax Number: (632) 837-2924
Email address: ethics.secretariat@yahoo.com

INTRODUCTION

The Philippines has witnessed significant scientific, technological and social advances – both locally and globally – since the release of the latest version of the National Ethical Guidelines for Health Research in 2006. These developments have brought about changes in the landscape of health research and have given rise to new ethical consideration. It is thus imperative that new ones be formulated to better protect the rights and dignity of the human participants involved in research. This move is also consistent with the policy of Philippine Health Research Ethics Board (PHREB), which espouses the revision of the guidelines every five years.

Upon the recommendation of PHREB, the Philippine Council for Health Research and Development (PCHRD) created an Ad Hoc Committee to spearhead the updating and revising of the guidelines (through PCHRD Special Order No. 029 Series of 2010). The said Committee is tasked to review and update the existing ethics guidelines by the National Ethics Committee (1995, 1996, 2000) and the Technical Working Group on Ethics (2006) to ensure adherence to universal ethical principles and values as well as respect for Filipino values and culture. In addition, assistance of specific contributors was likewise sought in revising specific topics that require certain expertise. A summary of these proposed revisions was presented during the Ethics Forum held on 10 August 2010 for comments and validation of the participants who were comprised mostly of members of institutional ethics review bodies.

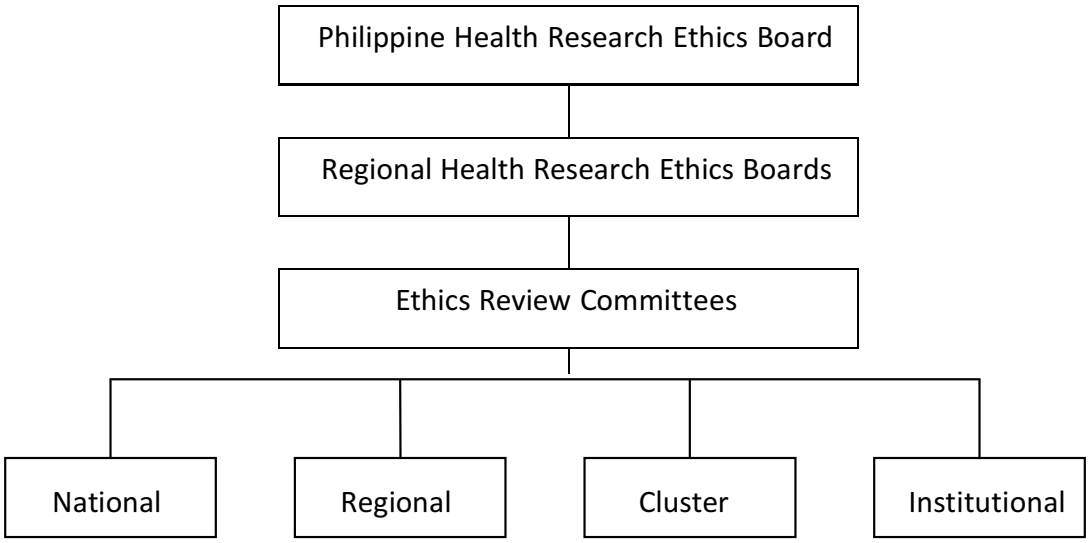
In view of the need to review, harmonize and consolidate all the inputs received from the Ad Hoc Committee members, contributors, users and other interested parties, conduct of a write-shop is being proposed. The 2011 version features reorganized and reformatted guidelines that is more user-friendly. Aside from the revised guidelines on the conduct of biomedical research on social sciences, herbal medicine, assisted reproductive technology, clinical studies and epidemiological studies, the 2011 edition includes new guidelines which are aimed for use in researches on minors, elderly, indigenous peoples, and other new topics like acupuncture, emergency and Intensive Care Unit settings, qualitative research, biosimilars, nanotechnology, among others.

Just like the earlier editions, these guidelines are meant to promote, and not to stifle, good and ethical scientific research. In the final analysis, all individuals concerned with research must resolve for themselves the omnipresent conflict between present risk and future benefits of the study at hand.

RESEARCH ETHICS AGENCIES

In 2003, the establishment of the Philippine National Health Research System (PNHRS) led to the creation of the Philippine Health Research Ethics Board (PHREB) as the national policy making body in health research ethics.

At present, relevant activities in ethics review in the Philippines are organized as follows:



Philippine Health Research Ethics Board (PHREB)

The Philippine Health Research Ethics Board (PHREB) has 13 members, including two ex-officio members , namely, the Department of Science and Technology (DOST)—PCHRD Executive Director and the Department of Health (DOH) Research Ethics Committee Chair. Except for the ex-officio members, appointments shall be for a term of three years (initially, five were appointed for three years and six members for two years). The members represent a balance of background, gender and disciplines (e.g., health research, philosophy, law, academe, medicine, public health/epidemiology, theology, social science and allied health sciences). There are also those who are from people's organizations and the youth sector. The Chair and Co-Chair have two-year terms.

The functions of PHREB are as follows:

- Formulate/update guidelines for the ethical conduct of human health research;
- Develop guidelines for the establishment and management of ethics review committees and standardization of research ethics review;
- Monitor and evaluate the performance of institutional ethics review committees in accordance with procedures outlined in a prior agreement;
- Promote the establishment of functional and effective ethics review committees;
- Provide advice and make recommendations to the PNHRS Governing Council and other appropriate entities (including the Food and Drugs Administration [FDA]) regarding programs, policies, and regulations as they relate to ethical issues in human health research;
- Initiate and contribute to discourse and discussions of ethical issues in human health research;
- Network with relevant local, national and international organizations.

Regional Research Ethics Boards (RREBs)

The Regional Research Ethics Boards will be constituted by the PNHRS Governing Council and will have a multidisciplinary, multisectoral, gender- and age-balanced membership that reflects the cultural and social milieu obtaining in the region they are in. They will be under the supervision of PHREB.

The Regional Research Ethics Boards will be established in key regions to act as a regional research ethics review policy-making authority. Their functions will, therefore, be similar to that of PHREB with the region as their area of responsibility.

Ethics Review Committees (ERCs)

The Ethics Review Committees include the National Ethics Committee, Regional Ethics Review Committees, Cluster Ethics Review Committees, and Institutional Ethics Review Committees.

National Ethics Committee (NEC)

The National Ethics Committee was constituted in 1984, through Special Order No. 84-053 issued by Dr. Alberto G. Romualdez, Jr., then Executive Director of the Philippine Council for Health Research and Development (PCHRD). It had both policy- making and review functions (for researches in institutions without ERCs) until its policy-making role was taken over by the Philippine Health Research Ethics Board. Its phase-out was initiated in July 2010; however, it will continue to monitor all ongoing approved researches until their completion. Accordingly, relevant documents shall be archived in the care of the Philippine Council for Health Research and Development.

Regional Ethics Review Committees (RERCs)

The Regional Ethics Review Committees operate under the auspices of the Regional Health Research and Development Consortia, at present, in Regions 1, 2, 3, 4, 6, 8, 9, 10 and 11. They shall take charge of ethical review of researches to be conducted in institutions without their own ERCs, and of community-based researches without a specific responsible institution.

Cluster Ethics Review Committees (CERCs)

Several institutions may form a common ethics review committee if it is not feasible to form their own. The management of CERCs and its areas of responsibility shall be covered by a memorandum of agreement among the involved institutions. Its functions shall be similar to that of an institutional ethics review committee.

Institutional Ethics Review Committees (IERCs)

Philippine institutions that engage in biomedical and behavioral research shall establish an Institutional Ethics Review Committee which shall provide independent, competent, and timely review of the ethics of the proposed studies. The main purpose of the IERC is to help "safeguard the dignity, rights, safety, and well-being of all actual or potential research participants" (WHO, 2000). To this end, it is important that "in its composition, procedures, and decision-making, the IERC shall be independent of political, institutional, professional, and market influences" (WHO, 2000).

The IERC should consider both the scientific and ethical aspects of the proposed research even when the IERC is distinct from the technical review committee (CIOMS, 2002).

Data from a recent survey of local institutions conducted by the Philippine National Health Research System Technical Working Group on Ethics (2003—2004) show that only 50 percent of these institutions have an IERC (Reyes, 2004). Of the 103 reported IERCs in the country, almost half (55) are in the National Capital Region. Lack of training in research ethics was cited as a major flaw of many IERCs. The efforts of DOST—PCHRD, DOH, and the University of the Philippines (with funding support from United States National Institutes of Health (NIH)-Fogarty International Center) in organizing intensive training courses in research ethics may answer the need for capacity building in this field.

As of January 2012, 200 Ethics Review Committees have been identified all over the Philippines. Of these, 103 are registered in the PHREB database.

Standardization of ethics review is an area of concern that the IERC should address. In this regard, the IERC may use as references the WHO Operational

Guidelines for Ethics Committees that Review Biomedical Research (2000), and the 2011 National Ethical Guidelines for Health Research. However, it should develop its manual of standard operating procedures.

Composition

1. The membership of the Institutional Ethics Review Committee should be multidisciplinary and multisectoral, including the relevant expertise, such as medicine and research, theology, social or behavioral science, law, philosophy, environmental science, and public health. It is recommended that the IERC should include a person who can represent the interests and concerns of the community and its values. At least one member should be independent of the institution or research site. The IERC should have at least five members and should consider age and gender distribution.

2. In addition to the committee members, there should be adequate support staff to carry out IERC's responsibilities.

Appointment

3. The officers and members of the IERC shall be officially appointed by the administrative head of the institution.

4. The appointing official shall indicate their functions, terms of office, scope of work, conditions of appointment, and compensation, if any.

5. Procedures for renewal of appointment, resignation, replacement; grounds for disqualification; and procedures in regard to conflict of interest due to financial gains shall be included in the manual of standard operating procedures.

6. Prior to serving as a regular member, each member of the IERC shall sign a disclosure document which states that he/she has no conflict of interest (e.g., financial interests in a pharmaceutical company) as a reviewer, as well as sign a confidentiality agreement.

7. The appointing official should consider "a fixed rotation system for members that allows for continuity, the development and maintenance of expertise within the committee, and the regular input of fresh ideas and approaches" (WHO, 2000).

External Consultants

8. The committee shall establish a list of external consultants who can provide Consultants special expertise regarding ethical, scientific, psychological or social aspects of researches for review.

9. In deliberations on research involving special participant groups or concerns (e.g., HIV, AIDS, the physically challenged), best efforts must be exerted to include participation of advocates.

Functions and Responsibilities

10. The IERC is responsible for "acting in the full interest of potential research participants and affected communities, taking into account the interests, needs of the researchers, and having due regard for the requirements of relevant regulatory agencies and applicable laws" (WHO Operational Guidelines for Ethics Committees that Review Biomedical Research, 2000). In the Philippines, the regulatory agencies include PNHRS—PHREB, DOH—FDA, and the National Committee on Biosafety.

11. The IERC's functions are as follows:

a. to evaluate the conduct of research in their institutions in accordance with international and national guidelines, local laws, standards of professional conduct and practice, and community morals, values, and needs;
b. to promote research integrity by identifying and resolving conflicts of interest;
c. to establish appropriate mechanisms in all stages of the research in order to:

    - ensure the safety, protect the rights, and promote the welfare and well-being of research participants
    - provide counsel to research participants, including proponents and researchers

- ensure prompt reporting of changes in the protocol and unanticipated problems
- ensure the proper documentation of and adherence to the confidentiality rule and policy on informed consent
- monitor the progress of ongoing research;

d. to report to the institutional or national authorities any matter that affects the conduct and ethics of research which in its view may affect the rights and safety of research participants;
e. to keep a systematic and organized record of all proposals reviewed, including actions taken and other pertinent information;
f. to submit an annual report to the Philippine Health Research Ethics Board through DOST—PCHRD, which will contain the following:

- the composition of the IERC, including a short curriculum vitae (name of the person, educational attainment, most recent ethics training/seminars attended), and term of office of each member;
- members of the IERC secretariat, office and email addresses, and contact numbers;
- number of meetings held during the year, including the date and venue;
- number of researches reviewed by the IERC during the year, categorized as follows:
    - researches approved without changes
    - researches for which the IERC required modifications or revisions before approval
    - researches disapproved;
- any other information as may be required by PHREB.

Meetings and Deliberations

12. The IERC shall regularly meet as a committee on a schedule that is determined based on the research cycle of the institution. There shall be a provision for holding special meetings to consider urgent matters as decided by the chair.

13. More than half of the members shall constitute a quorum, which should include the community representative and one member who is independent of the institution or research site.

14. Deliberations of the IERC shall be characterized by transparency and collegiality. A member who is involved in whatever capacity in the study or project under consideration should inform the committee and his/her further participation in the deliberations must be determined accordingly.

15. As much as possible, decisions shall be made by consensus.

Training and Continuing Education of Ethics Committee Members

16. Members of the IERC shall undergo continuing training on the ethics and science of biomedical research. Initial training must be required of new members. Continuing educational activities must be held at least once a year. These may be linked with those of other ethics committees within the province or region.

For the purposes of these guidelines, an activity is deemed to be research if it aims to develop or contribute to generalizable knowledge (including theories, principles, relationships), or any accumulation of information using scientific methods, observation, inference and analysis.

These general guidelines shall govern all health research involving human participants. Additionally, specific guidelines on clinical trials on drugs, devices and diagnostics (see pages 43-53), herbal research (see pages 54-58), complementary and alternative medicine research (see pages 59-61), research on assisted reproductive technology (see pages 62-64), emerging technologies (see pages 65-69), genetic research with a section on stem cell research (see pages 70-76), epidemiologic research (see pages 77-81), social research (see pages 82-87), conduct of research on specific populations (see pages 88-102), HIV and AIDS research (see pages 103-104), and international/collaborative research (see pages 105-109), have been formulated because of special concerns raised in these areas.

Health research involving human participants includes research on identifiable human material or identifiable data (Principle 1—Declaration of Helsinki, 2008). Considerations related to the well-being of the research participants should take precedence over the interests of science and society (Principle 6—Declaration of Helsinki, 2008). It is the duty of the researcher to protect the life, health, dignity, right to self-determination, privacy, and confidentiality of the research participants, and to safeguard scientific integrity (Principle 11—Declaration of Helsinki, 2008). Researchers should exercise care that their research does not exacerbate existing inequities such as gender based inequities (CIOMS, 2002).

Elements of Research Ethics

Informed Consent

1. For all research involving humans, the investigator must obtain the voluntary informed consent of the prospective research participant. In the case of an individual who is incapable of giving or who has diminished capacity to give informed consent, the permission of a legally authorized representative in accordance with applicable laws must be obtained.

As a general rule, the investigator must obtain a signed form as evidence of informed consent from each prospective research participant. Investigators shall justify any exceptions to this general rule and obtain the approval of the Ethics Review Committee.

When informed consent cannot be expressed in written form, a non-written consent must be documented and witnessed by an impartial person (Declaration of Helsinki, 2008 and CIOMS, 2002).

Waiver of informed consent is to be regarded as uncommon and exceptional, and must in all cases be approved by an ethics review committee (CIOMS, 2002).

In activities such as a survey, informed consent process requires the adequate information needed for participation for evaluation of an ethics review committee.

2. The investigator shall provide the following information to the potential research participant, whether orally or in writing, in a language that suits the participant's level of understanding (CIOMS, 2002):

- That the individual is invited to participate in the research, the reasons for considering the individual suitable for the study, and that participation is voluntary.

- That the individual is free to refuse to participate and is free to withdraw from the research at any time without penalty or loss of benefits to which he/she is entitled.

- The purpose of the research, the procedures to be carried out by the investigator, and an explanation of how the research differs from routine medical care.

- For controlled trials, an explanation of features of the research design (e.g., randomization, double blinding), and that the individual will not be told of the assigned treatment until the study has been completed and the blind has been broken.

- While the use of placebo in controlled trials may be accepted where no current proven intervention exists or for compelling and scientifically sound reasons (Declaration of Helsinki, 2008), it should be made clear to individual that a placebo means no treatment. Investigators should see to it that the individual will not be subjected to risks of serious or irreversible harm.

- Where medical research is justifiably combined with medical care, the investigator should ensure that another person explains and gets the informed consent from the individual and that there is no undue pressure or influence on the individual to participate in the research.

- The expected duration of the individual's participation (including number and duration of visits to the research center and the total time involved) and the possibility of early termination of the trial or of the individual's participation in it.

- Any foreseeable risks, pain or discomfort, or inconvenience to the individual (or others) associated with participation in the research (in both the control and experimental group), including risks to the health or well-being of the individual's spouse or partner;

- The direct benefits, if any, expected to manifest to individuals from participating in the research.

- 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.

- That after the completion of the study, the individual will be informed (if he/she so desires) of any findings related to his/her health status.

- The expected benefits of the research to the community or to society at large, or contribution to scientific knowledge.

- Whether, when, and how, any products or interventions proven by the research to be safe and effective will be made available to the individuals after they have completed their participation in the research, and whether they will be expected to pay for them.

- Any currently available alternative interventions or courses of treatment.

- The provisions that will be made to ensure respect for the privacy of research participants and the confidentiality of records in which they are identified.

- The limits, legal or other, to the investigator's ability to safeguard confidentiality, and the possible consequences of breaches of confidentiality.

- The sponsors of the research, the institutional affiliation of the investigators, and the nature and sources of funding for the research.

- The possible research uses, direct or secondary, of the individual's medical records; and the possible future use and final disposition of biological specimens.

- If the specimens collected will not be destroyed, then where, how, and for how long they are going to be stored.

- That the research participants have the right to decide about such future use, continued storage, or destruction of collected specimens.

- Whether commercial products may be developed from biological specimens, and whether the research participant will receive monetary or other benefits from the development of such products.

- Whether the investigator is serving only as an investigator or as both investigator and the research participant's physician.

- The extent of the investigator's responsibility to provide medical services to the research participant.

- 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.

- In what way and by what organization the research participants or the research participant's family or dependents will be compensated for disability or death resulting from such injury (or, when indicated, that there are no plans to provide such compensation).

- That an Ethics Review Committee has approved or cleared the research protocol (CIOMS, 2002).

3. After ensuring that the research participant has understood the information, the investigator should then obtain the research participant's freely given informed consent, preferably in writing. If the consent cannot be obtained in writing, the non-written consent must be formally documented and witnessed (Declaration of Helsinki, 2008).

4. Caution must be exercised in obtaining informed consent for a research project if the research participant is in a dependent relationship with the investigator (e.g., as a patient) to ensure that the consent is not given under duress or undue influence. The Ethics Review Committee may stipulate that the informed consent should be obtained by a well-informed physician who is not engaged in the investigation and who is completely independent of the relationship (Declaration of Helsinki, 2008).

5. The participation of children in research requires extra protection, as children cannot volunteer to participate in a research study in the same way as an adult can. While they cannot give informed consent, they can participate in the process of obtaining consent by being asked for their assent (see page 98).

6. In obtaining informed consent, sponsors and investigators have the duty to:

- avoid deception, undue influence, or intimidation;
- seek consent only after ascertaining that the prospective research participant has adequate understanding of the relevant facts and the consequences of participation, and has had sufficient opportunity to consider whether to participate or not;
- renew the informed consent of each research participant if there are any significant changes in the conditions or procedures of the research, or if new information becomes available that could affect the willingness of research participants to continue to participate;
- renew the informed consent of each research participant in long-term studies at pre-determined intervals even if there are no changes in the design or objectives of the research (CIOMS, 2002).

Risks, Benefits, and Safety

7. Health research is only justified if there is a reasonable likelihood that the population in which the research is carried out stand to benefit from the research results (Declaration of Helsinki, 2008).

8. Every health research project involving human participant should be preceded by a careful assessment of predictable risks and burdens in comparison with foreseeable benefits to the research participant or to others (Declaration of Helsinki, 2008).

9. Every precaution should be taken to minimize the negative impact of the study on the research participant's physical and mental integrity (Declaration of Helsinki, 2008).

10. There must be an assurance of reasonable availability of a research product within the local market.

Termination of Study / Premature Termination or Suspension of a Trial

11. Study can be terminated by the investigator, the sponsor or the Ethics Review Committee. The research participant should be promptly informed and assured of appropriate therapy and follow-up (ICH-GCP, 1996).

Community Care

12. The conclusion or termination of the research activity should not preclude the possibility of administering extended community care. This should be especially considered in researches involving depressed communities, ethnic groups or in international collaborative protocols (Bhutta, 2000).

Privacy and Confidentiality

13. Every precaution should be taken to respect the privacy of the participant and the confidentiality of the participant's information (DOH, 2008).

Disclosure of Research Results

14. Disclosure of research results to research participants should occur only when all of the following apply:

- the findings are scientifically valid and confirmed;
- the findings have significant implications for the participant's health concerns;
- the course of action to ameliorate or treat these concerns is readily available when research results are disclosed to its participants. Appropriate medical advice or referral should be provided.

Standard of Care

15. The particular needs of the economically and medically disadvantaged must be recognized in determining the standard of care that must be provided to them as research participants.

16. The benefits, risks, burdens, and effectiveness of a new method should be tested against those of the best current prophylactic, diagnostic, or therapeutic methods (Declaration of Helsinki, 2008).

Compensation for Research Participants

17. Compensation given to participants for lost earnings, transportation, and other expenses incurred in taking part in the study, and compensation for the inconvenience and time spent by those who do not have direct benefit from the research should not be so large; or the medical services so extensive as to induce the prospective individuals to consent to participate in the research against their better judgment (CIOMS, 2002).

Participant Groups that Require Special Consideration

18. Some populations require special protection because of characteristics or situations that render them vulnerable. Vulnerable groups should not be included in research unless (a) such research is necessary to promote the health of the population represented, and (b) such research cannot be performed on legally competent persons.

19. Investigators, sponsors, or Ethics Review Committees shall not arbitrarily exclude women of reproductive age from biomedical research. The potential for becoming pregnant during a study shall not, in itself, be used as a reason for precluding or limiting women's participation in research.

20. The following should be considered in enrolling women who may become pregnant during the research:

- A thorough discussion of risks to the pregnant woman and to her fetus is a prerequisite for the woman's ability to make rational decision to enroll in a clinical study.

- A pregnancy test shall be done and access to effective contraceptive methods shall be ensured before the research commences if participation in the research might be hazardous to a fetus or a woman if she becomes pregnant.

Where such access is not possible for legal or religious reasons, investigators shall not recruit for such possibly hazardous research participants who might become pregnant (CIOMS, 2002).

- Investigators and Ethics Review Committees shall ensure that prospective participants who are pregnant are adequately informed about the risks and benefits to themselves, their pregnancy, the fetus and their subsequent offspring, and 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 fetus, or of pregnant women in general and, when appropriate, if it is supported by reliable evidence from animal experiments, particularly as to the risks of teratogenicity and mutagenicity (CIOMS, 2002).

21. Competent advice and assistance shall be provided to participants who, by virtue of social, economic, political or medical disadvantages, are liable to give consent under duress or without the benefit of adequate information.

Absence of Direct Benefit

22. When there is ethical and scientific justification to conduct research with individuals capable of giving informed consent, the risk from research interventions that do not hold out the prospect of direct benefit for the individual participant should be no more likely and no 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 ethics review committee has approved them (CIOMS, 2002).

Ensuring Quality Research

Research Protocol

23. The research protocol should adequately address the four ethical principles: respect for persons, beneficence, non-maleficence, and

justice. It should be sufficiently detailed to serve as documentation of the study. Further, it should:

- justify the need for the study, that is, why the study should be conducted given the current state of knowledge;
- demonstrate the appropriateness of the proposed methods for testing the stated hypothesis;
- demonstrate the feasibility of doing the study as proposed, that is, that the study can be completed successfully in the specified time and with the available resources.

24. The purpose of the study, the design, the population, the methods of data collection, and the planned analyses shall be described in the protocol.

25. All procedures, whether invasive or not, should be satisfactorily described in detail.

26. The protocol should provide information on how the welfare of the participants shall be protected.

27. It is also advisable to include in the protocol the agreements on the time schedule, publication of research findings, and authorship (see Guidelines on Authorship and Publication, page 120-121).

Qualifications of Investigators

28. Persons engaged in health research involving human participants should be scientifically qualified. The investigator must have the ability and skills to conduct the proposed study and the knowledge of the literature on the subject of interest.

Role of the Ethics Review Committee

29. The ERC should:

- Review the scientific merit and ethical acceptability of any research involving human participants.

- Conduct further reviews as necessary in the course of the research as well as monitor the study's progress (CIOMS, 2002).

- Research approved by a foreign ERC for implementation in the Philippines shall also be subjected to ethics review. Ensure that the ethical standards applied are no less stringent than they would be if the research were to be carried out in the country of the sponsoring agency.

- Ensure that the proposed research is responsive to the health needs and priorities of the Philippines and that it meets the requisite ethical standards (CIOMS, 2002).

- Issue the ethical clearance required for the implementation of any research it has reviewed and approved.

- Review amendments/changes in the protocol of researches that have been previously approved.

Responsibilities of the Institution

30. The institutions should:

    - Provide a supportive environment and adequate and quality facilities for research.

    - Ensure the ethical conduct and monitoring of researches being undertaken in the institution.

    - Maintain an efficient recording system of research studies being done and their status and investigators involved in the study.

    - Establish an independent and competent Institutional Ethics Review Committee/Board and provide adequate administrative support for it.

    - Establish standard operating procedures (SOPs) regarding research studies to be done in the institution including fees to be charged.

    - Establish a safety monitoring system for research studies being done in the institution.

- Be updated regarding national and international polices and regulations and comply with them.

- Ensure that a system for the education and protection of human participants is in place in the institution.

Role of the Sponsor

31. The sponsor should:

- Initiate and design research studies according to ethical guidelines and regulations.

- Provide adequate financial support to conduct the research study, including management of adverse effects in human participants.

- Provide clear, relevant and understandable information to participants in designing the informed consent document.

- Inform the local site investigators of the safety record of the drug, device or other medical treatments to be tested, and of any potential interactions of the study treatment(s) with already approved medical treatments.

- Monitor the results of the study as they come in from the various sites, as the trial proceeds. In larger clinical trials, a sponsor will use the services of a Data Monitoring Committee (DMC, known in the US as a Data Safety Monitoring Board).

- Be responsible for collecting adverse event reports from all site investigators in the study, and for informing all the investigators of the sponsor's judgment as to whether these adverse events were related or not to the study treatment.

- Implement and maintain quality assurance and quality control systems with written SOPs.

- Be responsible for securing written agreements from all involved parties (investigators, site institutions, etc.) regarding the research study.

- Ensure the quality of collecting and processing of data and the ethical conduct of research.

Other Considerations

The National Unified Health Research Agenda (NUHRA)

32. In general, research should adhere to the National Unified Health Research Agenda and must be firmly grounded through a process of priority-setting (Margetts, Arab, Nelson, & Kok, 1999).

33. Government funding agencies must seriously consider conformity of the proposal with the National Unified Health Research Agenda for approval.

Community Participation

34. Community participation is not only ethical but has practical value. It aims to involve the communities themselves in the formulation of research questions and to link the research to their own development. Such a participatory process with the community is a continuum that includes community consultation in protocol development, appropriate information disclosure and informed consent, protection of confidentiality and right of dissent, and community involvement in the actual conduct of research and in the sharing of actual conduct of research and in the sharing of benefits (Wejer & Emmanuel, 2000).

Externally-Sponsored Collaborative Research

35. In externally-sponsored collaborative research, sponsors and investigators have an ethical obligation to ensure that biomedical research projects for which they are responsible for, shall contribute effectively to capacity building.

Review Fees

36. Ethics review must not be promoted as an institutional resource generation activity. Review fees are meant to support the operations of the ethics committee, training activities and the continuing education of its members. Charging review fees for other purposes

will put the ethics committee in a conflict of interest situation from which it may not be easy to extricate itself.

Referral Fees

37. Referral of potential research participants for a fee taints the research process and provides the wrong motivation for those involved in the activity. Such practice is discouraged.

Protection of the Environment and Biosafety

38. In the conduct of biomedical or behavioral research, appropriate caution shall be exercised to avoid harm or damage to the environment (Declaration of Helsinki, 2008).

Researches involving the use of biological and hazardous materials including those that involved genetic modification and manipulation of microorganisms and of animal and plant tissue cells must be reviewed and approved by the National Committee on Biosafety of the Philippines (NCBP) before implementation.

Welfare of animals

39. In regard to the use of animals for research, investigators shall abide by RA No. 8485 – Animal Welfare Act of 1998 and its Implementing Rules and Regulations [DA Administrative Order No. 40 series of 1998 and the Code of Practice for the Care and Use of Laboratory Animals in the Philippines, 2nd edition, 2002 developed by the Philippine Association for Laboratory Animal Science (PALAS)].

ETHICAL GUIDELINES FOR CLINICAL TRIALS ON DRUGS, DEVICES, AND DIAGNOSTICS

A clinical trial is a scientifically designed experiment that evaluates the safety and efficacy of a treatment. It consists of four phases:

- Phase I study refers to the first introduction of a drug into humans. Normal volunteer participants are usually studied to determine the levels of drugs at which toxicity is observed. Such studies are followed by dose-ranging studies in patients for safety and, in some cases, early evidence of effectiveness.

- Phase II investigation consists of controlled clinical trials designed to demonstrate efficacy and relative safety. Normally, these are performed on a limited number of closely monitored patients.

  Some innovative pharmaceutical companies have added an additional layer called Phase Ib/IIa before jumping to Phase II. It employs a placebo arm and employs surrogate biomarkers assumed to predict the drug's therapeutic or adverse effects in the disease target population. This allows the right endpoint to be selected for Phases II and III. Participants employed are patients with the target disease but some bridging studies employ additional normal healthy participants. The main objective of this transition phase is to evaluate the safety and pharmacokinetics of multiple doses of the drug and monitor any effects on biological markers of disease activity.

- Phase III trial is performed after a reasonable probability of a drug's effectiveness has been established. This type of trial is intended to gather additional evidence of effectiveness for specific indications and more precise definition of drug-related adverse effects. This phase includes both controlled and uncontrolled studies.

- Phase IV trial is conducted after the national drug registration authority (i.e., FDA) has approved a drug for distribution or marketing. This trial may include research designed to explore a specific pharmacological effect, establish the incidence of adverse reactions, or determine the effects of a long-term drug administration. It may also be designed to evaluate a drug

in a population (such as children or the elderly) not studied adequately in the pre-marketing phases, or to establish a new clinical indication for a drug.

The four conventional phases in clinical drug development present different ethical issues. Careful consideration should be noted and addressed in each phase as indicated in the International Conference on Harmonization (ICH) Harmonized Tripartite Guidelines for Good Clinical Practice, General Consideration for Clinical Trials (E8).

General Guidelines

1. All research involving human participants should be conducted in accordance with the General Ethical Guidelines for Health Research on pages 29-42 and must be cognizant of the Guidelines on the Research Ethics Review Process on pages 110-119.

2. All clinical trials must have scientific and social value and, therefore, shall be adequately justified.

3. The various phases of the pharmaceutical trial present different ethical issues that should be keenly looked into by the Ethics Review Committee. These issues include product toxicities in Phase I, use of placebo in Phases II and III, and professional integrity and conflict of interest in post-marketing activities in Phase IV.

Clinical Equipoise

4. Investigator(s) involved in clinical trials shall be governed by clinical equipoise. A state of clinical equipoise means that on the basis of available data, a condition of genuine uncertainty on the part of the clinical investigator(s) and/or a community of medical experts exists regarding the comparative therapeutic merits of each arm in a trial. Thus they would be content to have their patients/clients pursue any of the treatment strategies being tested since none of them have been clearly established as preferable.

GCP Training of Investigator

5. The investigator(s) should provide evidence of GCP training before commencing a study. GCP training should be done every three years.

It is preferred that GCP training be taken in the country. This is to ensure that the investigators are informed of the local regulatory requirements of the clinical trials.

Enlistment Period

6. The investigator(s) should have adequate time to enlist the necessary number of participants to the trial.

Adequacy of Staff and Facilities

7. The investigator(s) should have adequate and fully informed staff, and the appropriate facilities to accurately and carefully undertake the trial.

Compliance with Regulatory Requirements

8. A clinical research shall comply with the necessary regulatory requirements for the conduct of the clinical trial based on the current rules and regulations on the approval and conduct of clinical trials issued by the Department of Health--Food and Drugs Administration in Administrative Order 47-A dated 30 August 2011.

The investigator(s) and sponsor shall be responsible for complying with each of the applicable regulatory requirements of FDA.

9. Investigational and comparator products, whether produced locally or abroad, should be prepared in accordance with the principles of good manufacturing practice, of assured quality, fully described, appropriately packaged and stored, and acceptably safe. All pre-clinical studies or available non-clinical and clinical information about the product shall be made available for review.

10. Good laboratory practices shall be strictly observed when a clinical trial requires laboratory assay.

Agreement with the Sponsor

11. The investigator(s) shall establish with the sponsor an agreement on the protocol, standard operating procedures, monitoring, and auditing of the trial and allocation of trial-related responsibilities, including publication and authorship.

Protocol

12. The protocol should at least contain the following:

- General information about the trial such as investigator(s), sponsor(s), monitor(s), other qualified medical expert(s), diagnostic laboratories, and research institutions involved.

- Background information regarding the product under investigation, relevant current research findings and references to such information and data, potential risks and benefits, reason for the indicated route of administration, dosage, periods of treatment, population to be studied, a declaration regarding compliance with good clinical practice, and regulatory requirements.

- Objectives and purpose.

- Trial design, which substantially determines the scientific integrity of the trial and reliability of the data, and which shall include the following:

    a. description of the type of design and trial plan (double-blind, placebo controlled, parallel design) and diagram of procedures and stages;
    b. primary and secondary endpoints to be measured;
    c. measures to minimize or avoid bias, such as randomization and blinding;
    d. trial treatments and investigation product's dosage, packaging, labeling, and storage;
    e. estimated duration of individuals' participation in the trial;
    f. discontinuation rules for the participants and the trial;
    g. treatment randomization codes maintenance and rules on breaking the code;
    h. procedures for accountability for product being investigated, placebos, and comparators;
    i. other sources of data.

- Selection and withdrawal of research participants, which include inclusion, exclusion, and withdrawal criteria.

- Informed consent.
- Research participants' therapy or treatment, and monitoring procedures.
- Efficacy parameters, methods, and timing.
- Safety parameters, methods, timing, and procedures for recording and reporting as well as monitoring adverse reactions.
- Safety measures for research participants when they withdraw/or are withdrawn from the trial.
- Plan for data and statistical analysis.
- Statement regarding direct access to trial data and documents for monitoring, audits, institutional ethics committee reviews, and regulatory inspections.
- Ethical considerations.
- Data management and record keeping.
- Financing and insurance.
- Publication plans and procedures.
- Clinical trial participants' information sheet/brochure.

13. Any amendment(s) to the protocol should be resubmitted to the ERC and FDA.

Use of Placebo

14. Use of placebo is generally not acceptable when there are standard treatments available to a patient population. Thus, a placebo control may be used only when:

- standard therapy is unavailable;
- existing treatment is of unproven efficacy, or possesses unacceptable side-effects;

- there is compelling scientific reason to use placebo, the research participants who receive placebo will not be subjected to any risk of serious or irreversible harm (Declaration of Helsinki, 2008);

- the placebo itself is an effective therapy (e.g., placebo in pain);

- the disease has little adverse effect on the patient (e.g., common colds or superficial fungal skin infection);

- testing an add-on treatment to a standard therapy when all research participants get all treatments that would normally be given;

- the research participant has provided informed rejection or refusal of standard therapy for a minor condition for which the patient refuses treatment, and when such refusal for therapy will not lead to unjustified affliction or irreparable damage or harm.

Informed Consent

15. Refer to section on Informed Consent in the General Ethical Guidelines for Health Research (see pages 29-34).

In cases when HIV testing is required in the protocol, a separate informed consent must be obtained and pre- and post-test counseling must be provided.

Therapy versus Research

16. The difference between therapy and research shall be upheld throughout a clinical trial. The investigator(s) shall ensure that research participants comprehend this and ensure that they keep in mind that in a clinical trial, the drug is experimental and that its benefits are currently being proven.

In instances where medical research is combined with medical care, strong justification should be presented by the principal investigator

and that participation in such trial will not adversely affect the health of the research participant. It should be clearly defined in the informed consent document which are standard care and which are purely components of the trial. There should be separate informed consent for medical care and for the clinical trial component.

Research on Medical Devices, Diagnostic Procedures and Preventive Measures

17. Clinical trials of medical devices, diagnostic procedures, and preventive measures, including vaccines, raise similar ethical concerns especially on free and informed consent, and potential conflict of interest.

- Trials of critical medical devices such as implants which may present a potential serious risk to health, safety or welfare of the participant shall not be conducted on healthy volunteers. The current safety data on the medical devices shall be gathered and the risks posed by the device shall be considered and evaluated.

- Review of clinical trial protocols on medical devices should include an expert consultant (e.g., Bioengineer who should look into the material and design as well as electrical safety of the device). It must be noted that clinical investigation of medical devices aim to demonstrate safety and performance not efficacy. Thus, clinical trials on medical devices should show that the device performs according to its intended purpose as claimed by the sponsor/manufacturer, and in a safe manner. Randomized trials are not usually indicated. Follow up period for this type of trial is longer than drug trials and may last for several years especially for implantable devices. Although regulatory issues for medical devices may be different from those of pharmaceuticals, the ethical and moral issues are the same.

- Safety procedures in the introduction of such medical device in the patient shall be followed. The patient information sheet shall contain information on procedures to be adopted should the patient decide to withdraw from the trial. Medical

devices that are not used regularly have less risk-potential than those used regularly. Likewise, devices used outside the body have less risk than those used inside the body.

- In the case of contraceptive implant trials, adequate monitoring and counseling for removal of the implant shall be done when the trial is over or the paticipant has withdrawn from the trial. Children born as a result of failure of the contraceptive being investigated shall be followed up for any abnormalities and properly reported to monitoring authorities.

- Clinical trials done in an emergency room/ICU setting

  Research in an emergency room/ICU setting involves a highly diverse and critically ill patients, and thus are considered to belong in the vulnerable population. As such, the requirement to get an informed consent directly from the patient applies. However, in cases where the patient-participant, by the virtue of the nature of his disease, is unable to give consent (e.g., patient has delirium or the sensorium is impaired), consent must be obtained from the patient's legally authorized representative or the patient's surrogate decision maker prior to enrollment in the clinical trial. Once patient's sensorium improves during the course of management and is able to give informed consent, the investigator should seek a re-consent from the patient himself on whether to continue with or withdraw from the trial.

  There are situations however, especially in the emergency room setting, when the surrogate decision maker is not available at the time the patient is brought to the hospital. In such cases, every effort by the principal investigator to locate the patient's family/surrogate decision maker must be exerted and documented within the time allotted within the therapeutic window.

  ERCs must ensure that the protocol contains appropriate procedures to inform, at the earliest feasible opportunity the legally authorized decision maker and or family members of the participant's inclusion in the study and his/her right to discontinue participation in the research.

In rare instances, the ERC may grant exemption for the informed consent requirement only under all of the following conditions:

a. patient-participant have a life threatening condition for which available treatments are unproven effective or lacking and/or unsatisfactory;
b. prospect of direct benefit to the research participants;
c. when research participants are unable to give consent (e.g., impaired sensorium) and no surrogate decision maker/family is around or cannot be located;
d. the risks associated with the investigation are reasonable in relation to what is known about the emergent condition;
e. where to be effective, the intervention under investigation must be given right away upon admission to the emergency room/ICU or within the specified therapeutic time window

However, in the above situation, consent for continuing participation of the patient must be sought from family members/surrogate decision maker or from the research participant himself/herself as soon as feasible.

- Vaccine trials

In contrast to pharmaceutical trials where the objective is to find out if a drug is efficacious for individual use, vaccine trials are done to find out if the vaccine can be safely used as a public health tool. In vaccine trials, the burden of risks is mostly carried by the individual participant and benefits accrue mainly to the community. Direct benefit from the investigational vaccine is provisional -- only if that participant gets exposed to the infectious agent at some future time, and if he/she had received the active vaccine during the trial which sufficiently had protected him/her. It must be noted that most vaccine trials are done on children, who belong a vulnerable population (see pages 96-99).

Child bearing women who participate in vaccine trials should be properly advised on the use of acceptable contraception.

Should pregnancy ensue, adequate provision for prenatal care should be provided. Children born as a result of failure of contraception should be reported and followed up for any abnormalities.

For vaccine trials using active or live attenuated microorganisms, the research participants may be exposed to the specific infection for which the vaccine is being tested. As such, the vaccinated participants and/or legal guardians should be informed accordingly so that proper care can be given.

DNA vaccines and vaccines developed using recombinant DNA technology should have a prior clearance from the Biosafety Committee of the institution where research will be done or if none, such should be referred to the National Biosafety Committee.

- Clinical trials involving diagnostic agents using radioactive materials and X-ray should not unnecessarily expose participants to more radiation than normal and should be undertaken only on patients needing the procedure for diagnostic or therapeutic purposes. Clearance from the Philippine Nuclear Research Institute that the level of radiation from the radiopharmaceutical is within the allowable limits for human use should be secured and submitted to the ERC for considerations. Measures to safeguard research participants and others who may be exposed to radiation should be taken. Adequate provisions for detecting pregnancies to avoid risks of exposure to the embryo shall be given. ERCs should require that the informed consent document include the information that participation will involve exposure to radiation which may have impact on significant others and possible genetic damage to their offspring.

Publication of Clinical Trial Results

18. Clinical trial results shall be communicated in a timely fashion and published regardless of results or findings. Findings shall be brought into the public domain and generally made known through scientific

and other publications. Special effort must be exerted to share the results with the trial participants.

19. Preliminary reports that raise false hopes and expectations of product safety, efficacy, and immediate use shall not be made public.

20. The plan for publication and the actual publication of trial results shall not expose the identity of the research participants or their family and community, or imperil their privacy or confidentiality as individuals, family, or community.

ETHICAL GUIDELINES FOR HERBAL RESEARCH

The use of herbal remedies can provide a practical and inexpensive way of alleviating illness in countries, like the Philippines, that are rich in natural resources and has a fecund pool of indigenous healing practices.

Philippine Republic Act No. 8423, the Traditional and Alternative Medicine Act of 1997, declared the policy of the state "to improve the quality and delivery of healthcare services to the Filipino people through the development of traditional and alternative healthcare and its integration into the national healthcare delivery system." This law aims to 1) encourage scientific research on and develop traditional and alternative healthcare systems that have direct impact on public healthcare; and 2) promote and advocate the use of traditional, alternative, preventive, and curative healthcare modalities that have been proven safe, effective, cost-effective, and consistent with government standards of medical practice.

These legislated objectives have generated research activities on herbal remedies or preparations to evaluate their safety and effectiveness. Necessarily, these researches involve human participants for which ethics review is mandated. Some argue that ethical issues of researches on traditional medicine can not be resolved by using Western Bioethical Guidelines because the individual is not the participant alone but a complex network involving family or community.

Advocates of herbal medicine are convinced that herbal products can be used without subjecting them to the same rigorous scientific evaluation (e.g., requirement for pre-clinical trials) required in Western medicine. It is argued that the current universal scientific procedures and standards are not applicable to remedies with a long history of use in and have been accepted by communities.

Despite all the arguments against treating herbal research differently from Western Medicine, the safety and well-being of participants in herbal research must remain paramount over the desire by any researcher to prove their effectiveness. Thus, basic ethical guidelines as espoused by many International instruments are applicable. These ethical guidelines were formulated with the Traditional and Alternative Medicine Act as its political framework and Good Clinical Practice for its scientific underpinning.

These guidelines shall serve as parameters in the conduct of research on herbal remedies based on universally accepted ethical principles such as respect for persons, beneficence, non-maleficence and justice. It is expected that these principles will be considered in all the ethical reviews of herbal researches. Thus, an ethically sound research must satisfy a number of important procedural requirements of which the most important is a prior review by an independent and competent Ethics Review Committee. The latter requirement is what these ethical guidelines will attempt to describe.

General Guidelines

1. All research involving human participants should be conducted in accordance with the ethical principles in the General Ethical Guidelines for Health Research (see pages 29-42).

2. There must be proof of long history of use of the herbal plant/ remedy to be tested. An exhaustive literature search about the therapeutic or diagnostic value of the herbal plants must serve as the background or justification to the research proposal. Any documents supporting its putative actions and traditional use in the community must be incorporated in the research proposal. Proof of their use may be both in the written, oral or video form. Evidence regarding usage of the herbal preparation can be validated with the National Commission on Indigenous Peoples (NCIP), the National Museum or by an expert opinion, should the need arise from the Ethics Review Committee.

3. The original herbal preparations and manner of use by people in the community must be similar to that intended in the proposed research. For example, if the herbal plant is applied as a poultice for a condition to be studied, then it should be given in the same form to the research participants.

4. Once an active principle is identified from the herbal preparation and there are intentions to synthesize it for research and eventual commercial purposes, any studies thereafter need to be reviewed based on the International Conference on Harmonization—Good Clinical Practice Guidelines and Good Manufacturing Practice guidelines.

5. Although efficacy of herbal preparations is a major objective of herbal researches, adverse reactions such as side effects, tolerance profile, and interaction with other administered preparations should always be part of herbal research.

6. Research in herbal remedies should include standardization of the preparation and identification of markers to ensure that the ingredients being studied and assessed are the same.

7. In the absence of a standard for the test preparation, the geographic area, maturity of collection of the plant, and the method of its preparation must be clearly described.

8. The method of herbal preparation in the research study should be standardized. The source of the plant, the way it was prepared and the excipient and diluent used must be characterized. This method must be followed all throughout the research proper.

Specific Guidelines

Informed Consent

9. Uncertainty regarding product, namely, adulteration, interactions between herbal remedies and other entities, minimal toxicity data, and incomplete prior dose finding must be clearly disclosed to all concerned, particularly in the informed consent process (WHO , 2005).

Recruitment of Volunteers

10. When normal volunteers are recruited, participants must preferably come from the community where the herbal preparations are frequently used.

Participation of Traditional Healers

11. Cultural settings and expectations must be considered in the review of the proposal and this may require inviting a traditional healer or a known scholar of herbal medicines in the Ethics Review Committee. If there are three key players in research for ICH-GCP, namely, investigators, patients and sponsors, herbal research has

four. The traditional healer who is the community's steward of indigenous knowledge is the fourth.

Research Design

12. Placebo-controlled trials may be accommodated in consonance with the guidelines on the use of placebo as indicated in Ethical Guidelines for Clinical Trials on Drugs, Devices, and Diagnostics (see pages 47-48).

13. Effectiveness of herbal preparations may not only be measured with improvements in health or disappearance of physical symptoms and other disease-related variables. It may also be measured in terms of overall health and well-being. However, measuring the quality of life or improvement in well-being must be objectively measured.

Transport

14. No indigenous materials used in the research may be transported outside the country unless the source (represented by the community leader, government agency or institution) of the material and the recipient sign a material transfer agreement.

15. Researchers must comply with the transfer agreement if plant products or herbal preparations will be tested outside the country.

Benefit Sharing

16. When possible, the community from where the medicine originates should be consulted during the course of the research, and the results and benefits of the research should be shared with this community (WHO, 2005).

17. A memorandum of agreement regarding benefit sharing and patenting conditions, especially for indigenous plant products, must be set as early as during the planning stage of the research.

Commercialization of Herbal Preparations

18. Researchers must include provisions for conditions when the herbal preparations may likely be commercialized. They should be

guided by existing laws and regulations of the Philippine Intellectual Property Rights Office.

Safeguarding Indigenous Knowledge

19. It is recommended that the rich knowledge about indigenous herbal plants in a community must be documented, appropriately recorded and archived for posterity.

Social Relevance of Herbal Research

20. Social value, in the form of knowledge gained from the research, should be generalizable to improve health. At the outset, partners should specify to whom benefits will accrue and in what way. This suggests the need for a clear legislative framework for herbal, complementary and alternative medicine research.

ETHICAL GUIDELINES FOR COMPLEMENTARY AND ALTERNATIVE MEDICINE RESEARCH

Worldwide, there is a continuing popular interest in and utilization of complementary and alternative medicine (CAM). In the Philippines, promotion of the utilization of CAM is embodied in Republic Act No. 8423, the Traditional and Alternative Medicine Act of 1997, which declared that the state shall "improve the quality and delivery of healthcare services to the Filipino people through the development of traditional and alternative healthcare and its integration into the national healthcare delivery system."

The World Health Organization and national health authorities have looked to CAM as a source of accessible, cost-effective, and beneficial alternative to the expensive conventional methods of treatment. This perspective can go hand in hand with the call for the application of the rigors of scientific investigation before specific CAM modalities could be promoted for widespread use.

Complementary and alternative medicine is defined as a group of diverse medical and healthcare systems, practices, and products that is not presently considered to be part of conventional medicine. Complementary medicine is used together with conventional medicine, while alternative medicine is used in place of conventional medicine (NCCAM, NIH, & US Department of Health and Human Services 2006).

As opposed to CAM, traditional medicine (TM) is defined as the sum total of the knowledge, skills, and practices based on the theories, beliefs, and experiences indigenous to a particular culture, whether explicable or not, used in the maintenance of health, and in the prevention, diagnosis, improvement, or treatment of illnesses. However, the term complementary/alternative/non-conventional medicine is used interchangeably with traditional medicine in some countries (WHO, 2000). It will also be so used in these guidelines.

According to the National Center for Complementary and Alternative Medicine (NCCAM), CAM therapies include the following (NCCAM et al., 2011):

- biologically-based therapies such as dietary supplements, herbal products, animal products, and aromatherapy;
- manipulative body-based methods such as massage, acupressure, chiropractic, and osteopathic manipulation;

- mind-body interventions such as meditation, prayer, mental healing, art or music therapy;
- energy therapies such as qi gong, reiki, therapeutic touch, pranic healing, electromagnetic fields methods;
- other methods used in alternative medical systems such as in medical traditions developed in the West (e.g., naturopathy and homeopathy), and in Oriental traditional medicine (e.g., ayurveda, unani, and traditional Chinese medicine).

While some scientific evidence exists regarding some CAM therapies, for most there are key questions that have yet to be answered through well-designed scientific studies – questions such as whether these therapies are safe and whether they work for the diseases or medical conditions for which they are used.

General Guidelines

1. All research involving human participants should be conducted in accordance with the ethical principles in the General Ethical Guidelines for Health Research on pages 29-42 and must be cognizant of the Guidelines on the Research Ethics Review Process on pages 110-119.

Specific Guidelines

Participation of Traditional Medicine

2. The technical review committee should include an expert in the specific traditional medicine modality being considered in the research expert protocol.

Study Design

3. In contrast to conventional medicine, CAM modalities focus on beneficial effects (e.g., quality of life) rather than efficacy. In this context, study designs other than randomized controlled trials may be acceptable.

4. Blinding could be difficult to achieve in the application of certain CAM modalities, in which case the research protocol should provide mechanisms for blinding the clinical outcome evaluator.

Rescue Medication

5. The protocol must identify and describe the rescue medication which should be available to the research participants who may require such an intervention.

ETHICAL GUIDELINES FOR RESEARCH ON ASSISTED REPRODUCTIVE TECHNOLOGY

Research in assisted reproductive technology (ART) includes studies to improve ovulatory (ovulation) rates, ejaculatory efficiency including sperm quantity and quality, embryo viability, fertilization success, and uterine hospitability. It may also involve studies on the psychosociocultural aspects of reproductive technology. Research in the reproductive health field, in general, is studded with gender issues.

In general, research on assisted reproductive technology is ethically complex. This is because the research participants, in contrast to other health researches, include two individuals (i.e., the source of the ovum and the source of the sperm) and the fertilized egg in various stages of development, whose status as a moral agent has religious and ethical implications. This means that the ethical principles enunciated for health research, in general, must be equitably and equally applied to the research participants with special consideration for gender and religious issues.

The Philippine Obstetrical and Gynecological Society (POGS), in 2004, and the Philippine Society of Reproductive Endocrinology and Infertility (PSREI) have set requirements that must be satisfied by medical hospitals, clinics, centers, and/or other facilities that conduct assisted reproductive techniques/ technologies and related research. Additionally, it is emphasized that clinical and biological research involving assisted reproductive technology shall be carried out under the supervision of a qualified practitioner who has acquired adequate and up-to-date training in, and is sensitive to the technical aspects of using technology for assisted reproduction.

General Guidelines

1. All research involving human participants should be conducted in accordance with the ethical principles in the General Ethical Guidelines for Health Research on pages 29-42 and must be cognizant of the Guidelines on the Research Ethics Review Process on pages 110-119.

2. In accordance with the ethical principle of distributive justice, research on assisted reproductive technology should not divert resources in any form away from research on areas of health which impact more on Philippine society, in general.

Specific Guidelines

Research on Gametes

3. The use of gametes (sperm and ovum) in fertility research should be subject to ethical review with special attention to the potential harm and risks involved in the collection of specimens, its cultural and religious implications, and human rights issues.

Research on Human Zygotes and Embryo

4. The intentional creation of human zygotes, embryos or fetuses for study, research, and experimentation for commercial and industrial purposes is unacceptable (POGS, 2004).

5. The embryo becomes a unique human being at the time of fertilization; hence, it is entitled to full moral support equivalent to that of an adult human being. Research on the embryo, therefore, is unethical (POGS, 2004).

6. Research may be conducted on a human embryo if the objective is to discover and eliminate defects that will lead to their correction, and only for the purpose of improving that particular embryo's chances of being born alive and healthy (POGS, 2004).

7. The sale of human zygotes is unacceptable.

Research Participants

8. Special effort should be exerted to ascertain the emotional stability and maturity of research participants.

9. Gender-sensitive counseling should be made available and offered as an adjunct service to research participants.

Informed Consent

10. It should be the responsibility of the attending physician to ensure that consent of research participants is given freely and on the basis of adequate information and that potential conflict of interest is resolved.

11. The investigator must be sensitive to the general social condition characterized by the coercive and unfair pressure on women to bear children.

Privacy and Confidentiality

12. Researchers should uphold the dignity of research participants and protect their privacy by putting in place adequate mechanisms for upholding the confidentiality especially of the circumstances of conception of children born out of assisted reproductive technology.

Embryos from in Vitro Fertilization

13. Embryos formed by in vitro fertilization should be given respect commensurate to their status (POGS, 2004).

14. Extreme care should be exercised in the handling of human embryos.

15. Arrangements regarding unused embryos, sperms, and ova should be agreed upon by the investigator and the source(s) prior to the research, and should be an important part of the research protocol.

Nanotechnology, also known as molecular manufacturing, deals with the manipulation of molecular-sized materials to build new ones at the molecular level of matter (Porter et al., 2008). The term "nanotechnology" has evolved over the years via terminology drift to mean "anything smaller than microtechnology," such as things that are nanoscale in size. It involves the building, with intent and design, and molecule by molecule, these two things: 1) incredibly advanced and extremely capable nano-scale and micro-scale machines and computers, and 2) ordinary size objects, using other incredibly small machines called assemblers or fabricators (found inside nanofactories). By taking advantage of quantum-level properties, nanotechnology allows for control of the material world, at the nanoscale, providing the means by which systems and materials can be built with exacting specifications and characteristics. It represents the state of the art advances in biology, chemistry, physics, engineering, computer science and mathematics. The major research objectives in nanotechnology are the design, modeling, and fabrication of molecular machines and molecular devices.

Nanomedicine is the novel use of nanotechnology in pharmaceutical "constructs" (these may not necessarily be considered as drugs), disease treatment and nanomachine-assisted surgery. Potential applications can include nanodevices for tracking and targeted destruction of tumor cells, killing bacteria, tissue repair, improved imaging and immune enhancement.

The emergence of nanotechnology has numerous social, legal, cultural, ethical, religious, philosophical and political implications.

Biosimilar development is a process that requires close monitoring of the design, manufacture, testing and standards setting for alternative biologicals. Biological medicines (e.g., monoclonal antibodies, biosimilars, and recombinant vaccines) are produced using living cells or organisms. The molecules of a biological medicine are much larger, have more complex structures, and are much more diverse than classical chemical drugs. Because of that, they are very sensitive to any change such as changes in the manufacturing process, or use of different batches of cell cultures, which can alter everything starting from efficacy, tolerability and safety of the molecule.

Biosimilar medicines are follow-on versions of the original (innovator) drugs. Whoever wants to make a biosimilar would not have the access to the original process, since the original process is always patented. Biosimilar medicines

are independently developed after the patent protecting the original product has expired. Small changes in the manufacture of biopharmaceutical and biosimilar medicinal products can dramatically affect the safety and efficacy of the therapeutic molecule. This may make patenting necessary for biosimilar products due to the complexities involved.

Producing a biosimilar requires the manufacturer to have their own process that could produce the same efficacy, safety and tolerability. For the generic version of small molecules no such problems exist. They just need to meet the bioavailability profile and tolerability to the original small molecule within the regulatory guidance.

Appropriately designed preclinical and clinical studies are required to prove that a biosimilar product has the same clinical properties as the innovator's product. The manufacturer may be required to do some clinical studies in support of biosimilar drug's safety and effectiveness. In particular, the studies must address immunogenicity concerns. In addition the regulator might also be interested in post-market pharmacovigilance plans as part of approval commitments.

General Guidelines

1. Guidelines for Good Manufacturing Practice (GMP) should be clearly set for specific emerging technologies.

2. Data on pre-clinical and all phases of a clinical trial should be provided prior to full-blown application of emerging technologies for patient treatment.

3. Public education programs, with particular emphasis on research participant and family education should be required for the introduction of any emerging technology product.

4. Credentialing of physicians and healthcare professionals who will be responsible for the administration, monitoring and counseling of research participants regarding treatment with products (drugs or devices) of emerging technologies should be done.

5. Extensive and long-range post-marketing surveillance is needed to monitor the effectivity, impact, and unknown hazards of emerging technologies.

6. When biosafety issues are applicable, a certification from the Institutional Biosafety Committee should be required.

Specific Guidelines

Ethics in Nanotechnology

7. Nanotechnology research should be conducted with the least risk possible to human beings and public welfare.

8. Experimental work on nanomaterials should be done in contained and regulated facilities. Biosafety precautions specific to the handling and processing of nanomaterials should be strictly observed at all times in the research facility.

9. Safety standards should be set for all stages of research involving nanomaterials.

10. If a nanotechnology researcher is in a position to make the public aware that regulatory decision-making regarding nanomaterials and the environment has been made on non-scientific grounds, and if doing so might help prevent harm to the public, then he or she should bring that decision-making, as well as the most credible account of the benefits, costs, and risks of the situation, to public attention.

Ethics in Nanomedicine

11. Before nanomedicine products can be used in diagnosis, prevention, or treatment of disease, they must first undergo extensive pre-clinical and clinical testing.

12. Safety and risk issues must be thoroughly understood if society is to take advantage of the potential benefits of nanotechnology.

13. Risks posed by the use of nanotechnology products to human participants should be reasonable in relation to the potential benefits to the participants and society and these risks should be minimized, wherever possible.

14. Though in vivo animal experiments and ex vivo laboratory analyses can increase the understanding of different nanomaterials,

they cannot eliminate the uncertainty surrounding the first exposure of a human participant to a particular nanomedicine product in a Phase I clinical trial.

15. To minimize risks in clinical trials, strategies should include careful review of the relevant literature, sound research design, appropriate inclusion and exclusion criteria, clinical monitoring, well-trained personnel, timely adverse event reporting, protection of confidentiality, standard operating procedures, follow-up with participants after they complete the study, and a data and safety monitoring board.

16. The investigator should inform a potential research participant, or his or her representative, about the purpose of the study, procedures, benefits, risks, alternatives, confidentiality protections, and other information the participant would need to decide whether or not to participate.

17. If a nanomedicine clinical trial involves exposure to novel materials that have not been thoroughly studied, investigators should inform research participants that there may be some risks that cannot be anticipated.

18. Researchers should educate the public about how nanotechnology can be used in medicine, and the benefits and risks of nanomedicine.

Ethics in Research Development of Biosimilars

19. Manufacturers of biosimilars should conduct all phases of clinical studies in order to promote drug safety and efficacy. In particular, the studies must address immunogenicity concerns.

20. Informed consent taken from research participants in a study on biosimilars should fully disclose all the information needed to consider the substitution of a biosimilar in place of the reference product and the risks this would entail.

21. Because the inherent differences between a biosimilar and an innovator product may involve a greater risk to benefit ratio for certain patient populations (e.g., stem cell donors) than for others, extrapolation should be implemented on a case-by-case basis.

22. The approval of a biosimilar shall be based on the demonstration of comparable efficacy and safety to an innovator reference product in a relevant patient population.

23. Because there is a limited clinical database at the approval of a biosimilar, it is important to collect post-approval safety data for these drugs. This means conducting post-marketing surveillance studies to monitor the efficacy and safety of biosimilar products.

ETHICAL GUIDELINES FOR GENETIC RESEARCH WITH A SECTION ON STEM CELL RESEARCH

The health status of an individual results from the interaction of many factors, involving the environment, lifestyle, and genes. Genes are the biochemical instructions for the development and growth of individuals. When a gene is altered, it may cause or lead to an increased susceptibility for a disease.

Human genetic research aims to identify genes associated with health and disease, and elucidate their functions. The ultimate goal is to use the knowledge gained through research to discover ways of better diagnosis treatment and prevention of disease. Genetic research includes family studies, linkage analysis, candidate gene and genome wide association studies, pharmacogenetics and pharmacogenomics, behavioral genetics, population-based genetics, cloning and stem cell research. These types of researches can be either therapeutic or non-therapeutic in nature. The primary aim of therapeutic research is essentially diagnostic, that is, to treat and/or cure a disease and the desired benefit is direct in terms of treatment. In contrast, a non-therapeutic research aims to test a hypothesis or through data gathering contribute to the discovery of new knowledge. Ultimately, non-therapeutic genetic research must still have the objective of realizing some future benefit to participants.

Human stem cell research holds enormous potential for contributing to an understanding of fundamental human biology, leading to the possibility of novel treatment and ultimately, cures for many diseases. Special efforts should be made to promote equitable access to the benefits of stem cell research. Intellectual property regulations for stem cell research should set conditions that do not restrict basic research or encumber future product development.

The ethical considerations in reviewing genetic research are no different from those that arise when reviewing other types of research. However, in addition to those that apply to all research involving humans, there are ethical issues unique to genetic research. These arise from the nature of genes and genetic information which, though personal, are also shared with other family members and with unrelated individuals in the population.

These guidelines should assist research institutions, scientists, pharmaceutical companies, health researchers, and Ethics Review Committees for the ethical

pursuit of genetic research so that the expected benefits in the improvement of health and healthcare will be attained.

General Guidelines

1. All research involving human participants should be conducted in accordance with the ethical principles in the General Ethical Guidelines for Health Research (see pages 29-42).

2. Given the hereditary nature of genetic research, confidentiality, privacy, and security are important considerations in the ethics review of a genetic study.

Specific Guidelines

Collection of Samples from Humans

3. Human biological samples for genetic research include samples that can serve as DNA, RNA, and protein sources: solid tissues, biopsies, aspirates, scrapings, and body fluids such as blood, saliva, ocular fluids, and excretions. Samples may be collected, processed, used and stored only for the following purposes:

- therapeutic and non-therapeutic genetic research (i.e., epidemiological, prognostication, population-based genetic studies, anthropological or archeological studies);
- forensic medicine, in which case, use of samples shall be in accordance with domestic laws and consistent with laws on human rights;
- development of drugs, biomedical devices, molecular diagnostics, and medical technologies;
- others as dictated by local and/or international interests, or in the event of global health and technology trends, or other reasons of public interest

Informed Consent

4. Prior, voluntary, informed, and expressed consent, without inducement by financial or personal gain, should be obtained for the collection of biological samples, human genetic and proteomic data, and for their subsequent processing, use, and storage.

5. Research participants should be provided with proper and full but comprehensible information that explains the basics of genetics, the research in its various steps, and the benefits or potential benefits to the participants.

6. Potential research participants should be adequately informed about what will happen to any genetic material or information obtained as part of the study.

7. Research participants should be recruited as individuals in their own right rather than as a family group, and should consent as individuals.

8. In cases where identities of groups or communities may be linked with genetic traits under study, permission or endorsement may be obtained from an elected or recognized leader who will be responsible for making decisions on the participation of the group in the study.

9. Informed consent should not be required for those protocols for genetic research that use anonymous samples or samples that have no identifiers. Any sample that can be linked to an individual through an identifier, or through any person or institution that has the capability to link the sample with its source, is not to be considered anonymous.

10. It is required that all secondary and third party uses of biological samples are restricted to anonymized or anonymous samples, as above, and both still need ethical approval for use. Limited, non-identifying, demographic information may be retained on the sample.

11. Stored biological samples collected for purpose other than those stated in No. 3 above may be used to produce human genetic or proteomic data with the prior, free, informed, and expressed consent of the person concerned.

12. In case informed consent is withdrawn, the samples and data should be irretrievably unlinked from their source. This will be accomplished by the destruction of all identifiers.

13. If genetic markers are yet to be determined at some future date and not stated during the time that the consent was taken, this information should also be included in the consent form.

Informed Consent of Vulnerable Groups

14. Genetic studies involving indigenous groups should be guided by domestic and international regulations on respect for human rights and privacy, and protection from exploitation.

.

Genetic Counseling and Disclosure

15. The informed consent should include statements on the disclosure and sharing of the results and findings of the study, that is, to whom should the information be revealed, among others.

.

16. Genetic counseling (pre- and post-test) should be provided when there is a need to disclose the findings of the genetic study.

Privacy, Confidentiality, and Security

17. Researchers must ensure the confidentiality and privacy of stored genetic information or research results relating to identified or potentially identifiable participants in accordance with the domestic and international laws on human rights. Researchers should also ensure that safeguards are in place to avoid accidental disclosure of sensitive information.

18. No individual results will be given back to research participants and results of genetic research should never go into the medical record.

19. Disclosure of genetic information is sometimes impossible to avoid. Such information should be dealt with sensitively, and the possibility that such a disclosure may occur should be considered in the initial process of seeking consent.

20. Researchers should also ensure that the results of genetic testing and genetic counseling records are protected from access by third parties.

21. There is potential harm to research participants arising from the use of genetic information, including stigmatization or discrimination. Researchers should take special care to protect the privacy and confidentiality of this information.

22. Identifying genetic information must not be released to others, including family members, without the written consent of the individual to whom the information relates, or a person or institution which may legally provide consent for that person.

23. The research participant's right to privacy (researcher's duty for confidentiality) continues after the participant's death so that confidential information may be revealed after death only with proper legal authority. The only exception is the right to disclose information to a family member if there is a clear and urgent need to provide information to avoid a serious health risk.

Storage and Handling of Biological Specimen

24. Genetic research often involves the storage of DNA or other biological samples in "tissue" or "sample" collections. In some cases, samples can be anonymized so that the donors cannot be identified.

25. Handling and preservation of biological samples should be in accordance with standard scientific procedures.

26. Disposal of stored biological specimens should be in accordance with standards for handling biohazardous and infectious materials.

27. Transport, transfer, and disposal of all stored biological samples should be properly documented and filed.

28. Retention time for stored biological samples should be determined by the respective institution, provided that this is written in the informed consent.

29. All specimens in a tissue bank must be accompanied by a copy of the consent agreement signed by the donor.

30. No specimen shall be removed from a tissue bank for research purposes without an approved research protocol.

31. A researcher must not transfer genetic material or related information to another research group, unless:

- the researcher and the other research group are collaborating on research which has been approved by their respective Institutional Ethics Review Committee;
- the genetic material and information are provided in a form that ensures that participants cannot be identified.

32. An approved Material Transfer Agreement (MTA) or Limited Use Agreement (LUA) should accompany genetic researches of collaborative nature (see pages 105-109).

Ethical Considerations in Stem Cell Research

33. Securing stem cells for research, whether from children, adults or naturally aborted fetuses, must be done under conditions of the most rigorous integrity for at least these reasons:

- to protect the interests of the donors;
- to reassure the public that important boundaries are not being overstepped;
- to enable those who are ethically uncomfortable with elements of this research to participate to the greatest extent possible;
- to ensure the highest quality of research and outcomes.

34. Obtaining adult stem cells requires the same conditions as those required in the case of tissue donation, based on respect for the integrity of the human body and the free and informed consent of the donor.

35. Stem cells that are retrieved from the umbilical cord blood after delivery require that the donor (the woman or the couple concerned) is informed of possible uses of the cells for this specific purpose of research and that the consent of the donor is obtained.

36. Research with aborted fetuses and pre-implantation embryos is highly controversial and may be unacceptable to several sectors of society. Thus, where the research benefits may be obtained using adult and cord blood stem cells, the use of these acceptable alternative sources is strongly recommended.

37. Research participants and researchers should be able to avoid participating in stem cell use if the cells were derived in a way they consider unethical.

38. Documentation of the original source of the stem cells should be made readily available to researchers and potential recipients of stem cell-based therapies.

39. In clinical applications of stem cell research, the possibility that potentially harmful changes, which may be deemed irreversible, should be minimized.

40. Appropriate steps must be taken to protect and preserve the identity of both the donor and the recipient in stem cell research and use.

ETHICAL GUIDELINES FOR EPIDEMIOLOGIC RESEARCH

Epidemiology is the study of the determinants of the incidence of diseases in public health. A related study, clinical epidemiology, deals with the prevention, diagnosis, risk factor analysis, causation, and treatment of diseases. Epidemiological research aims at studying determinants of health and disease in human populations in order to improve people's opportunities for making choices.

A major segment of epidemiologic research involves collection of data from individuals which may or may not require procedural interventions. Although researchers may claim that epidemiologic research such as observational studies often do not involve interventions that may cause discomfort to eligible individuals, these studies still require the individual's time and attention and may encroach on the individual's right to privacy and confidentiality. There are also social risks that need to be considered. Most people who take part in public health epidemiological research gain no personal benefit and often may not have a disease that needs treatment.

Despite not being interventional, epidemiologic research should nonetheless have social value, scientific validity, fair participant selection, favorable risk- benefit ratio, independent review, informed consent, and respect for enrolled research participants (Emanuel, Wendler et al, 2000).

Considering the nature of observational epidemiologic studies, the principles that govern consent procedures need not be as strict as those for experimental study designs. However, when the investigator proposes selective disclosure of information, the ethics committee must review the protocol and decide on its adequacy.

Ethics committees and other appropriate authorities should set the conditions for the use of genetic and other biological materials collected in epidemiologic researches.

These guidelines are for consideration of ethics committees for the protection of participants in epidemiologic research involving humans, focusing primarily on non-experimental studies. Its main difference from other researches is in the nature and extent of the informed consent process.

General Guidelines

1. All research involving human participants should be conducted in accordance with the ethical principles in the General Ethical Guidelines for Health Research (see pages 29-42).

Justice

2. Researchers should ensure that no group is inequitably burdened with risks in research.

3. Researchers shall conduct epidemiological studies with due consideration for the personal dignity and human rights of all research participants.

4. Researchers shall not conduct epidemiological studies that are not scientifically sound or ethical, and shall provide explicit, detailed research protocols that fully account for and address these issues.

5. Researchers shall conduct epidemiological studies in compliance with all appropriate laws, these Guidelines, and the approved research proposal.

6. Researchers shall not select research participants by inappropriate or arbitrary means and the methods for selection should be detailed in the protocol.

7. Researchers shall properly manage and protect the personal data of all research participants.

Specific Guidelines

8. Non-disclosure of all the study objectives may be permissible if full disclosure of the study hypothesis could bias the investigation. Only the Ethics Review Committee can make the decision for non-disclosure, though authors may request for such exemption.

9. When feasible, debriefing of research participants should be included in a study that waived full disclosure. This may be done towards the end of the study so the results may be disseminated to those involved.

10. Researchers, in principle, shall obtain written informed consent from all research participants prior to conducting any epidemiological study.

11. Investigators shall stipulate in their research proposals: a) how a study is explained to the research participants involved, b) how informed consent will be obtained from the participants, c) and any other relevant issues concerning informed consent.

12. Consent may not be required for collection of information in the public domain. Only ethics review committees can make the decision for exemption from consent, though authors may request for such exemption. Public domain information may include common general data such as address, marital status, educational attainment, number of children, among others. It should be realized that communities differ in their definition of what type of information about citizens is regarded as public.

13. Data regarding income, personal habits, preferences, personal opinions, political and religious inclinations, among others, may be considered confidential and will require consent prior to collection.

14. Collection of data by questionable means, such as deception, should not be condoned.

15. Data gathered for administrative purposes (as long as the information is not sensitive) do not require consent and may be waived if getting consent is considered impractical or too expensive.

16. Review of medical records may be done without requiring consent if anonymity can be maintained and if information sought is considered non-sensitive (Gordis & Gold, 1980).

17. The appropriate permission for storing biological material for research must be obtained from the research participants. If the samples are to be used for research not covered by the original consent, an ethics committee should decide whether renewed consent is needed or if the analyses may be done on anonymized samples. Details regarding the collection and storage of biological material are covered in the document on ethical guidelines for genetics research.

18. A person of authority may be allowed to give consent for collection of data among children and other individuals who are temporarily or permanently unable to give informed consent by themselves, provided that the research does not involve more than minimal risks to the participants.

19. If the information is obtained by means of a questionnaire, and adequate information has been given to the research participant, there is no need for a written informed consent, since answering the questionnaire implies consent.

20. There are alternative methods of obtaining informed consent (e.g., verbal consent). These are covered by the document on Ethical Guidelines for Social Research (see pages 82-87).

21. Researchers should avoid identifying individuals or groups when release of information about them can expose them to possible harm or social stigma, unless required by law. This legal requirement shall be included in the information to be disclosed when soliciting informed consent.

Privacy and Confidentiality

22. Working with personal data is a privilege that calls for a high degree of data protection, especially in situations where data are used without personal consent.

A working standard for data protection that secures as little risk of disclosure as possible should be developed.

23. Timely release of information could be essential to benefit public health such as in cases of urgent or emergency situations. The general population can benefit from information required for timely control or prevention.

24. In no case, however, that protection of privacy and respect for confidentiality be waived. Removal of identifiers or keeping to the minimum data that could identify groups should be done to avoid

labeling or stigmatizing them. In cases where populations at risk have to be advised, researchers have to ensure that risks of harm outweigh the benefits.

Information shared with Participants

25. Important findings from the research should be made available to all the participants in a suitable form.

Compensation for Participants

26. Compensation commensurate to the time given and effort exerted for participation is encouraged while taking care not to use this as undue inducement.

ETHICAL GUIDELINES FOR SOCIAL RESEARCH

Social research aims to understand social phenomenon as this occurs in the context of individuals, groups, institutions or societies. Necessarily it involves individuals, groups, or societies, and for a great part is conducted in the field. Existing theories about social phenomena influence the political or philosophical perspective of researchers.

One way of classifying social research is by methodology: quantitative social research and qualitative social research. Many social researchers combine both methods.

While most ethical concerns in social research are basically the same as in other categories of research such as clinical research, there are ethical challenges specific to social research. There are also ethical issues specific to the method used.

General Guidelines

1. All research involving human participants should be conducted in accordance with the ethical principles in the General Ethical Guidelines for Health Research (see pages 29-42).

2. The relationship between the researchers and the people they study oftentimes involves an imbalance in power in favor of the researcher. The researcher is more articulate, more knowledgeable and has greater access to resources than the people they are studying. Measures should be undertaken to clarify and balance the personal and political power of those involved. An example of these measures would be by increasing the level of participation of the people being studied in designing the study.

Justice

3. Researchers should exercise care that their research does not exacerbate existing inequities (e.g., gender-based inequities). "Sponsors of research or investigators cannot, in general, be held accountable for unjust conditions where the research is conducted, but they must refrain from practices that are likely to worsen unjust conditions or contribute to new inequities" (CIOMS, 2002, p. 10).

Informed Consent

4. See General Guidelines (see pages 29-34)

a. Disclosure of information

Researcher should provide information to the potential research participants about the research that can serve as basis for their decision to participate or not to participate.

Information to be disclosed must include the number of interview sessions and the length of time involved.

b. Consent of minors and mentally incapacitated persons

In the case of potential research participants who are minors, the consent of the parent or guardian must be obtained as well as the assent of the minor. Such assent must be properly documented and attested to by an impartial witness of legal age.

In the case of potential research participants who are elderly, demented persons, or other mentally incapacitated persons, there should be independent screening of their capacity to make decisions on their involvement in the study. See General Guidelines (see pages 29-42).

Specific Guidelines

Research involving Prohibited Activities

5. The ERC should be able to identify researches with potential legal repercussions legal risks for both or either the researcher and research participants.

6. In these cases, the ERC shall carefully weigh the risks against benefits of the study and advise the proponent accordingly.

7. A protocol for a course of action should be established in the event that a criminal act is disclosed or discovered through data collection such as interviews.

Coercion, Undue Inducement

8. There should be no coercion or undue inducement in soliciting consent.

9. In situations where certain persons such as gatekeepers (e.g., local village officials) or male spouses can be the source of coercion, researchers should find a way of ensuring that individual freedom to decide is respected.

When Consent may be Waived

10. Prior informed consent may not be obtained in archival research or in research that uses the technique of covert observation in data collection.

11. Covert observation can only be done for activities or scenes that are public in nature such that any person can observe them without violating principles of confidentiality or privacy.

12. There should be disclosure to the community during community consultations prior to data collection that observation will be done of particular public scenes during the research. If it is a requirement of the research design that the scenes and time of observation should not be divulged, the researcher should explain to the community why such prior disclosure could not be done. In no case shall the researcher collect data through covert observation if the community forbids it. There are communities (e.g., indigenous) who consider certain public activities (as defined above) to be sacred and certain behaviors of outsiders, taboo.

13. Ethics committee should exercise extra caution in allowing covert observation. The researcher should be required to do the following:

- make a thorough justification for its use;
- show a plan on how the data collected will be used;
- ensure confidentiality and anonymity.

Withholding of Information

14. Researchers should avoid deception. If deception must be used, there should be an appropriate debriefing after.

15. In exceptional cases where the withholding of information is justified by minimal risk and benefits from the research, debriefing must be performed as soon as appropriate. In no case shall withholding of information to result to irreversible harm.

Privacy and Confidentiality of Information

16. Researchers must respect research participants' right to privacy. Unless required by law, the confidentiality of information shall at all times be observed. Information that links specific individuals to specific information shall not be released. This legal requirement shall be included in the information to be disclosed when soliciting informed consent.

17. Researchers should avoid identifying individuals or groups when release of information about them can expose them to possible harm or social stigma unless required by law. This legal requirement shall be included in the information to be disclosed when soliciting informed consent.

18. Ethics Review Committees should give careful attention to the methods used for which type of data. It should advise the researcher about the risks of group methods for certain types of data.

19. It might not be possible for researchers to ensure the confidentiality of information or the anonymity of research participants in group methods such as focus groups.

20. Ethics committee should also carefully examine the instruments for group methods such as the group discussion guide to ensure that there is no disclosure of information that could cause harm when confidentiality or anonymity is breached.

Data Protection Plan

21. The researcher should be required to describe his/her data protection plan. For example, the researcher should provide adequate and clear instructions to transcribers of audio recordings or translators of transcriptions. This is to ensure that they are aware and able to protect confidentiality of data and privacy of research participants.

Avoidance of Harm

22. Researchers must ensure that risks of harm to the research participants in their study are minimized.

23. When the research causes psychological stress to the research participants, there shall be provision of care or counseling.

24. Researcher should show how social stigma can be minimized if it is a risk. The description of the steps to be undertaken should be specific, and not only general statements on keeping records confidential.

25. Ethics committee should look for evidence of competence of the researcher to undertake the study (e.g., training or track record in the use of the specific method and on the subject matter). Competence here should include cultural and intellectual sensitivity to the ethical issues involved.

26. In case unforeseen situations arise during the study that requires its temporary or permanent cessation, researchers should stop the conduct of the study completely or resume it when the risk of harm is at a reasonable level. Researchers should undertake appropriate measures to prepare the research participants or community for exit of the study.

27. The ERC should be informed as soon as possible of any serious adverse events or of any increased levels of risks.

Access to Services or Benefits

28. In carrying out experimental or quasi experimental research, access to services or benefits provided to the experimental group should also be provided to the control group. If the intervention is a benefit at the same time the experimental tool, the withholding of the intervention to the control group should only be for the duration of the experiment.

29. In prevention trials or community intervention research, researchers shall maximize the use of participatory processes so that the group or community can participate in deciding on how benefits can be accessed or shared.

30. In the matter of possible commercial use of output, benefit sharing should be taken up with the participants during the solicitation of consent.

31. Ethics review committees should require researchers to include in the proposal a description of how the benefits will be shared with the study population.

32. Researchers should endeavor to inform the research participants or community they studied about their research findings. The findings should be presented in a language and style that is understandable to them (Declaration of Helsinki, 2008)

33. Ethics committees should require researchers to include in the proposal how the research findings/report will be shared with the people being studied.

Justice

34. Researchers should ensure that no group is inequitably burdened with risks in research.

ETHICAL GUIDELINES FOR THE CONDUCT OF RESEARCH ON SPECIFIC POPULATION

I. IN EMERGENCIES AND DISASTERS

These guidelines refer to population living in communities that have experienced extreme forms of stress due to emergencies, natural calamities, armed conflict, political repression, or criminal and domestic violence. The impact on these population may have lingering physical, social, and psychological consequences, including chronic poverty, deprivation of basic needs, violation of basic rights, vulnerability, and a profound sense of hopelessness and dis-empowerment.

Research involving population in emergencies and disasters must be guided by principles applicable to the practice of humanitarian assistance and work with vulnerable groups, in general. Of relevance are universal humanitarian imperatives of alleviating human suffering, preserving human dignity as well as protecting and respecting human rights regardless of race, creed, nationality or political belief. Work with research population in emergencies and disasters must place special attention on the unique needs and special concerns of victims, including their specific cultural, racial, and ethnic affiliations, so that services and opportunities are appropriate and acceptable to these individuals (where feasible and appropriate to the study question). Issues of possible repeat traumatization and potential risks (e.g., stigmatization and reprisals) for the study population should likewise be fully addressed.

These guidelines address the following issues: the potential for harm resulting from the research process and its sociopolitical implications, the potential for the exploitation of participants, conflicts of researchers' interest with that of the community being studied, the recruitment of participants and obtaining of valid informed consent, ensuring gender and cultural sensitivity, and the need for research to contribute to the healing and re-empowerment of the affected community.

General Guidelines

1. All research involving human participants should be conducted in accordance with the ethical principles in the General Ethical Guidelines for Health Research (see pages 29-42).

2. In deliberations on research involving populations in emergencies and disasters, a community representative or accepted and established advocate must be present.

3. In the course of research, professional help must be engaged to ensure that the psychosocial needs of the community are taken into account.

4. The different roles of the researchers, caregivers, and volunteer workers must always be clarified and the potential conflicts of interest identified.

5. The Ethics Review Committee must put in place a monitoring mechanism to ensure that the above guidelines are followed.

Specific Guidelines

Research Design

6. The research proposal must explain how its objectives relate to the priorities of the interests of the community.

7. The research methodology must ensure that the research process will not impede the healing or recovery of the community. It is advisable that the research contributes to the process of designing intervention programs.

8. The protocol must include provisions for withdrawal, including closure activities and a proper referral mechanism to deal with the health needs of research participants and members of the team.

9. Researchers must demonstrate familiarity with the community's situation and their cultural beliefs and practices.

- The research team must include a local community counterpart.
- The research team must describe a preliminary community mapping/scoping exercise to ensure familiarity with the situation of the community as well as identify local resources which will support the faithful implementation of the project.

- The research team must demonstrate ability to anticipate adverse reactions and facilitate appropriate interventions.

10. The researchers have the responsibility to identify the specific vulnerabilities of the research population relevant to the study and the mechanisms that are being put in place to address them.

11. Collecting personal data on traumatic experiences should not be allowed unless clearly justified in the protocol; it must be understood however that in many instances, people themselves want to talk about these as a form of therapy.

12. Group methods should be used with much caution because confidentiality and anonymity cannot be guaranteed (in all types of research), and in security sensitive situations, this takes greater importance. (For example, when recruiting Focus Group Discussion (FGD) participants, people with history of conflict should not be placed in the same FGD group.) Potential research participants must be informed that they can be identified and that their views could not be kept confidential.

Recruitment and Informed Consent

13. The researchers must consult the community and secure its permission before approaching individuals for their informed consent.

14. The research team must identify factors that serve as a barrier to the freedom of individual members of the subject population to give consent, and provide effective mechanisms to address them.

Community

15. In research involving people in emergencies or disasters, the participation of subjects is of prime importance. The highest possible degree of participation is advised. The study design should describe the involvement of the research participants in the study.

Non-disclosure of Information

16. The withholding or non-disclosure of pertinent information must be justified in the context of protecting the research participants

from specific harm or risks and must be done according to the Ethical Guidelines for Social Science Research (see pages 82-87), and with the approval of the Ethics Review Committee.

Addressing Security Risks

17. The security risks for studies on population in armed conflict situation should be clearly identified and included in the ethical considerations section, informed consent process and form, and risk-benefit assessment.

18. "Innocent" data such as family data (number of males, females in the family) could actually be highly sensitive. For example, some would not give information on number of males for fear that they can be forcibly recruited by any of the combatant groups.

19. Keeping data secure is top most priority. (An example of a risk of harm that could arise from insecure data is information about an arriving delivery of supplies that could lead to an ambush of the aid convoy.)

20. A protocol should be established for a course of action in the event that a criminal act is disclosed or discovered through data collection such as interviews.

II. INDIGENOUS PEOPLE

There are challenges in the use of mainstream standards/guidelines when indigenous people (IP) are involved as research participants. There are problems posed by the composition, standards, and procedures of ethics review committees where IP ethics is not represented because there may be IP norms and practices that could be inconsistent with existing research ethics guidelines.

General Guidelines

1. In deliberations on research involving special populations by any oversight body, the following considerations must be included:

a. Presence of a community advocate or representative

b. Psychosocial and cultural needs of the community

c. Identification of the different roles of various stakeholders such as the sponsors, researchers, caregivers, and volunteer workers must always be clarified and the potential conflicts of interest identified.

d. Assessment of compliance with existing national and local regulations and international guidelines relevant to the protection of rights of IP populations and a monitoring mechanism to ensure that the guidelines are followed; regulations and guidelines include the:

- Indigenous Peoples' Rights Act (IPRA) of 1997
- Council for International Organization of the Medical Sciences (CIOMS) International Ethical Guidelines for Biomedical Research and International Ethical Guidelines for Epidemiological Studies
- United Nations Declaration on the Rights of Indigenous Peoples (UNDRIP)
- Convention on Biological Diversity (CBD)

Specific Guidelines

Informed Consent

2. Research involving IP populations must maintain compliance with standard elements of free and prior informed consent such as competence, disclosure, comprehension of information disclosed, voluntariness, signification of consent (in the form of assent, signature, etc.), but must include special considerations for IP values and concepts, especially alternative decision-making processes, which may involve two interrelated processes here: community approval for the study to proceed on one hand, and individual consent to participate on the other hand. The first may be required by IP communities for the second to proceed.

3. Balance must be sought between community approval and individual informed consent so that the former does not compromise the latter. If a member of the community feels compelled to consent because the community has already approved the study, then such autonomy could be seen as compromised. However, if community approval was arrived at after several community meetings, discussions, consensus taking, where members freely participated, community approval could be seen as the representation of the members' decision. In this case, the group's decision strengthens individual decision rather than violates individual autonomy.

4. Community consultations are required for approval to conduct the study prior to approaching individual members for consent. Community consultations will provide the opportunity to the researcher to learn culturally appropriate ways of soliciting individual consent and at the same time to explain the rationale for individual consent. This may require iteration of the informed consent process to truly reflect community consultation, which the research budget should allow.

5. Other documents may be considered in lieu of the standard informed consent form (e.g. IPRA requirement of a MOA)

Competence of Researcher

6. The researcher must be familiar with the culture and preferably with the language of the particular indigenous people being studied. This competence should enable the researcher to approach the community, seek informed consent, develop a culturally-sensitive research design and conduct a study that does not violate their tradition while respecting individual autonomy.

7. Competence of researchers to conduct the study should be assessed as part of ethics review process. The researcher may be requested to appear before the ERC that is processing the application for ethical clearance and manifest required competence.

Respect for traditions

8. The researcher must demonstrate knowledge and appreciation of community traditions through the inclusion of an appropriate social preparation phase of the study.

9. The researcher should acknowledge and maintain respect for elders, which is a highly valued tradition in indigenous communities. This is part of the rationale why members would not participate in a study without the elders giving approval for the study to commence. Ignoring or bypassing the elders is seen as disrespect for their tradition. (See informed consent above)

10. The researcher should respect sacred places and rituals, including request of communities to conduct rituals as part of the community's decision making whether or not to allow the study.

11. The research design should not violate traditional practices. Methods like field observation could potentially trespass certain sacred places or taboos. Researchers should use alternative methods, and if there is none, to explain why field observation must be done and how the benefit outweighs the risk of harm that these methods could create.

Addressing vulnerability, risks, and safety

12. Risks and harms to normal populations should be included in the risk- benefit assessment.

13. IPs in the Philippines are generally vulnerable, therefore special attention should be given to their vulnerability. It is essential that procedures for informed consent taking and benefit sharing arrangements take into account this vulnerability.

14. Care should be exercised in disseminating information that could be used by vested interests in exploiting IP resources or violating their traditions. The IP community should consent to the dissemination plan and the information to be disseminated.

15. Risks to biodiversity must be examined, specifically whether the study poses risks of destruction of the biodiversity or alteration of the ecology in IP land.

16. The study should also take into consideration requirements for the protection of biodiversity already contained in the Ethical Guidelines for Natural Products and Herbal Medicine Research as well as other pertinent legislation.

Benefit sharing and ownership

17. The research plan should include explicit description of access and benefit sharing (ABS) and describe how the researcher will ensure that the community will have access to or get a fair share in whatever benefits will accrue from the study.

18. Information about ABS should be disclosed during the solicitation of individual consent and community consultations.

19. ABS agreements should be formalized as stipulations in a contract or memoranda of agreement between the IP community and other parties.

20. Researches must comply with Philippine laws on the transport and protection of indigenous materials.

21. In case communities or parties other than the study community make an ownership claim on the knowledge (and on the benefits), the researcher should undertake separate consultations and negotiations with these parties/communities.

22. Sponsors of the research should comply with all ABS agreements, and this compliance should be made part of the investigator's stakeholder responsibility. Additionally, the investigator should provide the community with the names and contact details of groups or institutions or individuals who can assist them in ensuring their rights in the agreement.

23. Dissemination and communication plans of the research should include a protocol for informing the community about the findings or outcomes of the study. A non-technical summary of the research findings, written in their language, should be provided to the community at the end of the study.

24. Community ownership of traditional knowledge should be acknowledged in any report in any medium.

Expertise of Ethics Committee

25. An ethics review committee (ERC) that processes the ethical clearance of research involving IPs must have adequate understanding of the application of the instruments cited in the

General Section of this guideline (see 2.d above). If necessary, the ERC should invite an expert to assist in the review of the study.

26. Expertise of the ERC could include articulate and empowered community representatives who genuinely embody the interest of the indigenous peoples to be studied. Empowerment of the representative is key because without it, the expert could be awed and inhibited in the presence of professionals in the ERC.

27. If an indigenous expert is available, there should be a preference for this person to inform the decision of the ERC, in which case, the ERC should consider using language that is familiar to the indigenous expert during its deliberations.

III. PEDIATRIC POPULATION (MINORS/CHILDREN) INCLUDING GUIDELINES ON ASSENT

Minors are considered a vulnerable population when it comes to research. The term "minor" is often interchanged with "child" or "pediatric" when in fact there are some nuances to these terms, namely:

- "Children" are persons who have not reached the legal age of 18 years and therefore cannot enter into contracts.
- "Minors" are persons under 18 years of age and the term is used interchangeably with the term "children." In some laws, "minors" include those who have reached the age of majority but are incapable of caring for themselves due to mental or physical infirmities.
- "Pediatric" as referred to by the Philippine Pediatric Society follows the WHO definition of a person below 18 years and 364 days (which is just a day before the age of 19).

Republic Act No. 6809 places the age of majority at 18 yrs of age at which time the person is emancipated from parental authority and is considered "qualified and responsible for all acts of civil life" and can thus enter into contracts.

A vital requirement in pediatric research that will involve individuals below 18 years old is the "assent" of the participant to be recruited to the research study. The assent shall be made expressly but may be in

the oral or written form. This section will touch on prevailing as well as recommended guidelines on assent for pediatric research in the Philippines.

General Guidelines

1. Research involving children should follow the general guidelines for research (see pages 29-42). In addition, general principles provided in international guidelines (Guideline 14 — CIOMS, 2002) should be followed.

2. The research cannot be carried equally well in adults. Examples include research on pediatric cancer, systemic lupus erythematosus, adolescent depression, childhood abuse, Down's syndrome, among others, where research on adults who had these illnesses in their childhood, will not elicit accurate results;

3. The purpose of the research is to obtain knowledge relevant to the health needs of children.

4. A parent or legal representative of each child has given permission. In default of parents or judicially declared guardians, this order of authority shall be followed:

- grandparents;
- oldest sibling over 21 years of age, unless unfit or disqualified;
- actual custodian over 21 years of age, unless unfit or disqualified.

5. Where the parents are both of minor age or themselves incapacitated to enter contracts giving consent to their children's participation in research, the guidelines on medical treatment of such children may be followed, where the parents as well as a legally capacitated third party both give consent (e.g.. the child's grandparents, physician, or the hospital administrator, as in emergency cases).

6. The child gives expressed assent to the participation in the research study in oral or written form.

7. The child's assent to participate in the study which he/she gives to the extent of his/her capabilities should be obtained without coercion.

8. A child's refusal to participate or continue in the research is respected.

Specific Guidelines

Assent

9. If the child is 7 to 12 years old a verbal assent is acceptable. At 12-15 years old, he/she will sign a simplified Assent Form different from the Informed Consent Form which the parents or guardians sign. The Assent Form should have been reviewed and approved by the ERC. The decision to have an Assent Form for participants below 13 years old rests on the ERC.

10. If the child is at least 15 years old, he/she can sign on the same informed consent document signed by the parents.

11. If the child is less than 7 years old, no assent is needed but a sign of dissent on the part of the child must be respected and documented.

12. At any age, any sign of dissent must be observed, and such children who dissent must not be recruited to the study except when they will directly benefit from the research, and the parents consent.

13. Information on the study to which the child's participation is sought and terms such as "research," "study design," "procedures," "adverse effect," "voluntary" should be explained in a manner and language the child understands for purposes of assent and dissent.

Determining the Age of the Child

14. The age of the child must be determined by documentary evidence as follows:

- child's birth certificate;
- child's baptismal certificate;
- any other pertinent documents such as, but not limited to, the child's school records, dental records, or travel papers.

15. In the absence thereof, competent testimonial evidence may be used.

16. In case of doubt as to the age of the child, after all measures are exhausted to determine it, the age shall be resolved in his/her favor.

17. All these presuppose that the child is mentally and physically capable of understanding what he/she is getting into. However, a competency examination of a child, motu proprio or by request of a party should be conducted, when there exists substantial doubt regarding the ability of the child to understand the nature and consequences of giving assent.

18. The protocol must include the procedure for obtaining the assent.

IV. OLDER PERSONS

The Philippines needs to prepare for the burgeoning population of older persons. The population 60 years and above has grown at a very rapid rate, increasing from 2.4 million in 1980 to 5.4 million in 2007 comprising 6.2 percent of the population. The older population is projected to increase rapidly in the future. By the year 2025, 10 percent of our population will be composed of senior citizens, at which time the country will be considered an aging society by UN definition (assuming that the medium-term assumptions of the Philippine population projections will hold true). However, there is inadequate representation of older persons in most researches including, but not limited to, biomedical, clinical, socio-psychological, and epidemiological. It is therefore appropriate to recommend the inclusion of older persons – 60 years and older, frail, ambulatory, homebound, and institutionalized – in these researches.

Ethical challenges in researches on older persons include the following:

- Variability of health status and functional capacity between the young old (60—69 years) to middle old (70—79 years), to the oldest old (80 years and above). This implies that researchers will need to design

protocols to take into consideration such variability and disaggregate data during the stage of data analysis. Also, with regard to drug trials, the presence of multiple chronic diseases and Polypharmacy (intake of five or more drugs) need to be considered as potential sources of drug-disease, drug-drug, and drug-patient interactions, leading to adverse drug events.

- Physical and sensorial disabilities such as blindness, deafness and mobility problems may inappropriately exclude such persons from needed participation in research.

- Neurological and psychiatric illnesses that affect mood, movement and cognition are accompanied by challenges in obtaining informed consent.

- Patients' expectations regarding participation in research, among persons with chronic, debilitating and incurable diseases may be unrealistic such that the research activities may be regarded as bringing cure rather than alleviation or stabilization of disease or disability.

- An increasing number of older persons living in long-term care institutions or home-bound may be inadvertently excluded from participating in researches, leading to recruitment bias.

- Socio-economic demographic characteristics may render the older persons more vulnerable and may affect their participation in research.

General Guidelines

1. Older persons with different health and functional status, including those who are terminally ill, regardless of venue of care, who will potentially benefit from the knowledge generated should be represented in such researches.

2. Researchers need to determine the capacity and competency of the patient to consent and participate in the study.

3. Researchers need to determine the best way by which consent will be obtained and continuing participation be ensured from a person who has difficulty with written or oral communication, mobility,

cognition, and emotion.

4. Researchers must be careful to clarify the purpose of the study in order to address participants' desires for therapeutic outcome, social contact, or practical help.

Specific Guidelines

Informed Consent

5. Researchers must be on the look-out for cognitive, psychiatric, and functional problems common among older persons that may affect their capacity to give informed consent. These should not necessarily exclude them from participation in the research.

6. The standard guidelines on informed consent must be followed (see pages 29-34).

7. In the event that capacity for an informed consent is doubtful, a cognitive assessment should be done. There are several tools that may be used to determine decisional capacity. To assess cognition, the ADAP (Alzheimer's Disease Association of the Philippines) recommends the use of Folstein's MMSE (score of 27/30 and higher) and the clock drawing test (score 4/4). To assess functional capacity, ADAP recommends Adapted-Functional Activities Questionnaire (A-FAQ). The researcher may also use the following guide to determine competency:

- LS1: the patient knows that he/she is faced with a choice;
- LS2: the patient has the capacity to make a reasonable choice comparable to that of a normal person;
- LS3: the patient is aware of the emotional consequences of his/her positive or negative choice;
- LS4: the patient is able to provide reasons for his/her choice;
- LS5: the patient has the capacity to understand the meaning of the information and the treatment situation.

No single tool is sufficient in determining ability to consent. The investigator's clinical judgement based on history and assessment is of utmost importance.

8. In the absence of capacity or competency to provide informed

consent, surrogate decision makers may provide consent in behalf of the research participant using the substituted judgment or best interest standard. Persons with movement disorders such as Parkinson's disease or stroke may give their consent through a thumb mark rather than a signature.

Design of Research

9. It is recommended that the study design consider representing the various subgroups such as age, gender, socio-economic, and functional status.

10. A thorough list of chronic diseases, prescription drugs, over the counter drugs, and supplements will help determine potential for adverse drug events. This is especially relevant in clinical trials.

11. The protocol should include safeguards that are proportionate to the impairment and experimental risk/benefit.

Conduct of the Research

12. Involve surrogate decision makers and primary caregivers in all phases of the research. This may mean regular, weekly communication between the study staff and the primary caregiver.

13. The research participant has the right to withdraw from the study at any time during the conduct of the study. The surrogate decision maker and/or researcher must be sensitive to signs of dissent from the research participant especially those with communication problems.

14. The investigator must ensure that the study compensation will directly benefit the research participants.

Dissemination of Research Output

15. The investigator must ensure that the research participants (with special attention to those who are institutionalized, homebound or those who have communication and mobility problems) are informed of the result of the study.

16. It must be in the form that is easily understandable to the participant.

ETHICAL GUIDELINES FOR HIV AND AIDS RESEARCH

HIV and AIDS research encompasses a wide range of health research that includes basic research on the infectious agent and its effect on individuals, clinical trials on vaccines and other therapeutic protocols, and investigations on the psychosociocultural aspect of HIV and AIDS. The basic principles of research ethics shall, therefore, apply in all these activities as they apply to other health research activities. However, institutional research ethics committees, researchers, and funding agencies should pay special attention to the issues of justice and respect for groups and individuals affected by HIV and AIDS as their condition gives them distinct vulnerabilities because of the cultural sensitivity of reproductive health issues.

For a more detailed discussion of ethical issues, the reader is referred to the Ethical Guidelines in AIDS Investigations in the Philippines published by the Philippine National AIDS Council and the AIDS Society of the Philippines, and the Philippine AIDS Prevention and Control Act of 1998.

General Guidelines

1. All research involving human participants should be conducted in accordance with the ethical principles in the General Ethical Guidelines for Health Research on pages 29-42 and must be cognizant of the Guidelines on the Research Ethics Review Process on pages 110-119.

Specific Guidelines

Identification Consent

2. The recruitment process should be sensitive to the social implications of being identified as a potential HIV and AIDS case or of belonging to a high-risk group. Specific mechanisms to protect the privacy of individuals should be described and put in place.

3. Special attention should be given to the possible sensitive nature of the information to be extracted from the research participants and, if applicable, the necessity of undergoing an HIV test. It is also important to determine the participant's willingness to be informed of the test result, the test's reportability, and the implication on his/her sexual activities if found positive. The research participant must

also be informed that he/she is free to withdraw from the study anytime.

Pre- and Post-test Counseling

4. Pre- and post-test counseling by well-trained, culture- and gender-sensitive research personnel should be put in place as part of the research protocol.

Standard of Care

5. In an interventional study, the control group should receive the standard of care accepted by the larger community. It is unethical to subject the control group of affected individuals to placebo treatment or be withdrawn from the current mode of treatment before the start of the study.

Research Benefits

6. Special effort should be exerted to make the beneficial findings of the research project accessible and available to participants under reasonable circumstances.

Use of Research Data

7. Special care shall be applied in the public use of research data and the publication of reports so that participant groups are not further stigmatized or become targets of blame. Reports shall be carefully examined for gender and culture bias.

ETHICAL GUIDELINES FOR INTERNATIONAL COLLABORATIVE RESEARCHES

Some major ethical issues on research involving developing countries have constantly been raised. Some of these controversies focus on the following:

- the standard of care that should be used in research in developing countries;
- the "reasonable availability" of interventions that are proven to be useful during the course of research trials;
- the quality of the informed consent.

The persistence of these issues have been partly because of the different interpretations of existing ethical guidelines as well as the varied perspectives and thinking of sponsors, funders and collaborators from developed and developing economies.

However, North-South research collaboration is currently plagued by differing interpretations of ethical standards of doing research in developing countries. Should new treatments be compared against Western standards of care or against local existing standards? Can communities benefit from research they have taken part in when they may not be able to afford the new interventions they have helped prove efficacious? How can researchers and institutions in developing countries be strengthened through international collaboration (Lansang and Crawley, 2000)?

One other major issue is that of inequitable funding – only 10 percent of global research funding goes to diseases, which make up 90 percent of the global burden. For this, three guideposts, Think action–Think local–Think long term, can be used (Torres-Edejer, 1999).

Scientific advances are not the only yardstick to measure success of North-South research collaboration: the choice of identified priorities as areas of work, the sustainability of the studied interventions outside the research setting, and the investment in local research capacity are becoming equally important as indicators of success (Torres-Edejer, 1999).

Although most of the ethical research issues center on North-South collaboration, there is also a growing interest and emphasis on South-South or intra-regional research collaborations. For example, based on a recent survey on the Association of South East Asian Nations (ASEAN) research initiatives and health technology researches done by the ASEAN Network for

Drugs, Diagnostics and Vaccine Innovation (ASEAN-NDI), most of the South-South regional research collaborations in the ASEAN region focus on just a few countries such as Singapore, Thailand and Malaysia, with the other ASEAN member countries lagging behind. This means that the "North" role of the partnership is being borne only by these aforementioned countries. This may result in an inequitable prioritization of researches skewed in favor of these countries. Although the running motto of the ASEAN as it moves towards regional harmonization and integration is – "ASEAN Help ASEAN", there is a need to be more conscious of potential ethical issues arising from intra-regional partnerships similar to issues arising from North-South research collaboration.

In order to support health research in developing countries that is both relevant and meaningful, the focus must be on developing health research that promotes health equity and developing local capacity in bioethics (Bhutta, 2000), whether they are North-South or South-South research collaborations.

There are 11 Research Partnership Principles proposed by the KFPE (Commission for Research Partnerships with Developing Countries) in 2010 that are widely used and recommended by many research programs. These were just recently updated to include the following:

1. set agenda together
2. be accountable
3. create transparency
4. clarify responsibilities
5. promote mutual learning
6. enhance capacities
7. share data and networks
8. disseminate results
9. pool profit and merits
10. apply results
11. secure outcomes

The aforementioned steps are all part of a framework for ethical research that includes eight principles and 31 benchmarks that systematically specify practical measures to determine the extent to which the research satisfies the principles (KFPE, 1998; 2010) (see Table 1).

Table 1: Ethical principles and benchmarks for multinational clinical research

Principles	Benchmarks
Collaborative partnership	• Develop partnerships with researchers, makers of health policies, and the community. • Involve partners in sharing responsibilities for determining the importance of health problem, assessing the value of research, planning, conducting, and overseeing research, and integrating research into the healthcare system. • Respect the community's values, culture, traditions, and social practices. • Develop the capacity for researchers, makers of health policies, and the community to become full and equal partner in the research enterprise. • Ensure that recruited participants and communities receive benefits from the conduct and results of research. • Share fairly financial and other rewards of the research.
Social value	• Specify the beneficiaries of the research (who). • Access the importance of the health problems being investigated and the prospective value of the research for each of the beneficiaries (what). • Enhance the value of the research for each of the beneficiaries through dissemination of knowledge, product development, long-term research collaboration, and/or health system improvements. • Prevent supplanting the extant health system infrastructure and services.

Scientific validity	• Ensure that the scientific design of the research realizes social value for the primary beneficiaries of the research. • Ensure that the scientific design realizes the scientific objectives while guaranteeing research participants the healthcare interventions to which they are entitled. • Ensure that the research study is feasible within the social, political, and cultural context or with sustainable improvements in the local health-care and physical infrastructure.
Fair selection of study population	• Select the study population to ensure scientific validity of the research. • Select the study population to minimize the risks of the research and enhance other principles, especially collaborative partnership and social value. • Identify and protect vulnerable populations.
Favorable risk-benefit ratio	• Assess the potential risks and benefits of the research to the study population in the context of its health risks. • Assess the risk-benefit ratio by comparing the net risks of the research project with the potential benefits derived from collaborative partnership, social value, and respect for study populations.
Independent review	• Ensure public accountability through reviews mandated by laws and regulations. • Ensure public accountability through transparency and reviews by other international and non-governmental bodies, as appropriate. • Ensure independence and competence of the reviews

Informed consent	• Involve the community in establishing recruitment procedures and incentives. • Disclose information in culturally and linguistically appropriate formats. • Implement supplementary community and familial consent procedures where culturally appropriate. • Obtain consent in culturally and linguistically appropriate formats. • Ensure the freedom to refuse or withdraw.
Respect for recruited participants and study communities	• Develop and implement procedures to protect the confidentiality of recruited and enrolled participants. • Ensure that participants know they can withdraw without penalty. • Provide enrolled participants with information that arises in the course of the research study. • Monitor and develop interventions for medical conditions, including research-related injuries, for enrolled participants at least good as existing local norms. • Inform participants and the study community of the results of the research.

This framework of principles and benchmarks is complex, because ethical evaluation of clinical research is complex. A single ethical principle is rarely absolute; most situations implicate multiple principles (KFPE, 1998; 2010). Consequently, the various principles and benchmarks will compete and must be balanced against each other – a process that inevitably requires judgment (KFPE, 1998; 2010).

This framework can probably be applied to all research, regardless of setting or sponsorship. Importantly, differences in health, economic, social, and cultural aspects of a research setting will affect application of the framework – specifically how much weight or priority is given to different benchmarks. Depending on a study's objectives and context, particular benchmarks will be given greater weight than others. Such balancing is inevitable whenever there are multiple ethical considerations (KFPE, 1998; 2010).

THE RESEARCH ETHICS REVIEW PROCESS

The Ethics Review Committee is the independent committee which reviews and approves proposals for the ethical conduct of health research involving human participants. The research proposal shall be clearly formulated in a protocol to be submitted to the ERC for approval before study implementation.

Since quality of the ethics review is an important concern, the ERC shall have a manual of standard operating procedures (SOPs) which should clearly describe all areas of its work. For the initial and continuing review of protocols, the ERC should indicate a reasonable time frame in their SOPs for completing the review process and provide the proponent a written, signed and dated feedback on its review, preferably within two to four weeks after receipt of the submitted documents. The review must be efficient, transparent, and timely.

1. Required documents for ERC review of an initial protocol submission

1.1. The principal investigator shall be required to submit to the ERC the following documents before ERC reviews his/her research proposal:

a. Application for review – this is a request letter addressed to the ERC. This may be a form letter or part of a registration form as described in the ERC's SOP;
b. Results of technical/ethical review from other ERCs (if applicable);
c. Research protocol - The protocol must include the title, significance of the study, literature review, objectives of the study, methodology and procedures, description of the study population, exclusion/inclusion criteria, ethical considerations, data analysis.

The Section on Ethical Considerations should state what relevant international and national guidelines will be used as reference in the study and include ethical issues like anticipated risks (how these will be minimized) and potential benefits; protection of confidentiality of data and privacy of the research participants; vulnerability of research participants; management of adverse events; and how informed consent will be obtained.

d. Informed consent/assent documents (see guideline on Informed Consent on pages 29-34, Research among Children on pages 96-99; and Appendix A on sample of ICD/assent forms). The informed consent/assent documents must be both in English and in a language appropriate to the level of understanding of the research participant (see General Ethical Guidelines, pages 29-42). A sample template of statements to be written in an ICF is found in Appendix A1.

e. Study tools (questionnaires, case report form, posters/ advertisements for recruitment, etc.);

f. Study drug/medical device information like investigator brochures/ published literature/ medical device manufacturer's design, if relevant;

g. Curriculum vitae of principal investigators and co-investigators, which will also include relevant training and proof of their GCP training (in case of a clinical drug trial).

h. Information regarding funding, sponsors, institutional affiliations, other potential conflicts of interest;

i. Contracts and approval of relevant offices (Memorandum of Agreement (MOA) if study is collaborative in nature; Materials Transfer Agreement (MTA), Intellectual Property approval, Investigational Device Exemption (IDE), when relevant;

j. Study/protocol budget.

1.2. The principal investigator shall submit to ERC the number of copies of the protocol package that is required by ERC for its review.

2. Initial review procedure

2.1. After receipt of the application form and protocol package, the ERC office should check the submitted documents for completeness. The submitted protocol should be officially recorded in a log book or an electronic database – date of submission, protocol title, principal investigator, sponsor, among others.

2.2. The ERC Chair or his/her representative shall determine the kind of review that will be done – full board review or expedited. The Chair should assign the reviewers for either type according to the SOP. The protocol package is then distributed to assigned reviewers. Assessment checklists for technical and ethical review of a protocol can be prepared by the ERC to guide reviewers.

a. Full Board Review – the SOP shall describe whether the protocol will be initially reviewed by all ERC members or only by two or three primary reviewers (to include a scientific and non-scientific or lay member) before the ERC meeting. After the initial review of the protocol, it is discussed fully during the ERC meeting before final action on the protocol is decided.

b. Expedited review can be done by the ERC for protocols that do not to need a full board review such as those involving:

- chart review
- survey of non-confidential nature
- review of laboratory/pathology samples or stored tissues where patients are not identified and not genetic in nature
- collection of small blood samples

Expedited review refers to the number of ERC members doing the actual review rather than the length of time it requires.

The ERC Chair can assign two to three reviewers (which may include the Chair) to the expedited review and if they approve the protocol, the result of the expedited review can just be reported during the ERC meeting. If modifications are required, it is communicated to the investigator and when the revised protocol is re-submitted, the same reviewers will again review the protocol. If reviewers cannot decide on the protocol or if a full board review is deemed necessary, they shall recommend to the ERC Chair a full board review.

Amendments, protocol revisions and informed consent changes can be subjected to expedited review. Re-submitted protocols which have addressed modifications required by ERC may also be done through expedited review.

After the protocol is approved in the expedited review, the ERC Chair will communicate this to the principal investigator even before the regular ERC meeting.

3. Protocol review

3.1. The reviewers should assess the protocol based on the criteria set by the ERC to include:

a. review of technical issues (including relevant policy issues and study tools to be used in the study and the technical review made by technical reviewers);

b. review of ethical issues (vulnerability of research participants, confidentiality, conflict of interest, qualification of proponent, use of placebo if relevant, etc.);

c. review of the informed consent documents. An ICD assessment checklist is highly recommended. Comments of the reviewer should be duly written, not only a ticking off on the list;

d. a determination of the risk and benefit ratio or degree of risk (minimal, moderate or high).

4. Preparation for ERC meeting

4.1. The ERC Chair should schedule the deliberation of the reviewed protocols in the next regular ERC meeting, reasonably within four weeks after the submission of the protocol package (SOP on ERC meetings).

4.2. The agenda for the ERC meeting will include the titles of protocols for full board review, reports on expedited reviews, re-submitted protocols, progress reports, final reports, serious adverse events (SAE) reports and other matters.

The agenda and the protocols to be discussed in the ERC meeting should be sent to the ERC members at a reasonable time for their study and preparation for the meeting. If there are only two or three primary reviewers assigned to review the whole protocol, abstracts

of the protocols in the agenda should be sent to other ERC members before the meeting.

5. Meeting proper

5.1. Before each ERC meeting, the presence of a quorum must be declared by the presiding person (usually the ERC Chair). The rule on quorum is set in the SOP and shall not only specify numbers but also require a balanced composition (scientific member, non-scientific member and a lay person should be present). Equally important is the determination and resolution of any conflict of interest before proceeding to deliberate on each protocol.

5.2. Usually, the ERC Chair will assign the primary reviewer to present a brief summary of the protocol and their review findings or assessment of the technical and ethical issues during the ERC meeting. The second reviewer (usually the lay or non-scientific member) will make additional comments especially on the informed consent document. Their presentation is followed by a discussion and comments by the other ERC members.

5.3. The ERC shall assess the protocol based on the set criteria and will be similar to the order of the individual review process (see Item No. 3). A decision by consensus is made by the ERC after each issue (approved, needs clarification/modification, revise, etc.).

5.4. The Presider/Chair summarizes the board decision on the protocol. It is advised that ERC decide by consensus, rather than by voting.

5.5. All deliberations including dissenting opinions are documented by the ERC secretary and must be reflected in the minutes of the ERC meeting which should be subsequently approved and signed by the Chair before it is filed.

6. Clarifications during review of protocol at ERC meeting

6.1. The principal investigator or sponsor can be invited to present their proposal or to clarify or explain where there are questions posed by the reviewers.

6.2. Independent consultants and technical reviewers may be asked to provide their expert opinion on the protocol.

6.3. The invited principal investigator, independent consultants or technical reviewers should be present only at the time that the protocol is for deliberation at the ERC meeting. A confidentiality agreement is signed by each non-ERC member guest before the meeting.

6.4. Guests cannot join in decision-making by the ERC and must leave the room when a decision is to be made regarding the protocol.

7. Action on proposals

7.1. The ERC should inform the investigator/proponent in writing of its action within two weeks after the ERC meeting. The ERC should include in its letter to the investigator: a) title of the proposal reviewed (revision/amendment, date, version number); b) name and title of applicant; c) documents reviewed; d) date and place of ERC meeting when decision was made; e) effectivity/time period of the ERC approval; and f) the name of the ERC making the decision.

7.2. The action of the ERC may be one of the following:

a. Approval

In case of approval, the ERC should inform the investigator, in writing, of the ERC's requirements for approved researches that must be complied with during the conduct of the research. These include the following:

- report of serious and/or unexpected adverse event(s) (SAEs, suspected unexpected serious adverse reactions (SUSARs)) related to the conduct of the research within a timeframe required by the ERC (hours/days after occurrence as stated in SOP);
- report of SAEs from other study sites or centers;
- in case of SAEs and SUSARs, a justification for why the research should continue;.

- any changes, deviations or amendments to the approved protocol and informed consent document. These shall need another review and approval by the ERC;
- progress report at least once a year or as requested by the ERC;
- notice of termination of the research before its anticipated completion date, and the reason for it;
- preparation for a possible site visit by ERC.

b. Modifications Required Prior to Approval

In case modifications are required, the ERC should clearly describe what revisions/changes are required or areas for improvement.

c. Disapproval

In case of disapproval, the ERC should clearly state its objections and the reason(s) for disapproval.

8. Appeal for reconsideration

8.1. In case of an unfavorable decision, the investigator may make oral or written representation to the ERC for reconsideration.

9. Withdrawal of prior approval

9.1. Prior approval may be withdrawn for the following reasons:

a. undue or significant number of serious adverse events directly or indirectly attributed to the research;

b. breach of previously agreed upon conduct of the research;

c. upon the recommendation of sponsor or other stakeholders but in consultation with the principal investigator.

10. Continuing review of the protocol

10.1. As part of its function, the ERC must monitor and continuously review a protocol that it has approved. The process includes review of amendments, revisions, and approval of such before implementation. The process also includes review and approval of reports (progress, termination, end of study, final reports, publications). The process of continuing review may be expedited or may need a full board review and decision.

10.2. All continuing reviews are reported (if approved through an expedited process) or put on the ERC meeting agenda for review and approval if full board decision is needed.

11. Site monitoring visit

11.1. The ERC or designated representative may also do onsite visit or audit on studies that it has approved. This may be done where there is significant number of serious adverse events, new study sites, non-compliance or suspicious conduct, failure to submit required reports, among others.

a. ERC should inform the investigators of the visit at a date agreeable to both.

b. The ERC should review the informed consent to see if an updated version is being used, examine study files, observe the informed consent process if possible, inspect the study site, and interview participants.

c. After the site visit, a report is given to the principal investigator and to ERC.

d. ERC may recommend corrective actions for observations made.

12. Review of SAE and SUSAR

12.1. The ERC should have SAE/SUSAR report forms available which may be used for reporting by the investigators. It will include determination of the causality of the SAE/SUSAR and relationship

to the study drug, health product or device used in the research. If deemed trial-related, the ERC shall determine what action to take. A log book for SAEs at the local study site should be kept by the ERC.

12.2. Both local and international SAE reports shall be evaluated by the ERC.

13. Premature termination / suspension of study (ICH-GCP, 1996)

13.1. If the trial is prematurely terminated or suspended for any reason, the principal investigator should promptly inform the ERC how this will be managed and ensure appropriate therapy and follow-up of participants. The principal investigator should submit a written detailed explanation of the termination or suspension.

14. Completion of the research

14.1. Upon completion of the report, the investigator should inform the ERC in writing that the study has been completed and shall furnish the ERC a copy of the final report. This should be duly reported during the subsequent ERC meeting.

15. Documentation and archiving

15.1. All documentation and communication of the ERC should be dated, filed and archived according to written procedures (WHO, 2000).

a. Agenda and minutes of ERC meetings should have templates to facilitate their preparation and filing.

b. Protocol study files should be separated into: 1) Protocols awaiting approval; 2) Ongoing approved studies; and 3) Completed or archived study files.

- The study files should include protocol and current version, ICD, amendments, all communications regarding application, decision, follow-up, SAE reports, continuing progress reports.
- Completed study files include all of the above and the final report. They are usually archived for a minimum of three years.

- Active and completed studies should be separately filed in a secure place.

c. ERC Standard Operating Procedures

d. International, national and local guidelines

e. Annual ERC reports

f. Curriculum vitae of ERC members including initial and continuing training in ethics review, GCP, among others, which should be updated, signed and dated.

g. Record of income and expenses of the ERC

h. Log books and electronic database to facilitate checking and follow-up of approved protocols

i. Log book for inquiries and complaints (dated) especially from study participants with their contact numbers

j. Log book for SAEs from local study site. Files of reports of SAEs from international sites are kept in another file.

k. Flow charts of ERC procedures should be clearly visible to guests.

l. Templates of various forms to be used in ethics review available electronically or in print.

GUIDELINES ON AUTHORSHIP AND PUBLICATION

The publication of research results gives rise to ethical problems and controversies when there are ambiguities regarding responsibility for various aspects of the research and the resulting publication. In order to provide guidance, the PHREB endorses the guidelines issued by the International Committee of Medical Journal Editors-Uniform Requirements for Manuscripts Submitted to Biomedical Journals: Ethical Considerations in the Conduct and Reporting of Research, Authorship and Contributorship (see http://www.icmje.org/ethical_1author.html).

Authorship and Publication

1. All qualified authors must be given due recognition by being included in the list of authors and all persons designated as authors should qualify for authorship.

2. Each author should have participated sufficiently in the work to take public responsibility for appropriate portions of the content.

3. In order to be named as authors, contributors must have provided substantial input to the following:

    a. conception and design, acquisition of data or analysis and interpretation of data;
    b. drafting the article or revising it critically for important intellectual content;
    c. final approval of the version to be published.

4. The following should not be regarded as sufficient grounds for recognizing authorship:

    a. acquisition of funding;
    b. collection of data;
    c. general supervision.

5. The list of authors should include a guarantor (usually the lead author) who will assume responsibility for the integrity of the whole paper.

6. The authors shall obtain the informed consent of research participants as a condition for the publication of photographs or identifiable information.

7. In submitting articles for publication, the authors must provide the following to the editor:

a. the specific contribution of each author to the paper;
b. an acknowledgment of the contributions made by people other than the authors;
c. a statement that the authors complied with all Ethics Review Committee requirements, the National Ethical Guidelines for Health Research, and pertinent guidelines on the care and use of animals.

GLOSSARY

active principle or ingredient(s) – The substance(s) in a medicinal preparation that brings about the clinical effects expected; the constituent(s) in a medicinal preparation that exert an effect pharmacologically as distinct from the fillers, wetting agents and other excipients included in the preparation. Similar terms used are active pharmaceutical ingredient (API) and bulk active in medicine or active substance in pesticide formulations.

adverse drug reaction – In the pre-approval clinical experience with a new medicinal product or its new usages, particularly as the therapeutic dose(s) may not be established, all noxious and unintended responses to a medicinal product related to any dose should be considered adverse drug reactions. The phrase responses to a medicinal product means that a causal relationship between a medicinal product and an adverse event is at least a reasonable possibility, that is, the relationship cannot be ruled out. Regarding marketed medicinal products, a response to a drug which is noxious and unintended and which occurs at doses normally used in human for prophylaxis, diagnosis, or therapy of diseases or for modification of physiological function (ICH–Guideline for Good Clinical Practice (E6, R1), art. 1.1) Current reporting required by FDA is in http://umis.doh.gov.ph/ adverse. *See also adverse events, serious adverse event, unexpected adverse event and suspected unexpected serious adverse reaction.*

adverse events – Any untoward or undesirable medical occurrence in a patient or participant in clinical investigation after use or administration of an investigational product. This is not necessarily caused by the treatment. *See also adverse drug reaction, serious adverse event, unexpected adverse event and suspected unexpected serious adverse reaction.*

AIDS – Acquired Immunodeficiency Syndrome. It is the clinical manifestations in the advanced stages of HIV infection characterized by the breakdown of the immune system.

alternative medicine or alternative healthcare modalities – Other forms of non-allopathic, occasionally non-indigenous or imported healing methods, though not necessarily practiced for centuries nor handed

down from one generation to another. Some alternative healthcare modalities include reflexology, acupressure, chiropractic, nutritional therapy, and other similar methods (Traditional and Alternative Medicine Act, 1997). *See also complementary and alternative medicine.*

amendment to the protocol – A written description of a change(s) to, or formal clarification of a protocol and changes on any other supporting documentation made from the originally approved protocol by the research ethics review body after the study has began. *See protocol amendment.*

anonymized – When processing of personal data ensures that association or connection with the subject or research participant cannot be traced and determined. *See also de-identified.*

anonymized sample or data – Biological sample or data that cannot be linked to an identifiable person through destruction of that link to any identifying information about the person who provided the sample or data.

approval – Favorable or affirmative decision of the Research Ethics Committee following a review of the protocol and other required documents and thus research may already be started and undertaken as set forth by the ethics committee, CPG, the institution, and relevant regulatory terms.

archival work – Research involving the examination of records or documents.

assent – Authorization for one's own participation in research given by a minor or another participant who lacks the capability to give informed consent. The assent is a requirement for research, in addition to consent, given by a parent or legal guardian. It is an agreement by an individual not competent to give legally valid informed consent like a child or cognitively impaired person to participate in research. *See also child's assent and surrogate assent.*

assisted reproductive technology – All treatment or procedures that include the in-vitro handling of human oocytes and human sperm or embryos for the purpose of establishing a pregnancy. For example, in-vitro fertilization and transcervical embryo transfer, gamete intrafallopian transfer, zygote intrafallopian transfer, tubal embryo transfer,

gamete and embryo cryopreservation, oocyte and embryo donation, gestational surrogacy.

autonomy – The right or power or ability or capacity to govern oneself or make an informed or uncoerced decision. *See also collective autonomy and shared autonomy.*

behavioral genetics – The study of genes that determine behavioral traits and phenotypes or study of whether and how behavior traits are inherited.

behavioral research – Studies that apply social and behavioral theories and principles to understand the actions or reactions of persons in response to external or internal stimuli or to an intervention. In health and medicine, it includes studies on basic biobehavioral mechanisms and social processes that are relevant to public health or disease prevention and promotion, etiology, diagnosis, treatment and rehabilitation. *See also social and behavior research.*

Belmont Report – A statement of basic ethical principles governing research involving human participants issued by the National Commission for the Protection of Human Subjects in 1978 on the conduct of biomedical and behavioural research involving human subjects including guidelines to ensure that research is conducted in accordance with the principles. (Retrieved from http://ohrp.osophs.dhhs.gov/humansubjects/guidance/belmont.htm)

beneficence – The ethical obligation to maximize benefits and to minimize harms. (CIOMS, International Ethical Guidelines for Biomedical Research Involving Human Subjects, 2002). It entails an obligation to protect persons from harm by maximizing anticipated benefits and minimizing possible risks of harm. The principle of beneficence can be expressed in two general rules: (1) do not harm; and (2) protect from harm by maximizing possible benefits and minimizing possible risks of harm. (IRB Guidebook, US Department of Health and Human Services, retrieved from http://www.hhs.gov/ohrp/irb/irb_glossary.htm). *See also ethical principles and benefits.*

benefits – Any direct or indirect good effect or something of positive value to health or welfare from the research study to the participants; something that promotes or enhances well-being. *See also direct benefits, indirect benefits and beneficence.*

bias – The systematic tendency of any factors associated with the design, conduct, analysis and evaluation of the results of a clinical trial to make the estimate of a treatment effect deviate from its true value [ICH Harmonized Tripartite Guideline, General Considerations for Clinical Trial (E8)].

bioavailability – The rate and extent to which the active ingredient or active moiety is absorbed from a drug product and becomes available at the site of action. For drug products that are not intended to be absorbed into the bloodstream, bioavailability may be assessed by measurements intended to reflect the rate and extent to which the active ingredient or active moiety becomes available at the site of action (Food and Drug Administration, US Department of Health and Human Services. (2009). Code of Federal Regulations, Food and Drugs, 21(5), Subchapter D, Part 320. USA: FDA).

bioequivalence – The absence of a significant difference in the rate and extent to which the active ingredient or active moiety in pharmaceutical equivalents or pharmaceutical alternatives becomes available at the site of drug action when administered at the same molar dose under similar conditions in an appropriately designed study. Where there is an intentional difference in rate (e.g., in certain extended release dosage forms), certain pharmaceutical equivalents or alternatives may be considered bioequivalent if there is no significant difference in the extent to which the active ingredient or moiety from each product becomes available at the site of drug action. This applies only if the difference in the rate at which the active ingredient or moiety becomes available at the site of drug action is intentional and is reflected in the proposed labeling, is not essential to the attainment of effective body drug concentrations on chronic use, and is considered medically insignificant for the drug (Food and Drug Administration, US Department of Health and Human Services. (2009). Code of Federal Regulations, Food and Drugs, 21(5), Subchapter D, Part 320. USA: FDA).

biologic or biological product – Any attenuated or inactivated virus or bacteria, or subcomponents attached to adjuvants, toxoids, hyperimmune serum and analogous products applicable to diagnosis, prevention, treatment, or cure of diseases or injuries to man, obtained or derived from living matter – animals, plants or microorganisms or parts thereof. It includes preparations primarily designed to develop a type of immunity or preparations that are concerned with immunity

(Department of Health (DOH) Administrative Order No. 47-A series of 2001, Rules and regulations on the registration including approval and conduct of clinical trials, and lot or batch release certification of vaccines and biologic products).

Biosafety Committee – An institutional committee that reviews and approves research projects involving the use of genetically modified organisms and biohazardous materials, including human tissue samples. The committee is in-charge of registration of clinical trials on recombinant DNA, pathogens, infectious agents, human and human primate materials, established cell lines, biological toxins, and human gene therapy/pathogen. It ensures that all activities involving these agents are conducted in a safe manner and in conformity with generally accepted standards to protect the researchers, laboratory workers, human research subjects, the public and the environment, including laboratory animals and other organisms, and to prevent damage to property.

biosimilar medicines – Follow-on versions of original biological medicines. They are independently developed after the patent protecting the original product has expired. Biosimilar medicines are intended to have the same mechanism of action as the original biological medicines, and are designed to treat the same diseases as the innovator product. The name, appearance and packaging of a biosimilar medicine differ to those of the biological reference medicine (Retrieved from http://www.europa-bio.be/Healthcare/HC_FAQ-biosimilars.htm).

blinding – Also known as masking, is a procedure in which one or more parties of the trial are kept unaware of the treatment assignment(s). Single blinding usually refers to the subjects being unaware which treatment he/she is receiving, while double-blinding usually refers to the subjects, investigator(s), monitor(s), and, in some cases, data analyst(s) being unaware of the treatment assignment(s) (ICH Harmonized Tripartite Guideline, Guideline for Good Clinical Practice (E6,R1)). *See also double blinding.*

Bureau of Food and Drug – The national regulatory agency under the Department of Health that is mandated to guarantee the safety and effectiveness of all pharmaceutical products, biologics, vaccines, and medical devices used in the diagnosis, treatment, and prevention of disease. It is now called the Philippine Food and Drugs Authority by virtue of Republic Act 9711 of 2009. *See also Food and Drug Administration.*

carrier testing – A test to identify individuals who carry recessive genes; testing designed for healthy people who have no symptoms of disease, but who are known to be at high risk because of family history.

case-control study – Type of investigation that attempts to look backward in time to identify characteristics that may have contributed to disease development by comparing responses of cases or those affected with the disease and controls or those unaffected persons. It is a study comparing persons with a given condition or disease (the cases) and persons without the condition or disease (the controls) with respect to antecedent factors (IRB Guidebook, US Department of Health and Human Services, retrieved from http://www.hhs.gov/ohrp/irb/irb_glossary.htm).

cellular metabolites – The molecular substrates and products of various cellular processes.

child's assent – An agreement or expressed willingness of a minor to take part in the research when a child cannot give full consent. Children often can understand some, but not all parts of a research study. Assent is the child's way of saying that he/she agrees to take part in the research to the degree that he/she understands it. It differs from consent since consent is the permission given by a parent or guardian to a child to take part in the research. Older children or youth may give their own consent if they are mature enough to completely or totally understand the research, and the consent or decision to participate is freely given with the premise that they are given enough information to make a choice and they understood the information provided to them (Retrieved from www.caringforkids.cps.ca/healthybodies/HealthResearch.htm and http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2606084/). The factors to be considered by the IRB are "age, psychologic state, and the maturity of the children involved" and to understand and determine whether and how assent must be documented. The assent can be an interactive process between the child and the researcher, involving disclosure, discussion, obtaining an understanding of the proposed research activity, and determining the child's preference regarding participation. The process involves "(a) providing information about the proposed research to the minor, (b) establishing shared decision-making by the child and the proxy concerning participation together with the proxy, (c) making an assessment of the child's understanding of the proposed research,

and (d) soliciting an expression of the child's willingness to participate in the proposed research" (Kon, A. A. (2006). Assent in Pediatric Research. Pediatrics, 117, 1806—1810. Retrieved from http://www.pediatrics.org/cgi/content/full/117/5/1806). *See also assent and surrogate assent.*

clinical equipoise – A state of clinical equipoise means that on the basis of available data, a condition of genuine uncertainty on the part of the clinical investigator(s) and/or a community of medical experts exists regarding the comparative therapeutic merits of each arm in a trial. Thus, they would be content to have their patients or clients pursue any of the treatment strategies being tested since none of them have been clearly established as preferable. In Freedman (1987), "The ethics of medical practice grants no ethical or normative meaning to a treatment preference, however powerful, that is, based on a hunch or anything less than evidence publicly presented and convincing to the clinical community. Persons are licensed as physicians after they demonstrate the acquisition of this professionally validated knowledge, not after they reveal a superior capacity for guessing."

clinical research – A study undertaken involving a particular person or group of people with the purpose of increasing knowledge and determining how well treatment or diagnostic test works in a particular patient population. Patient-oriented research involves a particular person or group of people or uses materials from humans. This research can include: studies of mechanisms of human disease; studies of therapies or interventions for disease; clinical trials; and studies to develop new technology related to disease. Epidemiological and behavioral studies examine the distribution of disease, the factors that affect health, and how people make health-related decisions. Outcomes and health services research seeks to identify the most effective and most efficient interventions, treatments, and services." (Retrieved from http://www.nichd.nih.gov/health/clinicalresearch)

clinical research organization – *See contract research organization.*

clinical trial – A planned scientific research or study among human volunteers to determine the effects of treatment or diagnostic test on their safety, efficacy, and its effect on quality of life. It is also a systematic study on pharmaceutical products in human subjects (including patients and other volunteers) in order to discover or verify the effects of and/or identify any adverse reactions to investigational

products, and/or to study the absorption, distribution, metabolism, and excretion of the products with the object of ascertaining their efficacy and safety (WHO, Guidelines for Good Clinical Practice for Trials of Pharmaceutical Products). It is also defined as investigative work to evaluate new drugs, medical devices, biologics, or other interventions to patients in strictly scientifically controlled settings. Clinical trials may be designed to assess the safety and efficacy of an experimental therapy, to assess whether the new intervention is better than standard therapy, or to compare the efficacy of two standard or marketed interventions. *See also clinical research.*

cloning human genes – Transfer of human DNA sequences of interest into non-human cells with the purpose of expression, genetic manipulation, and amplification.

Cluster Ethics Review Committee – An ethics review committee shared by (common to) several institutions where the volume of researches and resources do not make it feasible to have an ethics committee in each institution. The functions of the cluster committee and the respective institutional responsibilities shall be contained in a memorandum of agreement amongst the institutions concerned.

cognitively impaired – Having either a psychiatric disorder (e.g., psychosis, neurosis, personality or behavior disorders, or dementia) or a developmental disorder (e.g., mental retardation) that affects cognitive or emotional functions to the extent that capacity for judgment and reasoning is significantly diminished. Others, including persons under the influence of or dependent on drugs or alcohol, those suffering from degenerative diseases affecting the brain, terminally ill patients, and persons with severely disabling physical handicaps, may also be compromised in their ability to make decisions in their best interests (IRB Guidebook, US Department of Health and Human Services, retrieved from http://www.hhs.gov/ohrp/irb/irb_glossary.htm).

cohort – A group of individuals who have common traits or identical or similar in many characteristics such as birth year.

cohort study – A longitudinal study of the same group of people observed over time. This is a type of investigation in which exposure is assessed among the same unaffected persons and subjects and then observed for subsequent development of the disease over time. It compares a

particular outcome in groups of persons who are identical or similar in many characteristics but differ in many other ways.

collective autonomy – The exercise of decision-making by an indigenous people (IP) community as an autonomous group which decision-making is usually characterized by dialogue, consultations and consensus building among the group members. *See also autonomy and shared autonomy.*

comparator (product) – An investigational or marketed product (i.e., active control), or placebo, used as reference in a clinical trial (ICH Harmonized Tripartite Guideline, Guideline for Good Clinical Practice (E6,R1)); a pharmaceutical or other product (which may be a placebo) used as a reference in a clinical trials (WHO, Guidelines for Good Clinical Practice for Trials of Pharmaceutical Products).

compassionate use – Permission given by the national regulatory authority in particular the Bureau of Food and Drugs/Food and Drug Administration to make investigational new drugs and devices that are not yet approved for marketing for use of very or terminally ill patients having no other treatment alternatives. The US National Cancer Institute defines it as, "A way to provide an investigational therapy to a patient who is not eligible to receive that therapy in a clinical trial, but who has a serious or life-threatening illness for which other treatments are not available. Compassionate use trials allow patients to receive promising but not yet fully studied or approved cancer therapies when no other treatment option exists. Also called expanded access trial." (Retrieved from www.cancer.gov/dictionary)

compensation – Payment and/or medical care received or provided to subjects injured in research. Payment received by the research participants may include reimbursement for lost earnings, travel costs and other expenses incurred as a study participant, as recompense for inconvenience and time spent. It does not include remuneration for participating in the study. *See remuneration.*

competence – Technically, a legal term, used to denote capacity to act on one's own behalf; the ability to understand information presented, to appreciate the consequences of acting (or not acting) on that information, and to make a choice (IRB Guidebook, US Department of Health and Human Services, retrieved from http://www.hhs.gov/ohrp/irb/irb_glossary.htm).

complementary and alternative medicine (CAM) – A group of diverse medical and healthcare systems, practices, and products that are not generally considered part of conventional medicine. Conventional medicine (also called Western or allopathic medicine) is medicine as practiced by holders of M.D. (medical doctor) and D.O. (doctor of osteopathy) degrees and by allied health professionals, such as physical therapists, psychologists, and registered nurses. The boundaries between CAM and conventional medicine are not absolute, and specific CAM practices may, over time, become widely accepted. "Complementary medicine" refers to use of CAM together with conventional medicine, such as using acupuncture. "Alternative medicine" refers to use of CAM in place of conventional medicine. "Integrative medicine" (also called integrated medicine) refers to a practice that combines both conventional and CAM treatments for which there is evidence of safety and effectiveness. CAM practices are often grouped into broad categories, such as natural products such as variety of herbal medicines (also known as botanicals), vitamins, minerals, probiotics and other "natural products" which many are sold over the counter as dietary supplements; mind-body medicine are practices that focus on the interactions among the brain, mind, body, and behavior, with the intent to use the mind to affect physical functioning and promote health; and manipulative and body-based practices. Although these categories are not formally defined, they are useful for discussing CAM practices. Some CAM practices may fit into more than one category (Retrieved from http://nccam.nih.gov/health/whatiscam/#what).

complementary and alternative medicine research – Study done in human volunteers to determine the effects of and/or identify any adverse reactions to complementary and alternative medicine; study undertaken on a systematic and rigorous basis to generate new knowledge regarding diverse medical and healthcare systems, practices and products that are not presently considered to be part of conventional medicine.

conception – The period from fertilization to form a zygote up to birth of the infant;

– The period of pregnancy beginning from implantation of the fertilized ovum up to birth of the fetus.

conditional approval – Approval of the protocol by the Ethics Committee to proceed after certain conditions or modifications set by the EC are met.

confidentiality – The expectation from respondents and research participants that data or information relayed or communicated are kept secret. It also pertains to the treatment of information that an individual has disclosed in a relationship of trust and with the expectation that it will not be divulged to others without permission in ways that are inconsistent with the understanding of the original disclosure. (IRB Guidebook, US Department of Health and Human Services, retrieved from http://www.hhs.gov/ohrp/irb/irb_glossary.htm). It is the duty of healthcare providers and health researchers toward patients and research participants to protect privacy and to refrain from unauthorized disclosure of information pertaining to them. It is also the prevention of disclosure of the IEC/IRB information, deliberations and documents to non-authorized individuals.

conflict of interest – A conflict of interest arises when a member(s) of the Ethics Committee holds interests with respect to specific applications for review that may jeopardize his/her ability to provide free and independent evaluation of the research focused on the protection of the research participants. Conflict of interests may arise when an EC member has financial, material, institutional or social ties to the research. For example, serving as a member of the research team, receiving salary from the sponsor, having equity interest of and holding management position in the business entity, holding patent right or receiving royalties from such rights whose value may affect the value of the research outcome.

contract research organization – Also called Clinical Research Organization, a service organization with whom a drug or device manufacturer or sponsor contracts to perform clinical trial related activities which may include, among others, development of protocols, recruitment of patients, collection and analyis of data, and preparation of application documents to a national regulatory agency. It is a person or an organization (commercial, academic, or other) contracted by the sponsor to perform one or more of a sponsor's trial-related duties and functions (ICH–Guideline for Good Clinical Practice (E6, R1), art. 1.20). Likewise, the US FDA defines a CRO as "a person [i.e., a legal person, which may be a corporation] that assumes, as an independent contractor with the sponsor, one or more of the obligations of a sponsor, e.g., design of a protocol, selection or monitoring of investigations, evaluation of reports, and preparation of materials to be submitted to the FDA." [21 CFR 312.3(b)]

control – The standard by which experimental observation are evaluated. In many clinical trials, one group of patients will be given an experimental drug or treatment, while the control group is either given a standard treatment for the illness or a placebo (Retrieved from http://www.Clinicaltrials.gov/ct/info/whatis).

controlled trials – A trial in which one group of participants is given an experimental drug, while another group (the control group) is given either a standard treatment for the disease or a placebo; a prospective clinical trial comparing two or more treatments, or placebo and treatment(s) in similar groups of patients or within patients. A controlled trial may or may not use randomization to assign patients to groups, and it may or may not use blinding to prevent them from knowing which treatment they get (Retrieved from https://www.ecri.org/patient/references).

Convention on the Biological Diversity – Signed by 150 government leaders at the 1992 Rio Earth Summit, the Convention on Biological Diversity is dedicated to promoting sustainable development. Conceived as a practical tool for translating the principles of Agenda 21 into reality, the Convention recognizes that biological diversity is about more than plants, animals and microorganisms and their ecosystems – it is about people and the need for food security, medicines, fresh air and water, shelter, and a clean and healthy environment (Retrieved from http://www.cbd.int/convention/downloade).

conventional medicine – Also referred to as Western medicine, biomedicine, and allopathic medicine; A system in which medical doctors and other healthcare professionals treat symptoms and diseases using drugs, radiation, or surgery; also called allopathic medicine, biomedicine, mainstream medicine, orthodox medicine, and Western medicine. *See also Western medicine and complementary and alternative medicine.*

counseling – Non-coercive interaction between a health professional and a patient or client and/or family that is meant to clarify personal values and priorities, healthcare options, expectations, risks, benefits, and resources in order to help in decision-making. It needs to be offered prior to sensitive testing (pre-test counseling) and/or after testing (post-test counseling) for comprehensive care.

criminal violence – Behaviors by individuals that intentionally threaten,

attempt, or inflict physical harm on others (National Research Council's Panel on the Understanding and Control of Violent Behavior, citing Reiss and Roth, 1993, p. 2).

cultural bias – Prejudice based on community values and traditions.

culture – The way of life of groups of people that is defined by mores, shared values, traditions and sociopolitical structures and institutions.

debriefing – The process of obtaining information about an experience from an individual who has participated in, or observed particular events. It is also "giving subjects previously undisclosed information about the research project following completion of their participation in research. Note that this usage, which occurs within the behavioral sciences, departs from standard English, in which debriefing is obtaining rather than imparting information (Retrieved from http://virginia.edu/vpr/irb/hsr/glossary.html).

deception – An act characterized by dishonesty, fraud, trickery or sham for the purpose of manipulating another person into making a decision that he or she would not have made otherwise.

Declaration of Helsinki – A code of ethics for clinical research approved by the World Medical Association in 1964 and widely adopted by medical associations in various countries. This is World Medical Association's (WMA) response to the Nuremberg Code. The Declaration of Helsinki was adopted by the WMA in 1964 and has been amended five times, at regular intervals. A note of clarification about placebo-controlled trials was added in 2002 (Retrieved from http://www.wma.net/e/policy/b3.htm).

de-identified – Removal of elements connected with data which might aid in associating those data with an individual. Examples include name, birth date, social security number, home address, telephone number, e-mail address, medical record numbers, health plan beneficiary numbers, full-face photographic images (Applied Clinical Trials, 2009) (Retrieved from http://www.cdisc.org/stuff/contentmgr/files/0/be650811feb46f381f0af41ca40ade2e/misc/cdisc_2009_glossary.pdf). *See also anonimized.*

deoxyribonucleic acid (DNA) – The fundamental substance of which genes are composed. It is an antiparallel double helix of nucleotides

(having deoxyribose as their sugars) linked by phosphodiester (sugar-phosphate) bonds to adjacent nucleotides in the same chain and by hydrogen bonds to complementary nucleotides in the opposite chain.

deoxyribonucleic acid sequencing – Method of analyzing the base sequence composition and order of a DNA sample using chemical tagging and physical measurements.

descriptive study – A study that is not truly experimental in nature such as quasi-experimental studies, correlational studies, record reviews, case histories, and observational studies.

device – An instrument, apparatus, implement, machine, invention, implant, in vitro reagent, or other article intended for use in the diagnosis, treatment, or prevention of disease. A device is intended to affect the structure or function of the body, but it does not function through chemical action within or on the body (Retrieved from https://www.ecri.org/patient/references). *See also medical device*.

diagnostic – Procedure or technique used in the identification of a disease or determination of the health status of an individual.

direct benefits – Gain or advantage or good effect derived by a research subject immediately or closely arising from the use of an experimental substance or device. *See also benefits.*

disapproval – A negative action of the Ethics Committee on the protocol. The study cannot be implemented if it has been disapproved by the Committee.

disclosure of data – The giving of information in connection with proposed research undertaking or the sharing of the results of the study especially as they pertain to the individual's or the family's health situation.

discontinuation – The deed of terminating participation in a clinical trial by a research subject (dropout) earlier than the completion of all protocol-required terms. In some case, the discontinuation may be initiated by the investigator for a cause or inability to locate or follow up subject or by the sponsor.

disease allele – One of the variant forms of a disease gene at a particular

locus, or location on a chromosome. Different alleles produce variation in inherited characteristics such as hair color or blood type. In an individual, one form of the allele (the dominant one) may be expressed more than another form (the recessive one).

domestic violence – Or domestic abuse, is brutality or cruelness committed by one family/household member against another. It is violent conflict between household members resulting to physical harm, sexual assault, or fear of physical harm and other vicious action.

double blinding – One in which neither the subject nor any of the investigator or sponsor staff who are involved in the treatment or clinical evaluation of the subjects are aware of the treatment received [ICH Harmonized Tripartite Guideline, Statistical Principles for Clinical Trials (E9)]. *See blinding.*

drug – A substance used as medication or used in the diagnosis, cure, mitigation, treatment or prevention of disease.

dual-use research – Scientific studies undertaken for beneficial purposes but at the same time with harmful applications [WHO. (2009). Bulletin of the World Health Organization, 87(9)]. The legitimate technologies that are studied to promote scientific advances likewise create potential risks. The knowledge, tools, and techniques gained and used in these biotechnology researches can be utilized misappropriately or wrongly to create biological weapons or for bioterrorism.

duress – Wrongful and usually unlawful compulsion (as threats of physical violence) that induces a person to act against his or her will: "coercion" (Merriam-Webster's Dictionary of Law (c), 1996).

effectiveness – The degree to which a diagnostic test or treatment produces a desired result in patients in the daily practice of medicine (Retrieved from https://www.ecri.org/patient/references).

efficacy – An indication that the therapeutic effect of a clinical trial intervention is acceptable; that is, at least as good as the control intervention or standard of care to which it is compared. It is the ability of a treatment modality to produce an effect to alleviate a disease. This is the "degree to which a diagnostic test or treatment produces a desired result in patients under the idealized circumstances of a clinical trial." (Retrieved from https://www.ecri.org/patient/references).

eligibility criteria – The list of criteria or conditions that guide enrollment of participants into a study. The criteria describe both inclusionary and exclusionary factors (e.g., inclusion criterion – participants must be between 55 and 85 years old; exclusion criterion – must not take drug X three months prior to the study). (Retrieved from https://www.ecri.org/patient/references). *See inclusion criteria and exclusion criteria.*

embryo – The stage of human development following implantation (starting 10-14 days), when the primitive streak begins to form up to fetal stage.

energy therapy or medicine – One of five domains of "complementary and alternative medicine" (CAM) identified by the National Center for Complementary and Alternative Medicine (NCCAM) in the United States. There are two categories namely: biofield therapies, and bioelectromagnetic-based therapies. The former are therapies intended to affect energy fields that purportedly surround and penetrate the human body such as Qigong, Reiki, and Therapeutic touch. The later therapies involve the use of electromagnetic fields, such as pulsed fields, magnetic fields, or alternating-current or direct-current fields. *See complementary and alternative medicine*.

epidemiologic research – Investigative studies intended to establish "the distribution and determinants of disease frequency in human populations." It is a study undertaken on a systematic and rigorous basis to generate new knowledge regarding the determinants of the incidence of diseases as well as their related risk factors, etiology and causation. *See also clinical research.*

epidemiology – The basic medical science that focuses on the distribution and determinants of disease frequency in human populations (Raymond Greenberg, Medical Epidemiology, 1993).

equipoise – A state in which an investigator is uncertain about which arm of a clinical trial would be therapeutically superior for a patient. An investigator who has a treatment preference or finds out that one arm of a comparative trial offers a clinically therapeutic advantage should disclose this information to subjects participating in the trial (Retrieved from http://www.cdisc.org/stuff/contentmgr/files/0/be650811feb46f381f0af41ca40ade2e/misc/cdisc_2009_glossary.pdf). *See also clinical equipoise.*

ethical clearance – A certification that a research proposal has complied with ethical requirements; action of an ethics review committee on a research protocol that signifies approval and permission to proceed with the research. *See also approval.*

ethical principles – "Refers to those general judgments that serve as a basic justification for the many particular ethical prescriptions and evaluations of human actions" (National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research. (1979). The Belmont Report: Ethical Principles and Guidelines for the Protection of Human Subjects of Research. US NIH, Office of Human Research Subjects). Three basic principles, among those generally accepted, that are particularly relevant to the ethics of research involving human subjects are the principles of respect of persons, beneficence and justice. *See also respect of persons, beneficence and justice, autonomy and non-maleficence.*

Ethics review – The evaluation of a research protocol by an ethics review committee to promote the safety and protection of the dignity of human participants. This is a systematic process by which this independent committee evaluates a study protocol to determine if it follows ethical and scientific standards for carrying out biomedical research on human participants. It checks if the protocol complies with the guidelines to ensure that the dignity, rights, safety and well- being of research participants are promoted.

ethics review committee – Also called research ethics committee (REC), institutional ethics review board (IERB), independent ethics committee (IEC) or institutional review board (IRB); a committee constituted to review the ethical aspects of a research proposal and its possible implementation. This is an independent body whose responsibility is to ensure the protection of the rights, safety and well-being of human participants involved in a trial and to provide public assurance of that protection. *See also research ethics committee.*

exclusion criteria – Factors utilized to determine whether an individual is ineligible for a clinical trial or research study. *See also eligibility criteria.*

expedited review – An ethics review of research protocol by the IRB chair or a designated voting member or subgroup of voting members rather than by the entire IRB. This is done for some research involving no

more than minimal risk and maybe for minor changes in approved research, annual renewals of approved projects, approval of protocol amendments, research conducting health record review, and for confirming changes required by the ethics committee for approval of the protocol.

experimental design – The structure of research, identifying the various elements of a research project and how they relate to one another. The structure specifies treatment conditions or independent variables, the variables which are planned to be measured or the dependent variables and methods of assigning subjects to groups wherein these subjects are randomly assigned to treatment conditions.

family studies (in genetic research) – Mapping of disease genes through the establishment of genetic linkage within a family.

feasibility - Possibility or likelihood to be accomplished or implemented.

fetus – Stage of human development when the first neural cells start differentiating, that is, starting from six to eight weeks up to birth.

focus group discussion (FGD) – Qualitative method of eliciting in-depth information on concepts and perceptions on selected topics or issues by having a structured and/or unstructured group discussion of 6–12 persons facilitated by a trained professional.

Food and Drug Administration (FDA) – The new name and the reorganized and strengthened Bureau of Food and Drugs by virtue of the **"**Food and Drug Administration (FDA) Act of 2009" or Republic Act No. 9711 of August 18, 2009, "An act strengthening and rationalizing the regulatory capacity of the Bureau of Food and Drugs (BFAD) by establishing adequate testing laboratories and field offices, upgrading its equipment, augmenting its human resource complement, giving authority to retain its income, renaming it the Food and Drug Administration, amending certain sections of Republic Act No. 3720, as amended, and appropriating funds thereof." The FDA (Section 5) shall have the following centers and offices: (a) The Centers shall be established per major product category that is regulated, namely: (1) Center for Drug Regulation and Research (to include veterinary medicine, vaccines and biologicals); (2) Center for Food Regulation and Research; (3) Center for Cosmetics Regulation and Research (to include household hazardous/urban substances); and (4) Center for

Device Regulation, Radiation Health, and Research. These Centers shall regulate the manufacture, importation, exportation, distribution, sale, offer for sale, transfer, promotion, advertisement, sponsorship of, and/or, where appropriate, the use and testing of health products. The Centers shall likewise conduct research on the safety, efficacy, and quality of health products, and to institute standards for the same." *See also Bureau of Food and Drugs.*

full board review – Review of proposed research at a convened meeting at which a majority of the membership of the IRB are present, including at least one member whose primary concerns are in non-scientific areas. For the research to be approved, it must receive the approval of a majority of those members present at the meeting (IRB Guidebook, US Department of Health and Human Services, retrieved from http://www.hhs.gov/ohrp/irb/irb_glossary.htm).

gamete – Cell that fuses with another cell during conception; a reproductive cell containing half of the genetic material necessary to form a complete human organism. During fertilization, male (sperm) and female (ovum) gametes join together, producing a zygote.

gender – Socially defined feminine or masculine roles, attitudes, and values.

gender bias – Partiality, unfairness, prejudice manifested towards an individual or group of individuals based on sex and sexual orientation.

gender-sensitive counseling – Counseling that includes awareness of existing gender differences, issues and inequality in its framework for interaction with the patient or client.

gender sensitivity – The ability to perceive existing gender differences, issues, and inequality and to incorporate these into strategies and actions.

gene – The functional and physical unit of heredity passed from parent to offspring. Genes are pieces of DNA, and most genes contain the information for making a specific protein.

gene activity – The degree of expression of a particular gene or levels of transcription.

gene testing – Analysis done on affected persons or carriers within family already identified because of a history of high risk for having or transmitting a specific genetic disorder.

genetic association studies – Describes a situation in which a particular allele is found either significantly more or less frequently in a group of affected individuals than would be expected from the frequency of the allele in the general population from which the affected individuals were drawn.

genetic counseling – The provision of information and assistance to affected individuals or family members at risk of a disorder that may be genetic, concerning the consequences of the disorder, the probability or developing or transmitting it, and the ways in which it may be prevented or ameliorated.

genetic research – The study of the structure and functions of individual genes, genetic variation in human populations, and the applications of genetics in diagnosis and patient care.

genetic screening – A population-based method for identifying a subset of individuals at risk of developing or of transmitting a specific genetic disease or disorder.

good clinical practice (GCP) guidelines – An international ethical and scientific quality standards for designing, conducting, recording and reporting trials that involve the participation of human subjects. Compliance with these standards provide public assurance that the rights, safety, and well-being of trial subjects are protected, consistent with the principles that have their origin in the International Declaration of Helsinki, and that the clinical trial data are credible (CPMP/ICH/135/95). These are standards and procedures for clinical trials that encompass the design, protocol approval, monitoring, termination, audit, analyses, reporting, and documentation of human studies. It defines the responsibilities and activities of the sponsor, principal investigators and monitor involved in the clinical trials. The GCP ensures that the studies are scientifically and ethically sound, and all the clinical properties of the product under investigation are properly documented. For complete information, reference is made to the published WHO and International Conference on Harmonization Code of Good Clinical Practice (Department of Health Administrative

Order No. 47-A series of 2001, 30 August 2001). It is a standard for clinical studies which encompasses the design, conduct, monitoring, termination, audit, analyses, reporting and documentation of the studies and which ensures that the studies are scientifically and ethically sound and that the clinical properties of the pharmaceutical products (diagnostic, therapeutic or prophylactic) under investigation are properly documented (WHO, Guidelines for Good Clinical Practice for Trials of Pharmaceutical Products).

good laboratory practices – Standards and procedures whereby a laboratory achieves a defined consistent, and reliable standard in performing laboratory tests and activities (Department of Health Administrative Order No. 47-A series of 2001, 30 August 2001).

good manufacturing practice guidelines – National standards and regulations for licensing of laboratories engaged in the manufacture and production of drugs, vaccines and other pharmaceuticals intended for human administration or consumption. It is that part of quality assurance which ensures that products, including vaccines and biologics are consistently produced and controlled to quality standards appropriate for their intended use, including all phases of vaccine clinical trials, and as required by registration and marketing authorization. For supplementary guidelines for the manufacture of investigational pharmaceutical products for human studies, refer to WHO/Pharm/94.571 (Department of Health Administrative Order No. 47-A series of 2001, 30 August 2001). In the World Health Organization, Guidelines for Good Clinical Practice for Trials of Pharmaceutical Products; WHO Technical Report Series, No. 850, 1995, Annex 3, It is defined as that part of pharmaceutical quality assurance which ensures that products are consistently produced and controlled to the quality standards appropriate to their intended use and as required by marketing authorization.

government-sponsored health research – Health research that is undertaken using government funds or resources.

guardian – One who is legally responsible for the care and management of the person or property of an incompetent person or a minor or someone who can make important personal decisions in behalf of another person. *See also legally authorized representative.*

guidelines – A set of rules or recommendations intended to effect a course of action.

health equity – The absence of systematic disparities in health (or in major social determinants of health) among groups with different levels of underlying advantage/disadvantages, e.g., wealth, power, prestige.

health research – Generation of new knowledge (biomedical, clinical, social) to identify and deal with health problems, health systems and policies as well as those that impact on health such as socioeconomic, environment, energy and agricultural policies (PNHRS TWG Chairs, Feb 2004). This is composed of investigational activities that aim to generate data that shall contribute to improvement in the diagnosis, prevention and management of diseases, and in the delivery of care and for the enhancement of the quality of life of individuals and health conditions in communities. *See also clinical research.*

Helsinki Declaration – Guidelines adopted in 1964 by the 18th World Medical Assembly (WMA) held in Helsinki, Finland, and revised in 2000 by the 52nd WMA General Assembly, for physicians conducting biomedical research. This declaration outlines clinical trial procedures required to ensure patient safety, consent and ethics committee reviews in human subjects.

herbal medicine research – Study undertaken to generate new knowledge regarding the use of herbs and plants to prevent and treat diseases and ailments or to promote health and healing.

herbal medicines – Finished, labeled medicinal products that contain, as active ingredient(s), serial or underground part(s) of plant or other materials or combination thereof, whether in the crude state or as plant preparations (Traditional and Alternative Medicine Act of 1997, Republic Act 8423). Plant materials include juices, gums, fatty oils, essential oils, and other substances of this nature. Herbal medicines, however, may contain excipients in addition to the active ingredient(s). Medicines containing plant material(s) combined with chemically defined active substances, including chemically defined isolated constituents of plants, are not considered herbal medicines.

high-risk group – Social group known to have a high prevalence of a health

problem because of shared environmental, occupational, nutritional or genetic factors including practices that contribute to ill-health.

HIV (human immunodeficiency virus–type 1) – Viral infectious agent that causes destruction of cellular immunity in individuals acquired through tissue fluid transmission from infected persons.

HIV and AIDS research – Study undertaken on a systematic and rigorous basis to generate new knowledge regarding the prevention and/or treatment of HIV and AIDS.

HIV test – Immunology-based laboratory test that establishes the presence of HIV infection in an individual.

homeopathy – A system of medicine which involves treating the individual with highly diluted substances, given mainly in tablet form, with the aim of triggering the body's natural system of healing. Based on their specific symptoms, a homeopath will match the most appropriate medicine to each patient (Retrieved from www.hemeopathy-soh.org).

human immunodeficiency virus – *See HIV.*

human subjects – *See research participants and respondent.*

human zygote – *See zygote.*

hypothesis – A tentative explanation for an observation, phenomenon, or scientific problem that can be tested by further investigation.

Incapacity – A person's mental status and means, inability to understand information presented, to appreciate the consequences of acting (or not acting) on that information, and to make a choice. Often used as a synonym for incompetence (IRB Guidebook, US Department of Health and Human Services, retrieved from http://www.hhs.gov/ohrp/irb/irb_glossary.htm). *See also incompetence.*

inclusion criteria – The factors used to judge a participant's eligibility to be part in a trial or research. These factors are justified by the purpose of the researcher in conducting the research. *See also eligibility criteria.*

incompetence – Technically, a legal term meaning inability to manage one's

own affairs. Often used as a synonym for incapacity (IRB Guidebook, US Department of Health and Human Services http://www.hhs.gov/ohrp/irb/irb_glossary.htm). *See also incapacity.*

identifiable personal information – Information on a particular person who expects that such information shall be held in privacy such as culture, age, religion and social status, as well as their life experience and educational, medical, family, relationship, or employment histories.

independent consultant – An expert who gives advice(s), comment(s) and suggestion(s) upon review of the study protocols with no affiliation to the institute(s) or investigator(s) proposing the research proposal.

indigenous knowledge (IK) – The information base for a society, which facilitates communication and decision-making. Indigenous information systems are dynamic, and are continually influenced by internal creativity and experimentation as well as by contact with external systems (Flavier et al., 1995, p. 479); the local knowledge – knowledge that is unique to a given culture or society. IK contrasts with the international knowledge system generated by universities, research institutions and private firms. It is the basis for local-level decision-making in agriculture, healthcare, food preparation, education, natural resource management, and a host of other activities in rural communities (Warren, 1991).

indigenous peoples (IP) – Distinct communities, the land on which they live and the natural resources on which they depend are inextricably linked to their identities and cultures (World Bank). These are cultural groups that are continuously associated with a given geographic area and who formerly or currently inhabit the area and are independently or largely isolated from the influence of the existing governance, and have maintained, at least in part, their distinct cultural, social, organizational and/or linguistics attributes or practices so that they continue to be different in some degree from the prevailing or main culture of the country.

Indigenous Peoples Right Act (IPRA) – Republic Act No. 8371, known as "The Indigenous Peoples Right Act of 1997," was enacted to recognize, protect and promote the rights of Indigenous Cultural Communities (ICC) or Indigenous Peoples (IP). It also established the National Commission on Indigenous Peoples (NCIP), the lead government agency that formulates and implement policies, plans and programs

for the recognition, promotion and protection of the rights and well-being of Indigenous Peoples and the recognition of their ancestral domains. It also states that ICC/IP women shall enjoy land rights and opportunities with men in all spheres of life and provides for her participation in the decision-making process in all levels as well, full access to education, maternal and child care, health, nutrition, housing services and training facilities.

indirect benefits – An unintended or unlikely gain or advantage or good effect from participating in a research. *See also benefits and direct benefits.*

information in the public domain – *See public domain information.*

informed consent – The process of obtaining approval to participate in an investigative study or permission to a medical intervention. Consent must be freely given in verbal, video or written form. An important part of the process is the adequacy, appropriateness, and timeliness of the information for decision-making; It is "a decision to participate in research, taken by a competent individual who has received the necessary information; who has adequately understood the information; and who, after considering the information, has arrived at a decision without having been subjected to coercion, undue influence or inducement, or intimidation." (CIOMS, 2002)

Institutional Ethics Review Committee or Board – Ethics review committee organized in a particular institution to ensure that health research is conducted according to international ethical principles, national and institutional guidelines. This is an independent body constituted of medical, scientific, and non-scientific members, whose responsibility it is to ensure the protection of the rights, safety, and well-being of human subjects involved in a trial by, among other things, reviewing, approving, and providing continuing review of trial protocol and of the methods and material to be used in obtaining and documenting informed consent of the trial subjects (ICH E6 1.31). *See also research ethics committee and ethics review committee.*

intellectual property rights (IPR) – The Convention establishing the World Intellectual Property Organization (WIPO), concluded in Stockholm on July 14, 1967 (Article 2(viii)), that states, "intellectual property shall include rights relating to: literary, artistic and scientific works, performances of performing artists, phonograms and broadcasts,

inventions in all fields of human endeavor, scientific discoveries, industrial designs, trademarks, service marks and commercial names and designations, protection against unfair competition, and all other rights resulting from intellectual activity in the industrial, scientific, literary or artistic fields." WIPO Intellectual Property Handbook: Policy, Law and Use, WIPO Publication No.489. In the Intellectual Property Code of the Philippines, or Republic Act 8293, the term "intellectual property rights consist of: a) Copyright and Related Rights; b) Trademarks and Service Marks; c) Geographic Indications; d) Industrial Designs; e) Patents; f) Layout-Designs (Topographies) of Integrated Circuits; and g) Protection of Undisclosed Information (n, TRIPS). In the Traditional and Altenative Medicine Act of 1997, Republic Act 8423, IPR means the legal basis by which indigenous communities exercise their rights to have access to, protection, and control over their cultural knowledge and products, including but not limited to traditional medicines, and includes the right to receive compensation for it.

intellectual property sharing – To participate in, use, enjoy, or experience jointly or in turns the property that derives from the work of the mind or intellect or an idea, invention, trade secret, process, program, data, formula, patent, copyright, or trademark or application, right, or registration relating thereto (Merriam-Webster's Dictionary of Law (c), 1996).

intentional environmental exposure study – A controlled experiment that deliberately exposes human subjects to an agent (such as a chemical) found in the environment. The investigators control the amount of exposure (or dose), the length of the exposure period, the route of exposure (dermal, oral, respiratory), and other variables, such as the age, health, diet and activity of participants. Researchers carefully monitor the subjects' clinical signs and symptoms, and collect blood, urine, and other biological samples for biomedical testing (such as tests for the presence of a chemical or its metabolites, blood counts, etc.). Researchers conduct intentional environmental exposure studies to observe how the agents under investigation affect human beings, which can improve the understanding of the relationship between environmental exposures and disease. Other studies that are likely to have significance for public health include exposures to common allergens (such as dust, pollen, or animal dander), cosmetics, sunscreens, pesticide residues on food, insecticides applied to the

skin, and chemicals used in clothing, foods, food packaging, housing materials, and consumer goods (Resnik David, B (2009 in Pub Med Central), "Intentional Exposure Studies of Environmental Agents on Human Subjects: Assessing Benefits and Risks"; Account Res. 2007; 14(1): 35–55, retrieved from http://www.ncb.nlm.nih.gov/pmc/articled/PMC2681234). *See also intentional human dosing studies.*

intentional human dosing studies – Scientific studies that deliberately or purposely and calculatedly expose research subjects to environmental agents. *See also intentional environmental exposure study.*

interaction – The chemical or biological reactivity of the active principle or herbal preparation with other administered substances.

international collaborative research – Joint or shared conduct of research by at least two countries or governments (e.g., Philippines and one other foreign government/country). It is an investigative work conducted at an international level, with involvement by investigators coming from different countries.

intervention – A drug product or medicinal product, device, test articles, therapy, or process being investigated in a research or clinical study that is hypothesized to have an effect on the outcome(s) of the research being conducted.

intervention (interventional) study – A research that includes measures or technology to purposely affect the course of an illness. These measures aim to improve health or condition of an individual or a group of individuals or change the course of disease.

invasive procedure – Biological sampling using a method involving intrusion into the human body, such as obtaining a blood sample by using a needle and syringe (UNESCO International Declaration on Human Genetic Data).

investigational or study product – A pharmaceutical form of an active ingredient or placebo being tested or used as a reference in a clinical trial, including a product with marketing authorization when used or assembled (formulated or packaged) in a way different from the approved form, or when used for an unapproved indication, or when used to gain further information about an approved use (ICH

Harmonized Tripartite Guideline, Guideline for Good Clinical Practice (E6,R1)); Department of Health Administrative Order No. 47-A series of 2001, Rules and regulations on the registration including approval and conduct of clinical trials, and lot or batch release certification of vaccines and biologic products). Developmental or investigational vaccine or biologic refers to vaccine or biologic product that needs or is undergoing pre-clinical and clinical studies to determine safety, potency, efficacy and therapeutic/prophylactic value. It refers to a vaccine or biologic product which has never been registered or licensed by the national regulatory authorities, in particular FDA.

investigator – A person responsible for the conduct of the critical trial at a trial site. If trial is conducted by a team of individuals at a trial site, the investigator is the responsible leader of the team and be called the principal investigator (ICH Harmonized Tripartite Guideline, Guideline for Good Clinical Practice (E6, R1)). It is a person responsible for the trial and for the rights, health and welfare of the subjects in the trial. The investigator should have qualifications and competence in accordance with local laws and regulations as evidenced by an up-to-date curriculum vitae and other credentials. Decisions relating to, and to provisions of, medical or dental care must always be the responsibility of a clinically competent person legally allowed to practice medicine or dentistry (WHO Guidelines for Good Clinical Practice for Trials of Pharmaceutical Products). The investigator must be a qualified scientist who undertakes scientific and ethical responsibility, either on his/her behalf or on behalf of an organization, for the ethical and scientific integrity of a research project at a specific site or group of sites*. See principal investigator.*

justice – The ethical obligation to treat each person in accordance with what is morally right and proper, to give each person what is due to him or her. In the ethics of research involving human subjects, the principle refers primarily to distributive justice, which requires the equitable distribution of both the burdens and the benefits of participation in research (CIOMS, International Ethical Guidelines for Biomedical Research Involving Human Subjects, 2002), requiring fairness in distribution of burdens and benefits; often expressed in terms of treating persons of similar circumstances or characteristics similarly (IRB Guidebook, US Department of Health and Human Services, retrieved from http://www.hhs.gov/ohrp/irb/irb_glossary.htm). *See also ethical principles.*

legally authorized representative – One that represents another or others,

upon their permission in accordance with law, in a special capacity (Merriam-Webster's Dictionary of Law (c), 1996). This is the person who has authority, under the law, to stand for, or make decisions in behalf of another. *See also guardian.*

legally competent person – Qualified or fit to perform an act, in accordance with law, free from addiction or mental defects that renders one incapable of taking care or oneself or one's property (Merriam-Webster's Dictionary of Law (c), 1996). *See competence.*

linkage analysis – Gene hunting technique that traces patterns of disease in high risk families for the purpose of locating a disease-causing gene by identifying genetic markers of known chromosomal location that are co-inherited with the trait of interest.

masking – *See blinding.*

material transfer agreement – An agreement between the source institution (or community) and the recipient institution (agency or community) that defines responsibilities and ownership of the material under study.

medical device – A diagnostic or therapeutic article that does not achieve any of its principal intended purpose through chemical action within or on the body. Such devices include diagnostic test kits, crutches, electrodes, pacemakers, arterial grafts, intraocular lenses, and orthopedic pins or other orthopedic equipment. (IRB Guidebook, US Department of Health and Human Services, retrieved from http://www.hhs.gov/ohrp/irb/irb_glossary.htm). *See also device.*

minimal risk – A risk is minimal 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. For example, the risk of drawing a small amount of blood from a healthy individual for research purposes is no greater than the risk of doing so as part of routine physical examination (IRB Guidebook, US Department of Health and Human Services, retrieved from http://www.hhs.gov/ohrp/irb/irb_glossary.htm). The definition of minimal risk for research involving prisoners differs somewhat

from that given for non-institutionalized adults (See 45 CFR 46.303(d) and Guidebook Chapter 6, Section E, "Prisoners.").

minimal toxicity data – The lowest dose of the preparation that shall elicit toxicity signs and symptoms in human participants or in animals.

minors – Persons who have not yet reached the age of majority, 18 years old.

monitor – A person appointed by and responsible to the sponsor or contract research organization for monitoring and reporting progress of the trial and for verification of data (WHO, Guidelines for Good Clinical Practice for Trials of Pharmaceutical Products).

monitoring – The process of checking or scrutinizing research participants' health status during a clinical trial, and/or to oversee the progress of a trial or research and/or to check researcher's compliance with the protocol and regulatory requirements with in which the protocol is given ethical approval.

moral agent – Person competent of acting with reference to what is ethical or what is right and wrong; a sentient individual whose acts impact on others and are affected by the act of others.

multicenter trial – A clinical trial conducted according to a single protocol but at more than one site, and therefore, carried out by more than one investigator (ICH Harmonized Tripartite Guideline, General Considerations for Clinical Trial (E8)).

multifactorial inheritance – Heredity characterized by the involvement of several genes and environmental factors.

mutagenicity – The capacity of a chemical or physical agent to cause genetic alterations.

nanomedicine – An "offshoot of nanotechnology, that refers to highly specific medical intervention at the molecular scale for curing disease or repairing damaged tissues, such as bone, muscle, or nerve. A nanometer is one-billionth of a meter, too small to be seen with a conventional lab microscope. It is at this size scale – about 100 nanometers or less – that biological molecules and structures inside living cells operate" (Retrieved from http:/www.nihroadmap.nih.gov/

nanomedicine/index.asp). It is the application of nanotechnology in biomedicine for repair, construction, control and monitoring of biological systems on a molecular scale. It utilizes various different engineered nanoparticles.

nanotechnology – The understanding and control of matter at dimensions between approximately 1 and 100 nanometers, where unique phenomena enable novel applications. Encompassing nanoscale science, engineering, and technology, nanotechnology involves imaging, measuring, modeling, and manipulating matter at this length scale (Retrieved from http://www.nano.gov/html/facts/whatIsNano.html).

national healthcare delivery system – The country's total structures both private and public organizations, agencies, and individuals, including policies and mechanisms, that provide healthcare to individuals and communities.

National Unified Health Research Agenda (NUHRA) – An evolving plan that lists the priority research areas and topics that need to be addressed with in a five-year period based on global and national initiatives influencing the health sector like the Millennium Development Goals, the Medium Term Philippine Development Plan, the Health Sector Reform Agenda, and the National Objectives for Health and the Science and Technology Agenda. The list is drawn from multisector regional and national consultations involving representations from the government, academe, research institutions, professional organizations, non-government agencies, civil society and funding agencies. The list of topics is not comprehensive and final but an evolving list of research priorities in need of immediate action, given the current thrusts and realities. The selection of research concerns and topics serve as basis for: policy action and advocacy for achieving the critical goals and objectives of health; funding projects particularly by the government sector and other stakeholders from private and international organizations, as basis for academic work; collaboration between and among institutions; maximizing resource utilization among stakeholders and minimizing duplication of efforts with the delineation of responsible agencies; and the template to advocate for support from local, national and international organizations so health research can be mainstreamed as an essential component

in providing solutions that impact on the pressing health needs of the country and contribute to national development (Retrieved from http://www.pchrd.dost.gov.ph).

non-disclosure of data – The withholding of or refusal to reveal information derived from research.

non-invasive procedure – Biological sampling using a method which does not involve intrusion into the human body (e.g., oral smears).

non-maleficence – This principle proscribes the deliberate infliction of harm on persons (CIOMS, International Ethical Guidelines for Biomedical Research Involving Human Subjects, 2002). It is the duty of the researcher(s) to do no harm and to prevent harm. It is further defined as "the principle of doing, or permitting, no foreseeable harm including infringement of rights as a consequence of the research. It is the principle of doing no harm in the widest sense." (University of Arts London. (2010). Code of Practice in Research Ethics. Retrieved from http://www.arts.ac.uk/research/304.htm).

North-South research collaboration – The relationship or interaction between the developed and developing countries or rich and poor countries.

Nuremberg Code – A "code of research ethics developed during the trials of Nazi war criminals following World War II and widely adopted as a standard during the 1950s and 1960s for protecting human subjects (IRB Guidebook, US Department of Health and Human Services, retrieved from http://www.hhs.gov/ohrp/irb/irb_glossary.htm). It is a series of 10 principles for permissible medical experiments involving human subjects, articulated in 1947 as part of the judgment in Nuremberg against some of the physicians who led the experiments on inmates of the Nazi concentration camps (Retrieved from http://ohsr.od.nih.gov/guidelines/nuremberg.html).

participatory research – Research that involves the participation of the investigator in the activities of the research population. It could also involve research subjects in the definition of the research agenda, the conduct of research, monitoring and evaluation, and dissemination of results.

patent – Government instrument that assigns ownership of a product or creative work that is accompanied by certain rights.

patient-oriented research – *See clinical research.*

peer review – The examination of the research design and methodology of a research by expert(s) in the same field or similar level of expertise.

permit for clinical investigational use (PCIU) – A registration document issued by the FDA for the purpose of allowing the conduct of Phase I, Phase II and Phase III clinical trials of developmental or investigational biologic product in the country (Department of Health Administrative Order No. 47-A series of 2001, Rules and regulations on the registration including approval and conduct of clinical trials, and lot or batch release certification of vaccines and biologic products).

pharmacodynamics – The study of what a drug does to the body.

pharmacogenetics – The field of biochemical genetics concerned with drug responses due to genetically controlled variations.

pharmacokinetics – The study of what the body does to a drug.

Phase I clinical trial – The first trial(s) of a new active ingredient or new formulations in human, often carried out in healthy volunteers. Their purpose is to establish a preliminary evaluation of safety, and a first outline of the pharmacokinetic and, where possible, a pharmacodynamic profile of the active ingredients in humans (WHO, Guidelines for Good Clinical Practice for trials of pharmaceutical products). Also refer to the definition in the DOH Administrative Order No. 47-A series of 2001 "Rules and Regulations on the registration including approval and conduct of clinical trials , and lot or batch release certification of vaccines and biologic products" and need to secure a permit for clinical investigational use.

Phase II clinical trial – Trial(s) performed in a limited number of subjects, often at a later stage of a comparative (e.g., placebo-controlled) design. Their purpose is to demonstrate therapeutic activity and assess short-term safety of the active ingredient in patients suffering from a disease or condition for which the active ingredient is intended. This phase also aims at the determination of appropriate dose ranges or

regimens and (if possible) clarification of dose-response relationships in order to provide an optimal background for the design of extensive therapeutic trials (WHO, Guidelines for Good Clinical Practice for Trials of Pharmaceutical Products). Also refer to the definition in the Department of Health Administrative Order No. 47-A series of 2001, Rules and regulations on the registration including approval and conduct of clinical trials, and lot or batch release certification of vaccines and biologic products, and need to secure a permit for clinical investigational use.

Phase III clinical trial – Trial(s) in larger (and possibly varied) patient groups with the purpose of determining the short- and long-term safety/ efficacy balance of formulation(s) of the active ingredient, and of assessing its overall and relative therapeutic value. The pattern and profile of any frequent adverse reactions must be investigated and special features of the product must be explored (e.g., clinically relevant drug interactions, factors leading to differences in effect such as age). These trials should preferably be of a randomized double-blind design, but other designs may be acceptable (e.g., long-term safety studies). Generally, the conditions under which these trials are carried out should be as close as possible to normal conditions of use (WHO, Guidelines for Good Clinical Practice for Trials of Pharmaceutical Products). Also refer to the definition in the Department of Health Administrative Order No. 47-A series of 2001, Rules and regulations on the registration including approval and conduct of clinical trials, and lot or batch release certification of vaccines and biologic products, and need to secure a permit for clinical investigational use.

Phase IV clinical trial – Studies performed after marketing of the pharmaceutical product. Trials in this phase are carried out on the basis of the product characteristics on which the marketing authorization was granted and are normally in the form of the post-marketing surveillance, or assessment of therapeutic value or treatment strategies. Although methods may differ, these studies should use the same scientific and ethical standards as applied in pre-marketing studies. After a product has been placed on the market, clinical trials designed to explore new indications, new methods of administration or new combinations, among others, are normality considered as trials for new pharmaceutical products (WHO, Guidelines for Good Clinical Practice for Trials of Pharmaceutical Products). Also refer to the definition in the Department of Health Administrative Order No. 47-A

series of 2001, Rules and regulations on the registration including approval and conduct of clinical trials, and lot or batch release certification of vaccines and biologic products, and need to secure a permit for clinical investigational use.

Philippine Health Research Ethics Board – Created on 1 March 2006 through DOST Special Order No. 091 series of 2006 as a policy-making body for research ethics in the Philippines.

Philippine National Health Research System – Formally organized in 2004, it was conceptualized in support of a vibrant, dynamic, and responsible health research community working on a unified health research agenda with enhanced cooperation between the Department of Health, the Department of Science and Technology, and the Commission on Higher Education. The Philippine Health Research Ethics Board is one of the six groups working under its Governing Council.

placebo – A substance that is not biologically active, does not interact with other substances nor is it expected to affect the health status of an individual. It is an inactive pill, liquid, or powder that has no treatment value. In clinical trial, experimental treatments are often compared with placebos to assess the experimental treatment's effectiveness. In some studies, the participants in the control group will receive a placebo instead of an active drug or experimental treatment (Retrieved from http://www.Clinicaltrials.gov/ct/ info/whatis).

placebo-controlled trials – Clinical trials that assign the administration of a placebo to the control group while the test drug is given to the experimental group.

population-based genetics – The study of the distribution of genes in populations and of how the frequencies of genes and genotypes are maintained or changed.

pre-clinical trials or study – Investigation of the pharmacologic properties of a drug or preparation done in animals prior to human studies. Pre-clinical studies shall include pharmacodynamics, pharmacokinetics, and toxicity studies (BFAD, Guidelines for Registration of Pharmaceutical Products, 1997).

predictive testing – Determination of the presence of disease-associated genes prior to the onset or manifestation of the disease.

predisposition or risk testing – Determination of genetic parameters in an individual associated with increased risk of disease.

prenatal testing – Determination of whether a fetus has (or probably has) a designated condition for which an increased risk is indicated by later maternal age, family history, or other well-defined risk factors

principal investigator – The chief or person primarily responsible for the implementation of a research project. *See also investigator.*

prior dose finding – Quantity or dosage of the herbal medicine established in earlier studies or practice to be effective.

privacy – The right or claim or state or ability or condition of an individual or group or institution to conceal or seclude or hide themselves or information about themselves and thus reveal or expose themselves selectively. It is a conceptual space defining the individual's boundary as a person, intrusion of which is limited by human rights and by law. It is right to determine when, how, and to what extent information about someone is communicated to others.

product adulteration – Presence of foreign substances or impurities in the drug preparation that results in dilution or loss of its efficacy.

prospective study – Research that watches for outcomes, such as the development of a disease, during the study period and relates this to other factors such as suspected risk or protection factor(s). The study usually involves taking a cohort of subjects and watching them over a long period. The outcome of interest should be common; otherwise, the number of outcomes observed will be too small to be statistically meaningful (indistinguishable from those that may have arisen by chance). All efforts should be made to avoid sources of bias such as the loss of individuals to follow up during the study. Prospective studies usually have fewer potential sources of bias and confounding than retrospective studies (Retrieved from http://www.statsdirect.com/help/basics/prospective.htm). *See also retrospective study.*

protein – A macromolecule composed of subunits of linear chains of amino acids attached to each other by peptide bonds.

proteomic data – Information from the comprehensive analysis and cataloguing of the structure and function of all the proteins present in a given cell or tissue.

protocol – A document that provides the background, rationale, and objective(s) of a biomedical research project and describes its design, methodology, and organization, including ethical and statistical considerations. Some of these considerations may be provided in other documents referred to in the protocol (WHO, Operational Guidelines for Ethics Committees that Review Biomedical Research, 2000, TDR/PRD/ETHICS/2000, p. 22). A document that describes the objective(s), design, methodology, statistical considerations, and organization of a trial. The protocol usually also gives the background and rationale for the trial, but these could be provided in other protocol referenced documents (ICH–Guideline for Good Clinical Practice (E6, R1), art. 1.44). The formal design or plan of an experiment or research activity; specifically, the plan submitted to an IRB for review and to an agency for research support. The protocol includes a description of the research design or methodology to be employed, the eligibility requirements for prospective subjects and controls, the treatment regimen(s), and the proposed methods of analysis that will be performed on the collected data (IRB Guidebook, US Department of Health and Human Services, retrieved from http://www.hhs.gov/ohrp/irb/irb_glossary.htm) See also research protocol).

protocol amendment – A written description of a change(s) to, or formal clarification of a protocol (WHO, Operational Guidelines for Ethics Committees that Review Biomedical Research, 2000, TDR/PRD/ETHICS/2000, p. 22). *See also amendment to protocol.*

protocol approval by sponsor – The affirmative action of the sponsor on the protocol development when the technical and ethical reviewers have finally approved all the changes of the protocol. This usually act as the signal for the submission of the protocol and the other required documents to an IRB, national regulatory authorities and research sites as applicable. *See also approval.*

psychosocial needs – The needs of an individual pertaining to her social and psychological well-being.

public domain information – Data or information available and open to public observation like the list of names in the telephone directory, or events in streets and public transportation.

quality of life – A state or condition wherein an individual is able to live as how one normal person wants to live his/her life.

quasi-experimental design – A research design that does not make use of random assignment to groups, that is, it is like an experimental design but lacks the random assignment.

radiopharmaceuticals – Drugs that are used in the field of nuclear medicine as tracers in the diagnosis and treatment of certain diseases. Drugs that are labeled or tagged with a radioisotope that in many cases functions much like materials found in the body and do not produce special pharmacological effects. It can be radioactive tracer with medical applications that are administered like other drugs. It contain radioactive substances that is used in the diagnosis and treatment like cancer and in pain management of bone metastases or for enabling the production of a useful nuclear medicine image to diagnose a disease.

randomization, random assignment – The process of assigning trial subjects to treatment or control groups using an element of chance to determine the assignments in order to reduce bias (ICH Harmonized Tripartite Guideline, Guideline for Good Clinical Practice (E6, R1)). Random, random assignment, randomization, is the assignment of subjects to different treatments, interventions, or conditions according to chance rather than systematically (e.g., as dictated by the standard or usual response to their condition, history, or prognosis, or according to demographic characteristics). Random assignment of subjects to conditions is an essential element of experimental research because it makes more likely the probability that differences observed between subject groups are the result of the experimental intervention (IRB Guidebook, US Department of Health and Human Services, retrieved from http://www.hhs.gov/ohrp/irb/irb_glossary.htm).

Regional Health Research Ethics Board – Policy-making body for research ethics in a particular region in the Philippines. *See also Philippine Health Research Ethics Board.*

regulatory requirements – Necessary prerequisites for the approval and conduct of clinical trial by a national regulatory authority. For example,

for pharmaceutical and biologic products, it means obtaining a "permit for clinical investigational use" which is a "registration document issued by the FDA for the purpose of allowing the conduct of Phase I, Phase II, and Phase III clinical trials of investigational biologic products in the country" (Department of Health Administrative Order No. 47-A series of 2001, Rules and regulations on the registration including approval and conduct of clinical trials, and lot or batch release certification of vaccines and biologic products). *See also permit for clinical investigational use.*

remuneration – Payment for participation in research. *See also compensation.*

reportability (of test results) – The inclusion of an event (e.g., a diagnosis, evidence of violence against persons) in a list of items that are mandated by law to be reported to the Department of Health by designated individuals or health professionals because of their impact on public health and safety.

rescue medication – Quick-relief or fast-acting medications or procedure used to immediately manage or relieve symptoms when they occur.

research – Organized set of activities intended to generate data that are generalizable into new knowledge, principle or technology. Investigative work undertaken on a systematic and rigorous basis using quantitative and qualitative methods to generate new knowledge.

research ethics committee – An independent body (a review board or a committee, institutional, regional, national, or supranational), constituted of medical professionals and non-medical members, whose responsibility is to ensure the protection of the rights, safety and well-being of human subjects involved in a trial and to provide public assurance of that protection, by, among other things, reviewing and approving/providing favorable opinion on, the trial protocol, the suitability of the investigator(s), facilities, and the methods and material to be used in obtaining and documenting informed consent of the trial subjects (ICH–Guideline for Good Clinical Practice (E6, R1), art. 1.27). *See also Institutional Ethics Review Committee, cluster research ethics committee, ethics review committee.*

research involving traumatized populations – Study undertaken on a systematic and rigorous basis to generate new knowledge regarding

groups living in communities that have experienced hardships and stress due to natural calamities or human atrocities.

research on assisted reproductive technology – Study undertaken on a systematic and rigorous basis to generate new knowledge regarding reproduction that makes use of modern technology.

research participants or subjects – An individual who participates in a biomedical research project, either as the direct recipient of an intervention (e.g., study product or invasive procedure), as a control, or through observation. The individual may be a healthy person who volunteers to participate in the research, or a person with a condition unrelated to the research carried out who volunteers to participate, or a person (usually a patient) whose condition is relevant to the use of the study product or questions being investigated (WHO, Operational Guidelines for Ethics Committees that Review Biomedical Research, 2000, TDR/PRD/ETHICS/2000, p. 22).

research protocol – A document that provides the background rationale and objective(s) of a biomedical research project and describes its design, methodology and organization, including ethical and statistical considerations. Some of these considerations may be provided in other documents referred to in the protocol. *See also protocol.*

respect for persons – Involves a recognition of the personal dignity and autonomy of individuals, and special protection of those persons with diminished autonomy (IRB Guidebook, US Department of Health and Human Services, retrieved from http://www.hhs.gov/ohrp/irb/irb_glossary.htm). *See ethical guidelines.*

respondent – The person or group of persons answering or replying to research questions or providing the data that are collected during the research. They are also referred as subject or participant in a research and further as a unit, unit of analysis, experimental unit, during sampling or data analysis. *See also research participants.*

retrospective study – A research that looks backwards and examines exposures to suspected risk or protection factors in relation to an outcome that is established at the start of the study. Many valuable case-control studies, such as Lane and Claypon's 1926 investigation of risk factors for breast cancer, were retrospective investigations. Most sources of error due to confounding and bias are more common in

retrospective studies than in prospective studies. For this reason, retrospective investigations are often criticized. If the outcome of interest is uncommon, however, the size of prospective investigation required to estimate relative risk is often too large to be feasible. In retrospective studies the odds ratio provides an estimate of relative risk. Special care should be taken to avoid sources of bias and confounding in retrospective studies (Retrieved from http://www.statsdirect.com/help/basics/prospective.htm). *See prospective study.*

ribonucleic acid (RNA) – A single-stranded nucleic acid similar to DNA but having ribose sugar rather than deoxyribose sugar and uracil rather than thymine as one of the pyrimidine bases.

risk – The probability of discomfort or harm or injury (physical, psychological, social, or economic) occurring as a result of participation in a research study. Both the probability and magnitude of possible harm may vary from minimal to significant. Risks to research participants must be justified by the anticipated benefits to the subjects or to society. The investigator(s) and IRB must assess the risks and benefits of proposed research. *See also minimal risk.*

risk factors – Variables or conditions that increase the risk or chances of disease or infection; determinants of disease development. *See also risk.*

scientific review – Also called technical review, is the evaluation of the research protocol to ascertain scientific soundness and appropriateness of the objectives and design of the proposed study and the qualifications of the researcher. *See technical review.*

selective disclosure of information – Deliberate withholding of certain information from a patient or from a research participant usually justified by the principle of non-maleficence or, in the case of research, avoiding the introduction of bias on the part of the patient.

serious adverse event – Or serious adverse drug reaction, is an adverse event that results to death, life threatening incident or causes immediate risk of death from the event; results to inpatient or prolongation of hospitalization, causes significant disability, incapacity, and congenital anomaly or another episode which is considered a significant hazard to the participant. *See also adverse event or unexpected adverse*

event. Also, any untoward medical occurrence that at any dose: results in death, is life-threatening, requires inpatient hospitalization or prolongation of existing hospitalization, results in persistent or significant disability/incapacity, or is a congenital anomaly/birth defect (ICH–Guideline for Good Clinical Practice (E6, R1), art. 1.50). *See also adverse event, adverse drug reaction.*

shared autonomy – The autonomy of an individual member of an IP community that he/she exercises as part of a group. This concept is embedded with the notion that individual autonomy and group autonomy are complementary and not contradictory. *See also autonomy and collective autonomy.*

side effect – Undesired effect of a treatment which is either immediate or long-term.

single-gene diseases – A disorder that is determined by mutant alleles at a single locus.

site management organization (SMO) - is an organization that provides clinical trial related services to a contract research organization, a pharmaceutical company, a biotechnology company, a medical device company or a clinical site. The site is usually a hospital or a similar healthcare institution that has adequate infrastructure and staff to meet the requirements of the clinical trial protocol. The scope of an SMO's responsibility is limited to the "site" and hence the eponymous title. Some (but not all) of the responsibilities include: contract negotiations; submission for Institutional Review Board or Independent Ethics Committee (IRB/IEC) approval; patient counseling, recruitment and follow-up; informed consent form translation into vernacular languages; site initiation and trial close-out operations; trial-related documents archival and maintenance; reporting SAE to the CRO and the IRB/IEC; ensuring protocol compliance; advising and alerting investigators of potential protocol violations; advising and alerting investigators of potential ICH-GCP violations (Retrieved from http://en.wikipedia.org/wiki/Site_management_organization). *See also contract research organization.*

social and behavioral research – Study undertaken on a systematic and rigorous basis to generate new knowledge regarding the impact of sociological, psychological, anthropological and other social factors on health and well-being.

Critical Perspective – This perspective is recursive and focused on bringing about change in practices. Researchers utilizing this perspective generally have an agenda for social change. Studies under this perspective begin with an important stance about social issues and are aimed at creating political debate and discussion to bring about change. It is practical and collaborative.

Interpretive Perspective – This perspective holds that in seeking to understand their world, people develop subjective meanings of their experiences which are varied and multiple. The researcher then looks into the complexity of views rather than reducing them to a few ideas. Open-ended questions suit this perspective. Historical and social contexts are important to consider. The assumption is that the basic generation of meaning is always resulting from the interaction within social groups.

Positivist Perspective – This is sometimes referred to as the "scientific method" and is likewise called quantitative research, empirical science or postivist/postpositivist research. This reflects a deterministic philosophy which says that causes probably determine effects or outcomes. It is reductionistic because it reduces ideas into discrete sets to test in hypotheses and research questions. It utilizes careful observation and measurement of objective reality. Most of research in this perspective starts with test of a theory.

social research – Research covering broad range of disciplines and perspectives in sociology, anthropology, political science, economics, psychology, population studies, history, geography, linguistics, and other social sciences that are directly concerned with health issues. Interdisciplinary social research involves two or more of these disciplines utilizing both quantitative and qualitative approaches which are consistent with either positivist, interpretive or critical perspectives.

sponsor – An individual, a company, an institution or an organization which take responsibility for the initiation, management and/or financing of a clinical trial (ICH Harmonized Tripartite Guideline, Guideline for Good Clinical Practice (E6, R1)).

standard of care or treatment – Healthcare intervention or regimen that is generally accepted by health practitioners and experts as beneficial to

an individual needing such care. Standard treatment is the treatment that is currently thought to be effective in medical practice.

diagnostic – Professionally accepted level and type of examination to determine a patient's health condition.

prophylactic – Professionally accepted level and type of preventive management to prevent the occurrence of a particular health condition.

therapeutic – Professionally accepted level and type of treatment or assistance for a particular health condition.

stem cell research – The study of the properties, development, and transformation of primordial progenitor cells prior to establishment of specialized cells.

stigma – The negative regard (e.g., shame and dishonor) of the community or society to particular groups because of disability, illness, occupation, poverty, among others as dictated by culture.

study product – *See investigational product*.

surrogate assent – Necessary when an adult is not able to provide consent for themselves to participate in research due to: cognitive impairment, lacking capacity, or suffering from a serious or life-threatening disease. This is a protocol-specific request of the investigator, and must be reviewed and approved accordingly by the IRB (Retrieved from http://www.virginia.edu/vpr/irb/hsr/surrogate_assent.html). *See also assent and child's assent*.

susceptibility or predisposition (to disease) – The pathophysiological conditions and genetic inclination or condition that favor the development of a disease condition.

suspected unexpected serious adverse reaction (SUSAR) – A serious adverse reaction in research participants who were given a drug, that may or may not be dose related, but are not expected or anticipated since these reactions are not consistent with current information about the medicinal product in question. This may occur during clinical trials or clinical care. Current reporting required by FDA is in http://umis.

doh.gov.ph/adverse. *See also adverse event, adverse drug reaction, and unexpected adverse event.*

technical review – The process of examining, assessing or evaluating a research protocol by technical experts, seasoned researchers, statisticians and other relevant specialist or authority to ensure the scientific soundness and appropriateness of the objectives and design of the study and the qualifications of the investigator(s). *See scientific review.*

teratogenicity – The degree or measure of the ability to cause malformations of an embryo or fetus.

termination of the research – Ending or discontinuing a research study before its scheduled completion when the safety or benefit of the study participants is doubtful or at risk.

test preparation – The formulation or preparation of the herbal remedy or product that is going to be used in the study.

therapeutic window – The time period, based on available scientific evidence, during which the test article must be administered to have its potential clinical effect.

toxicity – Level or extent of being poisonous to a living organism or person; ability to cause grave harm or death.

traditional and alternative healthcare – The sum total of knowledge, skills and practices on healthcare, other than those embodied in biomedicine, used in the prevention, diagnosis and elimination of physical and mental disorder (Traditional and Alternative Medicine Act, 1997).

Traditional and Alternative Medicine Act (TAMA) – The 1997 law creating the Philippine Institute of Traditional and Alternative Health Care (PITAHC) to accelerate the development of traditional and alternative healthcare in the Philippines, providing for a Traditional and Alternative Health Care Development Fund and for other purposes including its integration to the national healthcare delivery system.

traditional healer – The relatively old, highly placed respected person in the community, with a profound knowledge of traditional remedies (Traditional and Alternative Medicine Act, 1997).

traditional medicine – The sum total of knowledge, skills, and practices in healthcare, not necessarily explicable in the context of modern, scientific, philosophical framework, but recognized by the people to help maintain and improve their health towards the wholeness of their being, the community and society, and their interrelations based on culture, history, heritage, and consciousness (Traditional and Alternative Medicine Act, 1997).

traditional medicine expert – A healthcare provider employing traditional medicine modalities to cure disease.

traumatized populations – Individuals who live in communities that have experienced extreme forms of life-threatening stress due to natural calamities or human atrocities such as armed conflict, political repression as well as criminal and domestic violence.

trial-related expenses – Expenses incurred by study participants related to their participation in a research study such as transportation, meals, loss of income.

undue influence – An inappropriate power, pressure or control or domination which may be mental, moral or physical that deprives a person of freedom of judgment, choice and thus, substitutes another's choice or desire in place of its own.

unexpected adverse event – An adverse reaction that has not been anticipated, nor previously experienced, or observed, and is not consistent with the informed consent, information sheets or applicable product information in the investigator's protocol or brochure, product or package insert or summary of product characteristic. *See also adverse event and serious adverse event.*

United Nations Declaration of Rights of Indigenous Peoples – A statement adopted by the UN General Assembly on Resolution 61/295 on 13 September 2007 affirming that indigenous peoples are equal to all other peoples, while recognizing the right of all peoples to be different, to consider themselves different, and to be respected as such; that indigenous peoples, in the exercise of their rights, should be free from discrimination of any kind; and that indigenous peoples have the right to the full enjoyment, as a collective or as individuals,

of all human rights and fundamental freedoms as recognized in the Charter of the United Nations, the Universal Declaration of Human Rights and international human rights law (Retrieved from http://www.un.org/sea/soc/dev/unpfii/en/drip.html).

voluntary – Free of coercion, duress, or undue inducement; used in the research context to refer to a subject's decision to participate (or to continue to participate) in a research activity (IRB Guidebook, US Department of Health and Human Services, retrieved from http://www.hhs.gov/ohrp/irb/irb_glossary.htm).

vulnerability – A substantial incapacity to protect one's own interests owing to such impediments as lack of capability to give informed consent, lack of alternative means of obtaining medical care or other expensive necessities, or being a junior or subordinate member of a hierarchical group (CIOMS, International Ethical Guidelines for Biomedical Research Involving Human Subjects, 2002).

vulnerable persons/groups – Individuals whose willingness to volunteer in a clinical trial may be unduly influenced by the expectation, whether justified or not, of benefits associated with participation, or of a retaliatory response from senior members of a hierarchy in case of refusal to participate (ICH–Guideline for Good Clinical Practice (E6, R1), art. 1.61). Vulnerable persons are those who are relatively (or absolutely) incapable of protecting their own interests. More formally, they may have insufficient power, intelligence, education, resources, strength, or other needed attributes to protect their own interests (CIOMS, International Ethical Guidelines for Biomedical Research Involving Human Subjects, 2002). These are also classes of individuals who have characteristics that lessen their capacity to protect their own interests or promote their own welfare; These are "persons whose situation or characteristics may make them unable to provide free and informed consent to participate in research. This group includes children, institutionalized persons, those who have cognitive impairments, and those in a position of inferiority" (Retrieved from http://www.pre.ethics.gc.ca.engish/tutorial/glossary.cfm#c).

waiver of informed consent – The act of intentionally or knowingly relinquishing or abandoning the right to consent to medical treatment by a patient or to participate in a medical experiment by a subject after achieving an understanding of what is involved, especially the risks (Merriam-Webster's Dictionary of Law (c), 1996). It is also

refers to the permission given by an Ethics Review Committee for research to be conducted without the informed consent of subjects, under exceptional circumstances, such as when research has to be undertaken in an emergency situation.

Western medicine – Or biomedicine, allopathy, regular medicine, conventional medicine, mainstream medicine, orthodox medicine or cosmopolitan medicine. *See conventional medicine.*

withdraw – Decision of the subject or respondent or patient to continue participating in research or clinical trial. *See discontinuation.*

zygote – The product of the biological union of the human sperm and egg (process of fertilization) until the blastocyst (32-cell) stage prior to implantation in the endometrium (0 to 4-5 days).

REFERENCES

Bhutta, Z. A. (2000). Ethics in international health research: A perspective from the developing world. *Bulletin of the World Health Organization,* 80(3), 114–120.

Braveman, P. & Gruskin, S. (2003). Defining equity in health. *Journal of Epidemiology of Community Health,* 57(4), 254–258.

Council for International Organizations of Medical Sciences (CIOMS). (2002). *International Ethical Guidelines for Biomedical Research Involving Human Subjects* (Guideline No. 4). Geneva: Council for International Organizations of Medical Sciences.

Department of Health. (2008). *Rules and regulations on the registration including approval and conduct of clinical trials, and lot or batch release certification of vaccines and biologic products* (Administrative Order 47-A s 2001). Manila: Department of Health.

Emanuel, E. J., Wendler D., Grady, C. (2000). *What makes clinical research ethical?* JAMA 283(20): 2701-11.

Forum for Ethical Review Committees in the Asian and Western Pacific Region (FERCAP). (2005). *International Conference on Standard Operating Procedures of Ethical Review Committee.*

Freedman, R. (1987). Equipose and the ethics of clinical research. *New England Journal of Medicine*, 317(3), 141–145.

Gertel, A., Block, P. B., Gawrylewski, H. M., Raymond, S. A., Quinn, T., Muhlbradt, E. (2009) CDISC Clinical Research Glossary Version 8.0. Applied Clinical Trials at appliedclinicaltrialsonline.com

Gordis, L. & Gold, E. (1980). Privacy, confidentiality, and the use of medical records in research. *Science*, 207, 153–156.

International Conference on Harmonization. (1996). Guidance for industry–E6 good clinical practice: Consolidated guidelines. Retrieved from http://www.fda.gov/downloads/regulatoryinformation/guidances/ucm129515.pdf

International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use. (1995). ICH harmonized tripartite guideline, structure and content of clinical study reports (E3). Retrieved from http://www.ich.org/fileadmin/Public_Web_Site/ICH_Products/Guidelines/Efficacy/E3/Step4/E3_Guideline.pdf

International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use. (1996). ICH harmonized tripartite guideline, guideline for good clinical practice (E6) (R1). Retrieved from http://www.ich.org/fileadmin/Public_Web_Site/ICH_Products/Guidelines/Efficacy/E6_R1/Step4/E6_R1__Guideline.pdf

International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use. (1997). ICH harmonized tripartite guideline, general consideration for clinical trials (E8). Retrieved from http://www.ich.org/fileadmin/Public_Web_Site/ICH_Products/Guidelines/Efficacy/E8/Step4/E8_Guideline.pdf

International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use. (2000). ICH harmonized tripartite guideline, choice of control group and related issues in clinical trials (E10). Retrieved from http://www.ich.org/fileadmin/Public_Web_Site/ICH_Products/Guidelines/Efficacy/E10/Step4/E10_Guideline.pdf

KFPE. (1998). Guidelines for Research in Partnership with developing Countries: 11 principles. KFPE, Berne

KFPE. (2010). Guidelines for Research in Partnership with developing Countries: 11 principles. KFPE, Berne (unpublished)

Lansang, M. A. & Crawley, F. P. (2000). The ethics of international biomedical research. *British Medical Journal,* 321, 777 –778.

Margetts, B., Arab, L., Nelson, M., & Kok, F. (1999). Who and what sets the international agenda for research and public health action? *Public Health Nutrition*, 2, 35–36.

National Center for Complementary and Alternative Medicine, National Institutes of Health, US Department of Health and Human Services. (2006). *Understanding CAM.* Retrieved from http://nccam.nih.gov/

National Center for Complementary and Alternative Medicine, National Institutes of Health, US Department of Health and Human Services. (2011). *What Is Complementary and Alternative Medicine?* Retrieved from http://nccam.nih.gov/health/whatiscam/D347.pdf

National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research. (1978). *The Belmont Report: Ethical principles and guidelines for the protection of human subjects of research*. US NIH–Office of Human Research Subjects. Retrieved from http://ohrp.osophs.dhhs.gov/humansubjects/guidance/belmont.htm

Philippine Obstetrical and Gynecological Society, Inc. (POGS), 2004. *Ethical Guidelines in Obstetrical Practice, Medical Education, and Research.*

Porter, A. L., Youtie J., Shapira P., Schoeneck D. J. (2008). *Refining search terms for nanotechnology.* Nanopart Res 10:715–728. DOI 10.1007/s11051-007-9266-y.

Reyes, M. V. T. (2004). *Directions in Philippine health research: Ethics review. In Proceedings of the First Philippine National Health Research System Assembly*. Manila: Philippine National Health Research System.

Rothman, K. (1991). *The ethics of research sponsorship*. Journal of Clinical Epidemiology, 44, 25S–28S.

South African Medical Research Council. (2005). *Guide to ethical considerations in medical research*. Africa: South African Medical Research Council.

Swiss Commission for Research Partnership with Developing Countries. (1998). *Guidelines for research in partnership with developing countries*. Berne: Swiss Academy of Sciences.

Torres-Edejer, T. T. (1999). *North-South research partnerships: The ethics of carrying out research in developing countries*. British Medical Journal, 319, 438–441.

Wejer, C. & Emanuel, E. J. (2000). *Protecting communities in biomedical research*. Science, 289, 1142–1144.

World Health Organization. (2000). *General guidelines for methodologies on research and evaluation of traditional medicine*. Retrieved from http://www.paho.org /Spanish/AD/THS/EV/PM-WHOTraditional-medicines-research-evaluation.pdf

World Health Organization. (1995). *Guidelines for good clinical practice for trials of pharmaceutical products* (WHO Technical Reports Series No. 850, Annex 3). Geneva: World Health Organization.

World Health Organization. (2000). (OGECRBR) *Operational guidelines for ethics committees that review biomedical research*. Geneva: World Health Organization.

World Health Organization. (2005). *Operational guidelines for the establishment and functioning of data and safety monitoring boards*. Geneva: World Health Organization.

World Health Organization. (2005). *Special Programme for Research and Training in Tropical Diseases*. Geneva: World Health Organization.

World Health Organization. (2005). *Special Programme for Research and Training in Tropical Diseases –Operational guidance: Information needed to support clinical trials of herbal products*. Geneva: World Health Organization.

World Medical Association. (2008). *Declaration of Helsinki–Ethical principles for medical research involving human subjects*. Retrieved from http://www.wma.net/en/30publications/10policies/b3/index.html

Other References

Conflicts of Interest: Retrieved from http://www.icmje.org/ethical_4conflicts.html

Editorship: Retrieved from http://www.icmje.org/ethical_2editor.html Peer

Review: Retrieved from http://www.icmje.org/ethical_3peer.html Privacy

and Confidentiality: Retrieved from http://www.icmje.org/ethical_5privacy.html

Protection of Human Subjects and Animals in Research: Retrieved from http://www.icmje.org/ethical_6protection.html

Nanotechnology: Retrieved from http://www.foresight.org/

SUBJECT INDEX

Appendix A1:
Template for Patient Information and Informed Consent Form

Project Title: _____

Sponsor: _____

Investigator(s): _____

Purpose and conduct of study

- Why is the study being done?
- What has been done previously?
- How will the present study be conducted?
- What is the nature and extent of involvement of research participants?

Risks and inconveniences

- Will there be discomforts? Are these described clearly?
- Will there be risks? Are these explained fully?
- Are there other effects the participants need to know in order to make a decision?

Possible benefits for the participants

- What benefits can the participants expect?

Compensation

- Will there be reimbursement of travel expenses? Compensation for loss of income? Meal expenses?
- Are there other financial considerations?

Provision for injury or related illness

- Will the participant be given free treatment in case of injury or illness incurred as a result of participating in the study?

Contact person

- Who is the person knowledgeable about the research and rights of the participant? How can he/she be contacted?

Voluntariness of participation

- Is the participant free of any coercion in participating?
- Is there assurance that the participant can withdraw anytime without affecting treatment/care due him/her?
- Is there provision for obtaining the informed consent from the legal representative in case of minors, the mentally handicapped or the incapacitated?

Confidentiality

- Is there a statement that describes the measures that will be taken to keep and ensure the confidentiality of the participant's records?

CONSENT FORM

I have read and understood the above information and had been given the opportunity to consider and ask questions on the information regarding the involvement in this study. I have spoken directly to my doctor who has answered to my satisfaction all my questions. I have received a copy of this Patient Information and Informed Consent Form. I voluntarily agree to participate.

Patient's
Signature:

Name of Patient	Signature of Patient	Date

Witness or Legal Guardian's Signature:
(Only when patient cannot read or sign this Informed Consent)

Name of Witness/ Legal Guardian	Signature of Witness/ Legal Witness	Date

Physician's Signature:

I, the undersigned, certify that to the best of my knowledge, the patient signing this consent form has read the above information sheet fully, that this has been carefully explained to him/her, and that he/she clearly understands the nature, risks, and benefits of his/her participation in this study.

Name of Physician	Signature of Physician	Date

Appendix A2:
Sample Checklist for the Assessment of the Informed Consent Form

Both the informed consent discussion and the written informed consent form and any other written information to be provided to subjects should include explanations of the following:

Are the following included in the written information provided to the subjects?

	Yes	No	Comment
a. That the trial involves research. b. The purpose of the trial. c. The trial treatment(s) and the probability for random assignment to each treatment. d. The trial procedures to be followed, including all invasive procedures. e. The subject's responsibilities. f. Those aspects of the trial that are experimental. g. The reasonably foreseeable risks or inconveniences to the subject and, when applicable, to an embryo, fetus, or nursing infant. h. The reasonably expected benefits. When there is no intended clinical benefit to the subject, the subject should be made aware of this. i. The alternative procedure(s) or course(s) of treatment that may be available to the subject, and their important potential benefits and risks. j. The compensation and/or treatment available to the subject in the event of trial-related injury. k. The anticipated prorated payment, if any, to the subject for participating in the trial. l. The anticipated expenses, if any, to the subject for participating in the trial. m. That the subject's participation in the trial is voluntary and that the subject may refuse to participate or withdraw from the trial, at any time, without penalty or loss of benefits to which the subject is otherwise entitled. n. That the monitor(s), the auditor(s), the IRB/IEC, and the regulatory authority(ies) will be granted direct access to the subject's original medical records for verification of clinical trial procedures and/or data, without			

	Yes	No	Comment
violating the confidentiality of the subject, to the extent permitted by the applicable laws and regulations and that, by signing a written informed consent form, the subject or the subject's legally acceptable representative is authorizing such access. o. That records identifying the subject will be kept confidential and, to the extent permitted by the applicable laws and/or regulations, will not be made publicly available. If the results of the trial are published, the subject's identity will remain confidential. p. That the subject or the subject's legally acceptable representative will be informed in a timely manner if information becomes available that may be relevant to the subject's willingness to continue participation in the trial. q. The person(s) to contact for further information regarding the trial and the rights of trial subjects, and whom to contact in the event of trial-related injury. r. The foreseeable circumstances and/or reasons under which the subject's participation in the trial may be terminated. s. The expected duration of the subject's participation in the trial. t. The approximate number of subjects involved in the trial.			

	Yes	No	Comment
Is the informed consent form written in a language understandable to the participants?			

	Yes	No	Comment
Does the informed consent process ensure that it is voluntary?			

Appendix B:
Ethics Review Committee's Standard Application Form for Ethical Evaluation of Proposed Study

General Instruction

Please accomplish ___(number) copies of this application form and attach them to copies of the proposal submitted for review.

1. Reference Number (To be assigned by the ERC): _____

2. Name of Applicant/Organization/Institution: _____

3. Address / Contact Numbers: _____

4. Project Coordinator or Principal Investigator:
   Name: _____
   Position: _____
   Address: _____
   Contact Numbers (Tel / Fax / Mobile / e-mail address): _____

5. Project Title: _____

   _____

6. Type of Study (basic research, clinical trial (randomized, placebo controlled, double blind), social research, epidemiology, survey, etc.)

   _____

7. Expected Number of Participants: _____

8. Planned Start Date: _____

9. Project Abstract (not more than 250 words):

10. Ethical Concerns (Are there any ethical issues that can be foreseen in the implementation of the project?):

11. Date of Submission: _____

12. Received By: _____

Note: The ERC evaluation will normally require eight weeks from receipt of the complete proposal from the proponent.

For further information, contact:

Name of Contact Person
Name of Institutional Ethics Review Committee
Address
Contact Number
Email Address

Appendix C:
List of Documents Required for Submission to the Ethics Review Committee

1. _____ (number) copies of the final protocol or amendments (when applicable)

2. _____ (number) copies of informed consent form (written in English and Filipino or dialect spoken and understood by research participants)

3. _____ (number) copies of Patient/Participant Information Sheet (written in English and Filipino or dialect spoken and understood by research participants)

4. Curriculum vitae of project investigator(s)

Appendix D:
Composition of the National Ethics Committee (2011)

Chair

MARITA V.T. REYES, M.D.
Professor, Department of Biochemistry and Molecular Biology, College of Medicine, UP Manila

Members

LEONARDO D. DE CASTRO, Ph.D.
Professor, Department of Philosophy, UP Diliman

JAIME C. MONTOYA, M.D., M.Sc.
Executive Director, Philippine Council for Health Research and Development

FILIPINAS F. NATIVIDAD, Ph.D.
Assistant Vice-President and Director, Research and Biotechnology Division, St. Luke's Medical Center

BENJAMIN C. VITASA, M.D., M.P.H., Ph.D.
Professor, Department of Environmental and Occupational Health, College of Public Health, UP Manila

SONNY MATIAS E. HABACON, M.D.
Clinician, Far Eastern University

FELICIDAD H. ROMUALDEZ
Community Representative

Appendix E:
Composition of the Philippine Health Research Ethics Board (2010–2013)

Chair

LEONARDO D. DE CASTRO, Ph.D.
Philosophy

Co-Chair

MARITA V.T. REYES, M.D.
Health Research

Members

ANGELES T. ALORA, M.D.
Academe

XERXES Z. ARCENAL
People's Organization

AGNES JOYCE G. BAILEN, Ll.B.
Law

WINSTON CHAM, M.D.
Allied Health

MIGUEL MANUEL C. DOROTAN
Youth

REINER W. GLOOR
Sponsor/Funding

JAIME C. MONTOYA, M.D., M.Sc., CESO III
Executive Director, PCHRD
(Ex-officio)

MICHAEL TAN, Ph.D.
Social Science

CECILIA V. TOMAS, M.D.
Medicine

CRISPINITA A. VALDEZ
Chair, DOH-Research Ethics Committee
(Ex-officio)

Appendix F:
Policies and Procedures for Registration and Accreditation of Research Ethics Committees

RATIONALE AND GOAL

An effective human research protection system must have appropriate mechanisms for oversight and proper recognition of research ethics committees.

Such mechanisms for oversight include registration and accreditation of Ethics Review Committees. Registration helps in monitoring performance and in the identification of research ethics committees that need assistance for further development in quality review. Accreditation, on the other hand, helps improve not only the substantive but also the procedural aspects of scientific and ethical review of research involving human participants.

It is for this reason that the Philippine Health Research Ethics Board established policies for registration and accreditation of research ethics committees in the Philippines.

The policies promote the establishment of procedures, mechanisms, and standards that enable ethics committees to conduct quality scientific and ethical review of research protocols and thereby ensure the safety and protection of the rights and welfare of the participants in research.

COVERAGE

These policies are meant for all research ethics review committees (RERCs) in the Philippines, categorized as follows:

- **Academic Institution-based ERCs.** These are ERCs that are organized in universities or colleges.
- **Hospital-based ERCs.** These ERCs function in a hospital.
- **Independent ERCs.** These IERCs exist and operate as individual units and are not affiliated with any institution.
- **Cluster ERCs.** These CERCs are formed by several institutions who, together, agreed to support and develop a common ERC. The management and administration of a CERC is determined by the memorandum of agreement among these institutions.

- **Regional ERCs.** These ERCs are organized as a consortium under the supervision of the Regional Health Research and Development Offices and function as ethics review committees for researches conducted in institutions (without their own ERCs) within the region.
- **Clinical research organization-based ERCs.** These ERCs are organized within a clinical research organization.
- **Contract research organization-based ERCS.** These ERCs are under a contract research organization.
- **Research site-based ERCs.** These research ethics committees operate within and for one or several research sites not covered by categories 1, 2 or 3. A research site-based RERC shall register and may apply for accreditation as a whole unit regardless of the number of sites or facilities the research will engage.
- **Private corporation-based ERCs.** These RERCs function in for-profit or non-profit corporations.

I. Registration

Registration of a research ethics committee is mandatory (DOST AO 001 Series 2008).

A. Documents to Submit

In applying for registration, the RERC shall submit the following:

1. documents pertaining to the composition of the RERC, including the curriculum vitae and research ethics review-related training certificates;
2. documents pertaining to the authority that created the RERC;
3. documents pertaining to the office and membership of the RERC Secretariat (including office/email address, and curriculum vitae and description of roles and responsibilities of personnel/secretariat);
4. data on type and number of research protocols to review per year;
5. information regarding review fees, if any.

These documents should be sent to the PHREB Secretariat, either through:
Mail: 3rd Floor, Room 306, DOST Main Bldg., Bicutan, Taguig City

Telephone: (632) 837-7537
Telefax: (632) 837-2924
E-mail: ethics.secretariat@yahoo.com

B. Processing Fee

The applicant shall pay a non-refundable processing fee of two hundred pesos (Php200.00). The fee is due at the time of filing of all the required documents.

C. Evaluation of Documents

The PHREB Committee on Standards and Accreditation shall evaluate the application and grant approval within 30 days following the submission of all required documents and payment of the processing fee by the RERC.

D. Certificate of Registration and Validity

The Certificate of Registration of an RERC is valid for three years unless sooner revoked.

E. Renewal of Registration

Requirements for renewal include submission of the updated documents, including CVs of members, certificates of training in research ethics review, and annual reports in the last three years.

An RERC may apply for renewal by complying with the requirements two months before the expiry of its registration.

Applications for renewal found to be sufficient in form and substance shall be approved and shall take effect on the day following the expiry of the previous registration.

Applications for renewal of registration should be sent to the PHREB Secretariat, either through:

Mail: 3rd Floor, Room 306, DOST Main Bldg., Bicutan, Taguig City
Telephone: (632) 837-7537
Telefax: (632) 837-2924
E-mail: ethics.secretariat@yahoo.com

F. Suspension or Revocation

Registration may be suspended or revoked for a valid and sufficient cause as determined by the PHREB Subcommittee on Standards and Accreditation Proper. Notice shall be served on the RERC whose registration has been suspended or revoked.

II. Accreditation

Accreditation is voluntary. Only a duly-registered RERC, however, may apply for accreditation. Accreditation ensures that the ERC is effective, efficient and independent in the performance of its duties.

A. Criteria for accreditation include:

1. functionality of the structure and membership of the ERC;
2. adequacy of the Standard Operating Procedures and consistency in its implementation;
3. adherence to international, national and institutional guidelines and policies;
4. completeness of the review process;
5. adequacy of the after-review procedures;
6. adequacy of administrative support for ERC activities;
7. efficient and systematic recording and archiving;

B. The Accreditation Process

There are four steps in the accreditation process: Application, Self-assessment, Onsite Assessment and Issuance of Accreditation Certificate.

1. Application

The ERC shall submit a letter indicating interest in undergoing the accreditation process and the following documents:

a. copy of the certificate of registration;
b. description of the Committee membership including names of members, officers, expertise, training, number of years of service;
c. written summary of the ERC standard operating procedures and policies;

d. summary of actions taken by the RERC within the immediate past year.

The application letter with the required documents should be sent to the PHREB Secretariat, through any of the following:

Mail: 3rd Floor, Room 306, DOST Main Bldg., Bicutan,
Taguig City
Telephone: (632) 837-7537
Telefax: (632) 837-2924
E-mail: ethics.secretariat@yahoo.com

The Committee on Standards and Accreditation shall inform the applicant ERC if its application has been approved (within two weeks) and therewith provide it with the self-assessment form to be accomplished by a responsible person from the ERC.

2. Self-assessment

Self-assessment consists of reviewing a list of items/ requirements deemed essential for an ERC to function effectively, efficiently, and independently. In accomplishing the form, the ERC indicates the degree to which it has complied with these requirements and its readiness for accreditation. This procedural step, therefore, makes the ERC aware of its deficiencies and presents an opportunity to correct them. This step may take up to six months, afterwhich the ERC should communicate whether it is ready for the next step or it wishes to defer its application.

Communications must be sent to the PHREB Secretariat, through any of the following:

Mail: 3rd Floor, Room 306, DOST Main Bldg., Bicutan,
Taguig City
Telephone: (632) 837-7537
Telefax: (632) 837-2924
E-mail: ethics.secretariat@yahoo.com

3. Accreditation Team Assessment Visit

A team of visitors from the PHREB SubCommittee on Standards and Accreditation shall conduct a scheduled onsite visit to ascertain the degree of compliance with the seven criteria of accreditation and to evaluate the correctness of the documents, the consistency of these documents with the actual practices of the ERC, and the manner in which documents are filed and stored.

Prior to the visit, the accreditation team shall identify the documents for review (e.g., written standard operating procedures, membership files, terms of reference of the members, representative protocols, minutes of meetings, communications, log book, if any) and the persons for interview (ERC chair and members, appointing authority and administrative staff). The team shall also specify the activities to be undertaken during the visit, e.g., opening and closing meetings, interviews and inspection of the ERC office including the archives. The visit lasts for two days.

The Accreditation team shall present its findings to the ERC during the closing meeting during which matters can be clarified for inclusion in the final report.

4. Issuance of Accreditation Certificate

The applicant RERC shall be notified of the final observations and recommendations and Status of the Application within 60 days after the onsite visit.

PHREB may issue any of the three categories of accreditation or withhold accreditation based on the findings during the onsite visit as follows:

Level 1 – The ERC has demonstrated sufficient competency and efficiency in ethical review and adheres to a set of appropriate standard operating procedures. However, it may not have an office and staff of its own.

Level 2 – The ERC has demonstrated sufficient competency and efficiency in ethical review, adheres to a set of appropriate standard operating procedures and has adequate administrative support – office, standard equipment and administrative staff.

Level 3 – The ERC has demonstrated sufficient competency and efficiency in ethical review, adheres to a set of appropriate standard operating procedures, has adequate administrative support, maintains an updated database of reviewed protocols and has established an informative and very good archival system.

Accreditation may be withheld pending satisfactory compliance with some requirements, afterwhich Level 1, 2 or 3 accreditation may be granted.

C. Levels of Accreditation

Level 3 accreditation gives the ERC the privilege to be part of the Ethics Review Resource Committees of the Philippine FDA. This means that it can be called upon by the FDA to conduct ethical reviews for the purposes of FDA or in behalf of the latter. Level 3 may also be required for ethics committees that review investigational new drugs (IND) or device protocols where results will be submitted in support of registration for marketing authorization. Such ECs are required to comply with ICH GCP standards.

Level 2 accreditation qualifies an ERC to review clinical trials protocols not intended for registration of new drugs. This shall include clinical trials conducted by doctors in hospitals to test safety and efficacy of clinical interventions, products, among others.

Level 1 accreditation qualifies an ERC to review researches involving human participants except clinical trials.

The ERC may apply for an upgrading of its accreditation by a formal presentation of the additional requirements.

D. Evaluation Fee

A non-refundable evaluation fee of _____shall be charged. The fee covers the costs of Evaluation and onsite visit.

The fee schedule shall be based on the size and complexity of the ERC being evaluated. They may be adjusted to reflect the costs of accreditation evaluation.

E. Period of Validity

The Certificate of Accreditation is valid for three years from the date of issuance unless sooner revoked or terminated.

F. Submission of Annual Report by an Accredited ERC

During the period of validity of its accreditation, the ERC must submit an annual report that includes the following information:

1. changes in committee chair and membership;
2. trainings attended by current members;
3. summary of types of protocols reviewed, approved, revised, disapproved;
4. summary of the criteria for disapproval;
5. summary of recognitions received by the ERC or significant events that have affected the performance of its duties.

Annual Reports should be sent to the PHREB Secretariat, either through:

Mail: 3rd Floor, Room 306, DOST Main Bldg., Bicutan,
Taguig City
Telephone: (632) 837-7537
Telefax: (632) 837-2924
E-mail: ethics.secretariat@yahoo.com

G. Renewal of Accreditation

Within two months before the expiry of its accreditation, an REC may apply for renewal. The Subcommittee on Standards and Accreditation shall evaluate the application for renewal based on the annual reports and performance in the past three years. The ERC shall be notified of

any follow-up action or of the approval of the application for renewal.

H. Suspension and Revocation

Accreditation may be suspended or revoked for a valid and sufficient cause as determined by the PHREB SubCommittee on Standards and Accreditation. Proper notice shall be served on the REC whose registration has been suspended, or revoked.

The status of accreditation of ERCs shall be regularly and periodically reported to the Philippine FDA for its guidance.

III. Posting or Displaying of Certificate of Registration and/or Certificate of Accreditation

An ERC is enjoined to post or display its duly-secured certificate of registration and accreditation in a conspicuous area within its office.

Any posting or display of an outdated, revoked, defaced or fraudulent certificate of registration or accreditation that might deceive or mislead researchers, sponsors, prospective participants, and other persons is considered a serious offense. Appropriate disciplinary action may be imposed on the concerned ERC.

Appendix G:
Standard Operating Procedures of Ethics Review Committees

The work of the ERC can be greatly helped by its Standard Operating Procedures (SOPs) which are detailed, written instructions, in a certain format, describing all activities and action undertaken by the ERC to achieve uniformity of the performance of its functions. The aim of the SOP is to simplify the organization and documentation of the operation of the ERC.

The objectives of ERC SOPs include:

1. define the process for formulating, writing, implementing and amending procedures within the ethics committee;
2. serve as an operating manual;
3. provide clear instructions in the ethical review process;
4. improve ethical review through consistent written procedures;
5. provide basis for continuous quality improvement of the research review process.

The ERC SOPs explain the processes for constituting the Ethics Review Committee, review procedures and meetings of the committee. These will facilitate management of protocol submissions, initial and continuing review, submission of final/completed study report, monitoring of the conduct of research study and filing of documents and archiving. Transparency of and communicating procedures to all stakeholders will be of benefit to all concerned and lessen the delay in the action of ERC as well as lessen possible areas of conflict.

SOPs shall be publicly available to all, both electronically and in hard copy. The ERC shall use the most recent approved version of its SOP manual while retaining all previous versions in its files. The SOP manual of an ERC must be made available to relevant bodies and individuals.

All kinds of forms to be used by ERC – application form templates, assessment checklists, communication letter templates, tables, among others should be included in the SOP manual, and if possible, made available to principal investigators electronically. Flow charts may be included in the SOP to make visible, at a glance, the sequence of processes/tasks to be done.

TOPICS

1. Preparing SOPs and Guidelines for Ethics Committee
   a. Writing, Reviewing, Distributing and Amending SOPs for Ethics Committee
   b. Preparation of Guidelines

2. Constituting an Ethics Committee
   a. Constitution, Duties and Responsibilities of ERC and Terms of Reference
   b. Confidentiality Agreement / Conflict of Interest Disclosure
   c. Training of ERC Members and Personnel
   d. Selection of Independent Consultants
   e. Resignation, Replacement and Disqualification of ERC Members
   f. ERC Fees and Compensation of IEC/IRB and Consultants (If applicable)

3. Initial Review Procedures
   a. Management of Protocol Submissions (Protocol Package Checklist)
   b. Use of Study Assessment Forms (Checklists for Technical Review , ERC Review Assessment , Informed Consent Document)
   c. Full Board Review of Submitted Protocols
   d. Expedited Review
   e. Review of New Medical Device Studies
   f. Review of Special Studies (e.g., indigenous communities, behavioral, genetics, pediatrics, etc.)

4. Protocol Amendments, Continuing Review and End of Study Review
   a. Review of Resubmitted Protocols
   b. Review of Protocol Amendments
   c. Continuing Review of Study Protocols
   d. Review of Final Reports (including termination, suspension or withdrawal of ERC approval, if applicable)

5. Monitoring Protocol Implementation
   a. Non-Compliance / Study Deviations/Violations
   b. Response to Participants' Requests/Complaints
   c. Management of Study Termination/Withdrawal of Ethical Approval

6. Monitoring and Evaluation of Adverse Events
    a. Reporting, Monitoring and Evaluation of Serious Adverse Events (SAEs) and Suspected Unexpected Serious Adverse Reports (SUSARs)

7. Site Monitoring

8. Preparation of Meeting
    a. Agenda Preparation
    b. Meeting Procedures and Minutes of Regular ERC Meetings
    c. Preparation and Conduct of Emergency/Special Meeting
    d. Preparation of ERC Meeting Minutes
    e. Management of Communications/Records

9. Managing of Study Files
    a. Maintenance and Storage of Active Study Files
    b. Archiving and Retrieval of Documents (Inactive/Terminated/ Completed Studies)
    c. Maintenance of Confidentiality of Study Files and ERC Documents

10. Maintenance, Storage, Disposal of Administrative Files, Logbooks and Forms

Appendix H:
Standard Operating Procedure (SOP) Template

	Institution (Name of Ethics Review Committee) STANDARD OPERATING PROCEDURES		
	SOP TITLE	SOP No.	
		Version No.	
		Version Date	
		Effectivity	

1. STATEMENT OF POLICY

2. OBJECTIVE/S OF THE SOP

3. SCOPE / APPLICABILITY

4. ROLES AND RESPONSIBILITIES

5. FLOWCHART

6. DESCRIPTION OF PROCEDURES

7. FORMS / TOOLS

8. HISTORY

9. GLOSSARY