



PHILIPPINE NATIONAL  
HEALTH RESEARCH SYSTEM



PHILIPPINE HEALTH  
RESEARCH ETHICS BOARD

# NATIONAL ETHICAL GUIDELINES

FOR HEALTH AND HEALTH-RELATED RESEARCH

# 2017

# **NATIONAL ETHICAL GUIDELINES FOR HEALTH AND HEALTH-RELATED RESEARCH 2017**

Prepared by the  
Philippine Health Research Ethics Board  
**Ad Hoc Committee for Updating the National Ethical Guidelines**

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Philippine Health Research Ethics Board  
c/o Philippine Council for Health Research and Development  
Department of Science and Technology  
Bicutan, Taguig City 1631, Philippines

## RESOLUTION

### **“RECOGNIZING DR. MARITA V.T. REYES AND THE MEMBERS OF THE AD HOC COMMITTEE FOR THEIR EFFORTS ON THE REVISION OF THE NATIONAL ETHICAL GUIDELINES”**

**WHEREAS**, the Ad Hoc Committee for the Updating of the National Ethical Guidelines was created to update the existing ethical guidelines to ensure adherence to local, national, and international principles and values and respect for Filipino morals and culture;

**WHEREAS**, the Ad Hoc Committee for the Updating of the National Ethical Guidelines was created on 13 January 2015, with Dr. Marita V.T. Reyes as Chair and the following as members: Dr. Rosario Angeles T. Alora, Dr. Leonardo D. de Castro, Prof. Edlyn B. Jimenez, Dr. Ricardo M. Manalastas, Jr., Dr. Evangeline O. Santos, and Dr. Cecilia V. Tomas;

**WHEREAS** the Ad Hoc Committee has completed its draft and the Philippine Health Research Ethics Board (PHREB) has approved the National Ethical Guidelines for Health and Health-Related Research 2017 (NEGHHR 2017);

**WHEREAS**, the PHREB recognizes the dedication, thoroughness, and perseverance of the Ad Hoc Committee in putting the NEGHHR 2017 together, engaging in extensive consultations, and finalizing the document for final approval;

**The Philippine Health Research Ethics Board hereby:**

**CONVEYS** its sincere gratitude and appreciation to the Ad Hoc Committee for Updating the National Ethical Guidelines for successfully completing its tasks.

**APPROVED**, ad referendum on 29 July 2017.

  
**PROF. LEONARDO D. DE CASTRO, PHD**  
Chair

## RESOLUTION

### **APPROVAL OF THE “NATIONAL ETHICAL GUIDELINES FOR HEALTH AND HEALTH RELATED RESEARCH 2017” PER 46TH PHREB MEETING DATED 7 JUNE 2017**

In accordance with its mandate under Republic Act No. 10532, otherwise known as the Philippine National Health Research System Act of 2013, of which Section 12 states that the Philippine Health Research Ethics Board (PHREB), created under DOST Special Order No. 091 s. 2006, shall ensure adherence to the universal principles for the protection of human participants in research.

**AWARE** that the National Ethical Guidelines for Health and Health-Related Research needs to be updated every five years due to scientific, technological, and social advancements and changes in the national and international guidelines;

**MINDFUL** of the need to provide more specific guidance for research in the areas of cosmetics, environmental health, online and digital tools, mental health, military, people with disabilities, genetic and genome, biobanks, registries, and databases;

**TAKING** into account the continuing rapid developments in health and health-related science and technology;

**AND ENSURING RESPECT** for the rights and welfare of all individuals and communities involved as participants in health and health-related research;

**The Philippine Health Research Ethics Board hereby:**

**APPROVES** and promulgates these guidelines, which shall be known as the **NATIONAL ETHICAL GUIDELINES FOR HEALTH AND HEALTH-RELATED RESEARCH 2017 (NEGHHR 2017)**;

**DIRECTS** the PHREB Secretariat to cause the publication of the NEGHHR 2017 in the Official Gazette of the Republic of the Philippines, and its registration in the Office of the National Administrative Register, UP Law Center.

These revised Guidelines shall take effect fifteen (15) days after the publication in the Official Gazette;

**ADOPTED**, ad referendum on 29 July 2017.

  
**PROF. LEONARDO D. DE CASTRO, PHD**  
Chair

## FOREWORD

The preparation for the 2017 edition of the National Ethical Guidelines has been inspired by two major developments: the enactment of the Philippine National Health Research System (PNHRS) Law of 2013, that provided a legal framework for the institutionalization of the Philippine Health Research Ethics Board (PHREB) as the national policy-making body for health research, and the palpable groundswell of public support for ethical health research in the country. The latter became evident through the record-breaking massive participation of various stakeholders in local and international events: The First PHREB National Conference (also known as the 14th International Conference of the Forum for Ethics Review Committees in Asia and the Western Pacific) that was held in Tagaytay City in November 2014, and the Global Forum on Research and Innovation for Health that was held in Manila in August 2015. The revision of the National Ethical Guidelines gained urgency after the release of the 2013 Declaration of Helsinki and the Council for International Organizations of Medical Sciences (CIOMS) initiative leading up to revision of the CIOMS International Ethical Guidelines for Biomedical Research Involving Human Subjects in 2016.

The work of the Drafting Committee, chaired by Dr. Marita V. T. Reyes, has been rendered more meaningful by PHREB's intensified campaign for the accreditation of Research Ethics Committees (RECs) alongside its training programs for health researchers as well as members of RECs. A number of accredited RECs have organized themselves into the Philippine Health Research Ethics Network (PHREN) that now serves as a forum for sharing experiences and gathering consensus regarding issues and challenges encountered in ethics review. The accredited committees have provided experience-based feedback, enhancing the form and content of these guidelines.

This edition of the National Ethical Guidelines seeks to address the question as to what constitutes health research while plugging gaps in areas not sufficiently covered in previous editions. The current version also gives due course to the nuances in principles and regulations as they apply to different fields, types, and methodologies of research. This is partly the reason why there is some measure of duplication that may be seen as one moves from

one section to another. It is hoped that the duplication serves the purpose of elaborating, rather than merely repeating.

The 2017 National Ethical Guidelines aim to balance the need to protect human participants from harm with the imperative to facilitate the conduct of beneficial health research. This aim is served partly by enabling RECs to determine which specific research proposals can be considered exempt on the basis of the general criteria provided. The 2017 National Ethical Guidelines also have a detailed section on health-related social science research, thus recognizing the broad understanding of health and of the dimensions of disease and illness. In this connection, the Ad Hoc Committee listened to expert representatives of different health and health-related disciplines. The contributions of all the experts consulted cannot be underestimated. The PHREB is fully cognizant of the help extended by all who sent in their comments and suggestions as it extends its gratitude to the Chair and Members of the Ad Hoc Committee for doing all the groundwork, and eventually consolidating all the various sections that make up this document that should be expected not only to provide guidance, but also to serve as a handbook for everyone who has a stake in the conduct of ethical health research in the country.



**PROF. LEONARDO D. DE CASTRO, PHD**  
Chair, PHREB

## MESSAGE

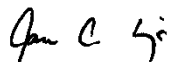
Since the establishment of the Philippine Health Research Ethics Board (PHREB), by virtue of the Philippine National Health Research System (PNHRS) Act of 2013, PHREB has been true to its mandate to “ensure adherence to the universal principles for the protection of human participants in research.” One of the fundamental roles of PHREB is to formulate and update guidelines for the ethical conduct of human health research as a response in the growing and evolving complexity of the health research environment in the country. These guidelines have come to be known collectively as the National Ethical Guidelines for Health and Health-Related Research.

Now in its 2017 version, the guidelines cater to the newly-identified specialized areas of health-related research including research involving military personnel, mental health, environmental health, cosmetics, and biobanking among others. This version also updated the current guidelines on research involving herbal medicine, alternative medicine, assisted reproduction, emerging technologies, genetics, stem-cell, epidemiology, social science, specific population (e.g., Indigenous People, Elderly, etc.) studies, HIV/AIDS, and clinical trials. This is definitely an affirmation of PHREB’s efforts to address emerging ethical issues in the conduct of health research.

PHREB anticipates that the landscape of health and health-related research will continually change as newfound knowledge and impacts of modernized society become more relevant than before. With these changes, PHREB assures that it will be relentless in promoting the principles of health research ethics in protecting the welfare of human participants above all.

The Department of Science and Technology - Philippine Council for Health Research and Development (DOST-PCHRD) commend the dedicated efforts of the PHREB and its Ad Hoc Committee members in steering the revision of the guidelines.

Mabuhay!



**JAIME C. MONTOYA, MD, MSC, PHD, CESO III**  
Executive Director, DOST-PCHRD



## MESSAGE

Our battle cry “All for Health towards Health for All” underscores the partnerships needed to achieve universal health coverage (UHC) - our ceaseless commitment to the Filipino people. To deliver health outcomes, ensure financial risk protection, and adequately respond to the legitimate expectations of our people, we need frontline health workers to deliver services, health managers and policymakers to design an enabling system, and civil society organizations to actively promote the interests of the people.

But what needs to be emphasized in this relentless pursuit towards UHC is the importance of health research. Evidences supported by well-designed and conducted research are vital for health workers, managers, and policymakers to make better and informed decisions and ultimately advance clinical care, health polices, and programs in the country. However, evidence generation in medicine inevitably involves human participation which entails possible health risk. Oftentimes, the poor and the sick are the ones subjected to these tests, experimental procedures, and drugs. It is thus in the Department of Health’s (DOH) interest - as the steward of health - to ensure that people are safeguarded from potential and unintended harm.

Therefore, allow me to extend our deepest gratitude and congratulations to the Philippine Health Research Ethics Board (PHREB) for its tireless commitment to update the National Ethical Guidelines for Health and Health-Related Research. This new publication shall foster rigorous but judicious scientific exploration in the field of medicine, upholding the rights and best interest of the Filipinos.

This certainly allows us to benchmark ourselves to the rest of the world and brings us a step closer to universal health coverage. But as a champion of public health, allow me to challenge the PHREB community further to strengthen guidelines for health policy and system research.

Again, my sincerest congratulation to the member of the Ad Hoc Committee for their trailblazing work! Let us continue to work together for our shared vision of “All for Health towards Health for All.”

Mabuhay!



**PAULYN JEAN B. ROSELL-UBIAL, MD, MPH, CESO II**  
Secretary, DOH

## MESSAGE

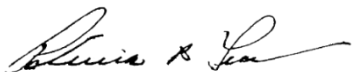
Greetings to the Philippine Health Research Ethics Board (PHREB) as it publishes its recent revision of the National Ethical Guidelines.

Titled “National Ethical Guidelines for Health and Health-Related Research”, this publication responds to changes in the health research landscape since the last revision of the Guidelines in 2011. It also ensures adherence to universal ethical principles in all phases of health research - important undertaking that promotes and protects the dignity of health research participants.

As the fields of science and technology continue to evolve globally, the role of the research in processing, recording, and producing new information becomes more significant. Ground- breaking innovations in healthcare technology – robotic surgery, mitochondrial DNA (mtDNA) transfer, micro-sampling of blood, among others – no doubt provide for stimulating contemporary health research environment. The principles provided by these Guidelines ensure better protection of the rights and dignity of the human participants involved in research. With the guidance it provides, ethical considerations in research are addressed and accountability in research conduction is ensured.

The Commission on Higher Education (CHED) commends the PHREB for this periodic undertaking of updating the health research guidelines. The Board’s efforts to aid researchers in the pursuit of relevant health findings that address the nation’s health problems attest to its role of being an important ally in national development.

Mabuhay!



**PATRICIA B. LICUANAN, PHD**  
Chairperson, CHED

## MESSAGE

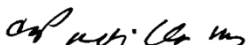
The University of the Philippines Manila (UP Manila), being a cradle of ideas, knowledge, and innovations in health research and a hub for health policy, advocates for an enabling and conducive environment for research. The integral part of such an environment is the protection of the rights, safety, and well-being of human participants in research.

As one of the implementing institutions of the Philippine National Health Research System (PNHRS), UP Manila supports national initiatives and programs in research ethics review of the Philippine Health Research Ethics Board (PHREB). We commend the PHREB for its continuing efforts to come up with clear, relevant, and harmonized guidelines for the conduct of health-related research in the country. The university commits to sustaining partnership with stakeholders towards strengthening research ethics policies nationwide; and contributes much needed resources, especially systems and scientific expertise, towards this end.

UP Manila has embedded a framework for ethical research in the university through the University of the Philippines Manila Research Ethics Board (UPMREB) and the restructured Research Grants and Administration Office (RGAO), which created a cohesive research management system that mandates and facilitates applicable ethics approval for all health research conducted by UP Manila personnel. In the last three years alone, through UPMREB and RGAO, the university is able to benchmark compliance with local and international regulatory and quality standards in human research oversight.

On behalf of UP Manila researchers and support staff, I thank the PHREB for leading the revision and publication of the National Ethical Guidelines for Health and Health-related Research 2017. Your hard work supports UP Manila's efforts to conduct relevant health researches that help advance the country's health.

The 2017 Guidelines will facilitate greatly UP Manila's growth and development as a health research university towards its broader mission of improving the health of Filipinos.



**CARMENCITA D. PADILLA, MD, MAHPS**  
Chancellor, UP Manila

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## HOW TO USE NEGHHR 2017

The National Ethical Guidelines for Health and Health-Related Research 2017 (NEGHR 2017) 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, methodology, and populations.

Nineteen appendices (A to S) are provided in these Guidelines. Appendices A and B are excerpts from the PNHR Act of 2013 (RA 10532), and its implementing rules and regulations (IRR) that are pertinent to the creation of PHREB. Appendices C and D are memorandums related to ethics review of research involving human participants. Appendices E, F, and G provide the guidelines and policies for accreditation of RECs as well as the recommended content and format of their SOPs. Appendices H and I are sample templates for application of ethics review and writing of research proposals respectively. Appendices J, K, L, M, and N are sample templates of documents relevant to the review of research (i.e., Worksheet for Protocol Assessment and ICF Checklist Assessment), and informed consent and assent forms. Lastly, Appendices O, P, and Q show the composition of the NEC, PHREB, and the Ad Hoc Committee for Updating the NEG.

It is important for the readers to familiarize themselves with the General Guidelines (pages 10 to 68), 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 (e.g., genetic studies), are fully described in the Special Guidelines respectively. The Special Guidelines complement those in the General Guidelines, and should not be considered as separate from it.

The different provisions are serially numbered for each specific section and may be cited by stating the section title followed by the provision number. For examples:

- The provision, *“The study design, methodology, and data collection, overall, should be able to generate information supportive of the objectives of the study. Social value can only be realized if the study is scientifically valid”* in the Elements of Research Ethics can be cited as (NEGHR 2017, Elements of Research Ethics, Guideline 3)



- The provision, *“All clinical studies must be adequately justified by reference to priority health needs of the country”* in the Guidelines for Clinical Research can be cited as (NEGHHR 2017, Clinical Research, Guideline 1).

The technical terms defined in the Glossary (pages 246 to 262) must be understood and used in the context of the specific provisions in the NEGHHR 2017. The entries in the Glossary may not be used outside of the said context.

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

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# INTRODUCTION

## *Background*

The National Ethical Guidelines is a distinct manifestation of the country's commitment to the protection of the rights, welfare, and well-being of human participants in research, and to research integrity.

Usually, time (like five years after the last revision) should be enough justification for an update. However, in the present endeavor, more than the time element, the international and local developments in research ethics pushed the “usual suspects” to come together and work, yet again, on the edition that should follow the 2011 National Ethical Guidelines for Health Research (NEGHR 2011).

The key international developments included the following: the release of new version of the Declaration of Helsinki last October 2013, the article on “Reforms of Clinical Research Regulations,” by E. J. Emanuel in the New England Journal of Medicine published on 4 November 2015, the approval of the text of CIOMS International Ethical Guidelines for Health-Related Research Involving Humans by the CIOMS Executive Committee during the CIOMS XXII General Assembly on 29 November 2016, and formally released on 6 December 2016.

At home, The PNHR Act of 2013 (RA 10532) became effective on 1 June 2013. This institutionalized the PHREB as the national policy-making body in research ethics. Thence, in accordance with its mandate, PHREB issued its new set of Requirements for Registration and Accreditation of RECs on 2 February 2014, and updated it on 7 September 2016. Further, PHREB developed a Workbook on Writing SOPs in 2015.

The passage of the Data Privacy Act of 2012 (RA 10173) went unnoticed until the promulgation of its IRR on 24 August 2016. The provisions of this law have clear implications on how human research data are collected, stored, accessed, and used.

The release of the National Commission on Indigenous Peoples (NCIP) Administrative Order No. 1 Series of 2012 “The Indigenous Knowledge

Systems and Practices (IKSPs) and Customary Laws (CLs) Research and Documentation Guidelines”, and NCIP Administrative Order No. 3 Series of 2012 “The Revised Guidelines on Free and Prior Informed Consent and Related Processes of 2012” effectively gave details on procedures to be followed in doing research among indigenous people and in their communities.

The natural disasters experienced by Filipinos in the past few years, i.e., floods, typhoons, and an earthquake, not only called attention to the need for disaster preparedness, but also for guidelines in social and public health research conducted in the affected areas. Questions on whether the present guidelines are clear about the responsibilities of these researchers and whether the affected communities are adequately informed about their participation have been raised.

Further, professional groups have raised concerns regarding a perceived absence of a regulatory framework on innovative stem cell therapy. There was worry over the vulnerability of potential clients especially because of the exorbitant fees that patients had to pay. The health sector needed to be guided on whether innovative stem cell therapy should be considered a research activity and therefore fall within the purview of the PHREB research ethics review system.

There were clear gaps identified in the guidance for several types of research in various domains. These include mental health research, environmental health research, emergency medicine research, research among military personnel, research among older persons, externally-sponsored collaborative research, biobanking, clinical registries, and online research.

One often repeated issue is the timeliness and efficiency of ethics review.

The Ad Hoc Committee for Updating the National Ethical Guidelines for Health Research, was reconvened to consider all the above developments and issues in the determination of relevant material in the revision of the research ethics guidelines. The core members of this committee are Dr. Rosario Angeles T. Alora, Dr. Leonardo D. de Castro, Prof. Edlyn Jimenez, Dr. Ricardo M. Manalastas, Jr., Dr. Marita V. T. Reyes, Dr. Evangeline O. Santos, and Dr. Cecilia V. Tomas. Topic experts (see List of Contributors) were invited

to prepare working papers, and/or to review old versions. Special mention must be given to the tedious and exacting work of Prof. Edlyn Jimenez as language editor, and to the unrelenting efforts of Atty. Marcia Ruth Gabriela Fernandez to ensure consistency of the guidelines with existing laws and practices in the conduct of research involving indigenous peoples, and the acceptability and clarity of the guidelines when applied to social science research. It must also be said that work on the revision of the National Ethical Guidelines was made possible and feasible by the dedication and commitment of Mr. Andronico Lear B. de Guzman whose technical assistance was truly invaluable!

Before the revision was finalized, the 2017 National Guidelines for Health and Health-Related Research underwent several reviews by stakeholders that included a general consultation during a special session of the Philippine Health Research Ethics Network (PHREN) Scientific Conference on 24 October 2016. Comments and suggestions from the public were also gathered through the PHREB website at <http://ethics.healthresearch.ph>. All comments were documented, discussed, evaluated, and finally adopted when deemed suitable. The public consultation generated a host of suggestions and recommendations that resulted into the present much-improved guidelines. Those who participated in the public consultation are listed in Appendix S (page 245).

## **Scope**

The National Guidelines 2017 define “research” as an activity that aims to develop or contribute to knowledge that can be generalized (including theories, principles, relationships), or any accumulation of information using scientific methods, observation, inference, and analysis.

“Research involving human participants” include any social science, biomedical, behavioral, or epidemiological activity that entails systematic collection or analysis of data with the intent to generate new knowledge in which human beings: (1) are exposed to manipulation, intervention, observation, or other interaction with investigators, either directly or through alteration of their environment; or (2) become individually identifiable through investigators’ collection, preparation, or use of biological material or medical or other records. This means that “research

involving human participants” does not only mean direct interaction of the researcher with an individual or groups of individuals, but also includes research using identifiable human material and data (adapted from Preamble 1, Declaration of Helsinki 2013).

Health research encompasses all research that seeks to understand the impact of processes, policies, actions, or events originating in any sector on the well-being of individuals and communities; and to assist in developing interventions that will help prevent or mitigate their negative impact, and in so doing, contribute to the achievement of health equity and better health for all (adapted from the RA 10532 Joint IRR). It implies that improving health outcomes requires the involvement of many sectors and disciplines. On the other hand, a research is considered “health-related” if it is outside of the aforementioned description for health research, but where the research procedures and outcomes can affect the well-being of the participants and the community.

Notwithstanding the very broad definition above, some sectors may question whether these guidelines, which are intended for health and health-related research, would apply to research that are clearly neither about health nor are health-related. Since, research ethics principles are now adopted by almost all disciplines (biomedical, natural, social, behavioral, business and management sciences) whose members conduct research involving human beings, it must be surmised that it is the requirement for ethics review that is the main issue. This is an institutional responsibility and decision. There are institutions who see the value of ethical review, and would opt to establish the oversight system, even for research that many would not see as health or health-related research. PHREB welcomes these institutions, and extends its hand for assistance. Indeed, PHREB looks forward to the day when researchers and institutions would regard ethical review as a process they want because it is needed to render quality assurance in their research work and programs.



**MARITA V. T. REYES, MD**

Chair,

Ad Hoc Committee for Updating the National Ethical Guidelines

## LIST OF ACRONYMS

|        |  |
|--------|--|
| ADAP   | Alzheimer’s Disease Association of the Philippines                   |
| AIDS   | acquired immune deficiency syndrome                                  |
| AFP    | Armed Forces of the Philippines                                      |
| AO     | Administrative Order   |
| ART    | assisted reproductive technology                                     |
| ASA    | Association of Social Anthropologists of the UK and the Commonwealth |
| CAM    | complementary and alternative medicine                               |
| CHED   | Commission on Higher Education                                       |
| CIOMS  | Council for International Organizations of Medical Sciences          |
| CBD    | Convention on Biological Diversity                                   |
| COPE   | Committee on Publication Ethics                                      |
| COI    | conflict of interest   |
| CRO    | Clinical Research Organization<br>or Contract Research Organization  |
| CV     | curriculum vitae   |
| DA     | Department of Agriculture  |
| DNA    | deoxyribonucleic acid  |
| DOH    | Department of Health   |
| DOST   | Department of Science and Technology                                 |
| DSWD   | Department of Social Welfare and Development                         |
| DSMB   | Data and Safety Monitoring Board                                     |
| EO     | Executive Order  |
| FDA    | Food and Drugs Administration  |
| FERCAP | Forum for Ethical Review Committees in Asia and the Pacific Region   |
| FGD    | focus group discussion   |
| GCP    | Good Clinical Practice   |
| GMP    | Good Manufacturing Practice  |
| HBRD   | human biobanks, registries, and databases                            |
| HIV    | human immunodeficiency virus   |
| ICC    | indigenous cultural communities                                      |

|         |   |
|---------|---|
| ICD     | informed consent document   |
| ICF     | informed consent form   |
| ICH     | International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use |
| ICH-GCP | International Council on Harmonisation-Good Clinical Practice                                       |
| ICMJE   | International Committee of Medical Journal Editors  |
| ICU     | intensive care unit   |
| IDE     | investigational device exemption  |
| IP      | indigenous peoples  |
| IPOPHL  | Intellectual Property Office of the Philippines   |
| IPRA    | Indigenous Peoples' Rights Act  |
| IRR     | implementing rules and regulations  |
| IUI     | intra uterine insemination  |
| KFPE    | Commission for Research Partnerships with Developing Countries                                      |
| LAR     | legally authorized representative   |
| LUA     | limited use agreement   |
| MARP    | most-at-risk-population   |
| MMSE    | mini-mental state examination   |
| MOA     | memorandum of agreement   |
| MOU     | memorandum of understanding   |
| MTA     | material transfer agreement   |
| mtDNA   | mitochondrial deoxyribonucleic acid   |
| NAST    | National Academy of Science and Technology  |
| 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   |
| NEDA    | National Economic Development Authority   |
| NEG     | National Ethical Guidelines   |
| NEGHHR  | National Ethical Guidelines for Health and Health-Related Research                                  |
| 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                          |
| PLHIV   | persons living with HIV  |
| PNHRS   | Philippine National Health Research System                       |
| PNRI    | Philippine Nuclear Research Institute                            |
| POGS    | Philippine Obstetrical and Gynecological Society                 |
| PSREI   | Philippine Society of Reproductive Endocrinology and Infertility |
| RA      | Republic Act   |
| REC     | research ethics committee  |
| REMB    | Regional Ethics Monitoring Board                                 |
| RNA     | ribonucleic acid   |
| RNE     | reportable negative event  |
| RUHRA   | Regional Unified Health Research Agenda                          |
| SAE     | serious adverse event  |
| SOP     | standard operating procedure                                     |
| SUSAR   | suspected unexpected serious adverse reactions                   |
| TAMA    | Traditional and Alternative Medicine Act                         |
| TM      | traditional medicine   |
| TWG     | technical working group  |
| UHC     | universal health coverage  |
| UNDRIP  | United Nations Declaration on the Rights of Indigenous Peoples   |
| UPM     | University of the Philippines Manila                             |
| UPM REB | University of the Philippines Manila Research Ethics Board       |
| WHO     | World Health Organization  |



# **GENERAL GUIDELINES**

## ELEMENTS OF RESEARCH ETHICS

Ethical assessment of health and health-related research requires a framework that may consist of principles, values, and key procedures. The following elements that constitute such a framework are based on Philippine experience in the conduct of research ethics review.

### Social Value

1. The participation of human beings in research can only be justified if the study has social value. Social value refers to the relevance of the study to an existing social or health problem such that the results are expected to bring about a better understanding of related issues, or contribute to the promotion of well-being of individuals, their families, and communities.
2. The significance of the study shall be clearly described in a separate section of the protocol with an accurate and updated description of the status of the social or health problem, and how the study will help arrive at a solution.
3. The study design, methodology, and data collection, overall, should be able to generate information supportive of the objectives of the study. Social value can only be realized if the study is scientifically valid.
4. A dissemination plan for the study results shall be included in the protocol. Dissemination is essential to achieving social value.
5. The REC shall determine the appropriateness and the practicability of the dissemination plan, as well as the suitability of the recipient(s) of the information.

### Informed Consent

6. Informed consent is a decision of a competent potential participant to be involved in research after receiving and understanding relevant information, without having been subjected to coercion, undue influence, or inducement.

7. Obtaining informed consent is a process that is begun when initial contact is made with a potential participant and continues throughout the course of the study. By informing the potential participants, by repetition and explanation, by answering their questions as they arise, by ensuring that they understand each procedure, and by obtaining agreement from them, researchers elicit their informed consent, and in so doing manifest respect for their dignity and autonomy.
8. For all research involving humans, the researcher shall 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 researcher must exert effort to obtain his or her assent and the consent of a legally authorized representative (LAR), in accordance with applicable laws.
9. In obtaining informed consent, sponsors and researchers shall have the duty to avoid deception, undue influence, or intimidation.
10. Informing the potential participant shall not be simply a ritual recitation of the contents of a written document. Rather, the researcher shall convey the information, whether orally, in writing, or other modes of communication, in a language and manner that suit the individual's capacity and level of understanding.
11. The researcher shall ensure that the prospective participant has adequately understood the information. The researcher shall give each one the full opportunity to ask questions, and should answer them honestly, promptly, and completely.

### *Essential information for participants*

12. The researcher 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:
  - 12.1. That the individual is invited to participate in the research which is being undertaken by the researcher (name of

researcher) from the institution (name of institution);

- 12.2. The reasons for considering the individual suitable for the study, and that participation is voluntary;
- 12.3. That the individual is free to refuse to participate in the research without penalty or loss of benefits to which he or she is entitled;
- 12.4. The purpose of the research, the procedures to be carried out by the researcher, and an explanation of how the research differs from routine medical or health care;
- 12.5. 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 study, or of the individual's participation in it;
- 12.6. 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;
- 12.7. The direct benefits, if any, expected to manifest to individuals from participating in the research;
- 12.8. 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;
- 12.9. The expected benefits of the research to the community or to society at large, or contribution to scientific knowledge;
- 12.10. Whether, when, and how, any intervention proven by the research to be safe and beneficial 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;

- 12.11. The provisions to ensure respect for the privacy of research participants and the confidentiality of records in which they are identified, including documentation through taking of pictures and recording of the interview and that these might be displayed in publications and conferences or fora;
- 12.12. Legal or other limits to the researcher's ability to safeguard confidentiality, and the possible consequences of breaches of confidentiality;
- 12.13. The participants are free to withdraw from the research at any time without having to give any reason, and without penalty or loss of benefits to which he or she is entitled;
- 12.14. The sponsors or funders of the research, the institutional affiliation of the researchers, and the nature and sources of funding for the research;
- 12.15. The possible research uses, direct or secondary, of the individual's medical or health records, and the possible future use and final disposition of biological specimens;
- 12.16. If the specimens collected will not be destroyed, then where, how, and for how long they are going to be stored;
- 12.17. That the research participants have the right to decide about future use, continued storage, or destruction of collected specimens and/or personal information;
- 12.18. Whether commercial products may be developed from biological specimens, and whether the research participant shall receive monetary or other benefits from the development of such products;
- 12.19. The extent of the researcher's responsibility to ensure needed services to the research participant;

- 12.20. That treatment and rehabilitation 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 medical service or organization that will provide the treatment and whether there is any uncertainty regarding funding of such treatment;
- 12.21. That a PHREB-accredited REC has approved or cleared the research protocol; and
- 12.22. The contact information of persons designated to respond to the following:
  - 12.22.1. Queries on the details of the protocol;
  - 12.22.2. Issues relating to the human rights of participants;
  - 12.22.3. Related concerns and grievances; and
  - 12.22.4. Management of research-related injuries.

#### *Documentation of consent*

13. As a general rule, documentation of informed consent includes an actual signature or thumbmark of the prospective participant on the informed consent form.
14. When the use of an informed consent form is not feasible or unacceptable to the prospective participant, a description of the process, attested by a witness, may be an alternative that needs prior approval of the REC.

#### *Waiver of the informed consent*

15. Waiver of individual informed consent is to be regarded as exceptional, and must be approved by an REC.
16. The informed consent process may be waived in specific research

contexts, such as:

- 16.1. Archival research involving publicly available documents;
- 16.2. Research that uses the method of naturalistic observation (often described as “covert” method) in data collection provided that all of following requirements are complied with:
  - 16.2.1. Thorough justification for the use of naturalistic observation;
  - 16.2.2. Plan for how the data collected will be used;
  - 16.2.3. Assurance that risks to participants are unlikely; and
  - 16.2.4. Mechanism to ensure confidentiality and anonymity of observed individuals and their data (e.g., observations are recorded in such a way that the individuals involved are not identifiable).
17. Some or all of the elements in the informed consent may be waived or altered (with prior approval of the REC) if all these conditions are met:
  - 17.1. The research presents no more than minimal risk;
  - 17.2. The waiver or alteration will not adversely affect the rights and welfare of the participants;
  - 17.3. The research cannot be practicably carried out without the waiver or alteration; and
  - 17.4. The participants will be provided with additional pertinent information after their participation (whenever appropriate).

### *Renewing consent*

18. The informed consent of each research participant shall be renewed under the following conditions:

- 18.1. If there are any significant changes in the circumstances or procedures of the research; or
- 18.2. If new information becomes available that could affect the willingness of research participants to continue to participate; or
- 18.3. In long-term studies at pre-determined intervals even if there are no changes in the design or objectives of the research.

### **Vulnerability of Research Participants**

19. Vulnerable participants shall require special protection because of certain characteristics or situations that render them as such. Vulnerable participants are those who are relatively or absolutely incapable of deciding for themselves whether or not to participate in a study for reasons such as physical and mental disabilities, poverty, asymmetric power relations, and marginalization, among others and who are at greater risk for some harms.
20. Vulnerable groups shall not be included in research unless such research:
  - 20.1. Is necessary to promote the welfare of the population represented; and
  - 20.2. Cannot be performed on non-vulnerable persons or groups.
21. Researchers, sponsors, or RECs 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.
22. 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. Caution shall be exercised in obtaining informed consent



for a research project if the research participant is in a dependent relationship with the researcher (e.g., as a research participant) to ensure that the consent is not given under duress or undue influence.

### **Risks, Benefits, and Safety**

23. Research is justified if there is a reasonable likelihood that the population from which the participants are derived stand to benefit from the research.
24. All research involving human participants shall be preceded by a careful assessment of predictable risks, burdens, and foreseeable benefits to the research participant or to others.
25. Every precaution shall be taken to minimize the negative impact of the study on the research participant's wellbeing.
26. Research shall be conducted only if there is an acceptable positive benefit-risk ratio.
27. The researcher/funder/sponsor shall endeavor to ensure the reasonable availability and accessibility of favorable research outcomes to the community.
28. 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 shall 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 the REC has approved them.

### **Privacy and Confidentiality of Information**

29. Researchers shall adhere to the principles of transparency, legitimate purpose, and proportionality in the collection, retention, and processing of personal information (Data Privacy Act of 2012).

30. Researchers must respect participants' right to privacy. Unless required by law, the confidentiality of information shall at all times be observed. Records that link individuals to specific information shall not be released. This requirement shall be included in the informed consent form.
31. Researchers shall refrain from identifying individuals or groups when release of information about them can expose them to possible harm or social stigma unless required by law.
32. Where there is some likelihood or opportunity for the researcher to observe the occurrence of illegal or harmful behaviors (e.g., child abuse, substance use, self-harm, or suicide ideation), the researcher shall:
  - 32.1. Explicitly indicate the limits of confidentiality in the informed consent process, such as when the researcher is ethically and legally obligated to disclose the identity of the respondent to forestall imminent harm to self or others;
  - 32.2. Emphasize the right of the respondent to withdraw from the study or withdraw his or her data, and to refuse to answer any question; and
  - 32.3. Prepare a concrete and realistic protocol for reporting and referral in the event that imminent harm and/or a criminal act is disclosed or discovered in the process of data collection.
33. Researchers shall recognize that collecting data using group methods (e.g., FGDs) has implications for the privacy and confidentiality of individuals. As it might not be possible for researchers to ensure the confidentiality of information or the anonymity of research participants, the researcher shall ensure that the nature of the study and the questions would cause minimal harm should confidentiality or anonymity be breached.
34. The researcher shall describe his or her data protection plan in the protocol, including the steps to be taken so that all who have access to the data and the identities of the respondents can safeguard privacy and

confidentiality. For example, the researcher shall provide adequate and clear instructions to research assistants, transcribers of audio recordings, or translators of transcriptions.

## **Justice**

35. In research involving human participants the principle of justice refers primarily to distributive justice, which requires the equitable distribution of both the burdens and the benefits of participation in research. That is, it should not be the case that one group in society bears the costs of research while another group reaps its benefits. Research should not worsen existing health and social inequities.
  - 35.1. There shall be fair selection in the choice of population, sampling, and assignments.
  - 35.2. There shall be provision of appropriate care to research participants regardless of their economic status, gender, race, or creed.
  - 35.3. There shall be just compensation for harms brought about by participation in the research.
  - 35.4. Research participants shall be reimbursed for lost earnings, travel costs, and other expenses incurred when taking part in a study. Where there is no prospect of direct benefit, participants may be given a reasonable and appropriate incentive for inconvenience. The payments shall not be so large as to induce prospective participants to consent to participate in the research against their better judgment (undue inducement).
36. Individuals and communities shall have access to benefits related to participation in the study.

## **Transparency**

37. Ethical research shall be characterized by transparency. It is imperative for all parties to be transparent about matters relating to their

involvement. Transparency is not diametrically opposed to privacy. On the contrary, transparency is an element of ethical research that promotes confidence in the research enterprise, even when privacy and anonymity need to be preserved about sensitive matters. The need for transparency also entails disclosure of research results.

38. Researchers must be transparent about aspects of a study that may have an impact on the rights, health, and safety of participants, or in respect to information that may have a bearing on the decision of participants to give or withhold their informed consent.
39. Disclosure of research results to research participants shall occur only when all of the following apply:
  - 39.1. The findings are scientifically valid and confirmed;
  - 39.2. The findings have significant implications for the participant's well-being; and
  - 39.3. The course of action to ameliorate these concerns is readily available when research results are disclosed to its participants.
40. Transparency imposes responsibilities on researchers to disclose information about their affiliations, financial interests, or other loyalties that may affect their objectivity and the integrity of their research output.
41. At the same time, transparency imposes responsibilities on research participants to be truthful in declaring their health conditions, and to be candid in expressing their concerns about their involvement in research.

# ENSURING QUALITY RESEARCH

## The Research Protocol

The protocol is the definitive document of the research or study. It provides guidance for those who will conduct the research, reference for evaluators and reviewers, template for validation, substantiation for intellectual property claims, and legacy of the proponent. As such, it should be rigorously conceptualized, carefully crafted, and elegantly formulated.

1. The research protocol shall be sufficiently detailed to serve as documentation of the study. Further, it shall:
  - 1.1. Justify the need for the study, that is, why the study shall be conducted given the current state of knowledge;
  - 1.2. Establish the appropriateness of the proposed methods for investigating the research problem;
  - 1.3. Provide evidence for 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;
  - 1.4. Describe the recruitment process (where, who, how); and
  - 1.5. Describe the dissemination plan for research results and outcomes.
2. The purpose of the study, the design, the population, the methods of data collection, and the planned analyses shall be clearly described.
3. All procedures, whether invasive or not, shall be satisfactorily described in detail.
4. The research protocol shall adequately address the elements of research ethics as part of the Ethical Considerations section.

5. The protocol shall provide information on how the safety and welfare of research participants shall be protected.

## Qualifications of Researchers

The researcher is the individual who is ultimately responsible and accountable for the research. The ethical discomfort in the use of human participants in a research is alleviated by the assurance that the researcher is qualified. Such qualifications need to be vetted by the researcher, the REC, and the sponsors.

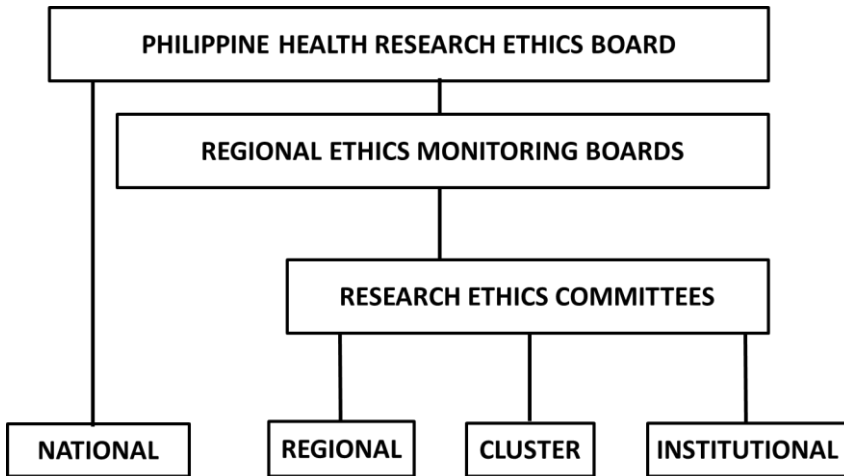
1. Persons engaged in research involving human participants shall have moral fortitude, scientific competence, social awareness, cultural sensitivity, intellectual humility, vigilance, and preparedness in safety issues.
2. The researcher shall have the training, ability, and resources to conduct the proposed study.
3. The researcher shall be knowledgeable of the literature on the research topic.

## The Research Ethics Review

### ***National Governance in Research Ethics Review***

The establishment of the Philippine National Health Research System (PNHRS) began in 2003 when a memorandum of understanding was set up between Department of Science and Technology (DOST) and Department of Health (DOH), and completed in 2007 when the Commission on Higher Education (CHED) and the University of the Philippines Manila (UPM) were drawn in as implementing agencies. PNHRS was legislated through the PNHRS Act of 2013 (RA 10532) which was enacted on 23 July 2012, and signed by then President Benigno Simeon Aquino on 7 May 2013. The PNHRS Law led to the creation of 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:



#### **1. Philippine Health Research Ethics Board**

PHREB has 12 members, including the DOST - Philippine Council for Health Research and Development (PCHRD) Executive Director as an *ex-officio* member, and representatives from the DOH, and CHED. Except for the *ex-officio* member, 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), and includes representatives from people's organizations and the youth sector. Both 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 RECs and standardization of research ethics review;
- Monitor and evaluate the performance of institutional RECs in accordance with procedures outlined in a prior agreement;
- Promote the establishment of functional and effective RECs;
- Provide advice and make recommendations to the PNHRG 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; and
- Network with relevant local, national, and international organizations.

## **2. Regional Ethics Monitoring Boards**

The Regional Ethics Monitoring Boards (REMBs) shall be established in key regions to serve as a regional arm of PHREB for monitoring purposes.

The REMBs shall have a multidisciplinary and multisectoral membership that reflects the cultural and social milieu in the region. Majority of the members should have been members of PHREB Accredited RECs. REMBs shall be under the supervision of PHREB.

PHREB and the REMBs, in consultation with RECs, shall develop and

agree on indicators of good performance, which shall be used in ensuring and monitoring quality ethics review in health research (Rule 23, PNHRIS IRR).

REMBs shall be located within existing regional DOST, DOH, and CHED offices or any designated institutions. For 2016, three (3) REMBs shall be established to assist PHREB with the following functions:

1. Information dissemination, training, and advocacy;
2. Monitoring performance of RECs in their respective regional areas;
3. Submission of annual reports to PHREB;
4. Development of quality assurance in review of RECs in the region;
5. Implementation of policies and directions for health research ethics set by PHREB; and
6. Other functions or tasks as deemed necessary.

### **3. Research Ethics Committees**

RECs include the National Ethics Committee (NEC), Regional RECs, Cluster RECs, and Institutional RECs.

#### *A. National Ethics Committee*

The NEC 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 research in institutions without RECs) until its policy-making role was taken over by the PHREB. In 2010, the NEC was temporarily phased out (DOST Special Order No. 383) only to be reactivated on 9 December 2013 because of the pressing need for a national body to review researches which are of national importance.

## B. *Regional Research Ethics Committees*

The Regional RECs operate under the auspices of the Regional Health Research and Development Consortia. They shall take charge of ethical review of research to be conducted in institutions without their own RECs, and of community-based research without a specific responsible institution.

## C. *Cluster Research Ethics Committees*

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

## D. *Institutional Research Ethics Committees*

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

The REC should consider both the scientific and ethical aspects of the proposed research even when the REC is distinct from the technical review committee.

As of August 2017, more than 200 RECs have been identified all over the Philippines. Of these, 77 have been accredited by PHREB.

## ***Guidelines for Research Ethics Committees***

RECs are essential components of a human protection system in research. As such, institutions or entities shall have policies regarding research, and ensure that RECs are established and given adequate support according to standards. RECs should be able to provide independent and quality review and monitoring of all health-related research involving human participants.

Institutional RECs shall have a manual of SOPs to make REC operations transparent, accountable, competent, timely, and consistent (WHO, 2011).

### **Composition**

1. The REC shall be constituted by the institutional authority in accordance with its policies on research and international and national standards. The institution's organizational chart shall include the location of the REC, in relation with other institutional units, to show under whose administrative oversight it belongs as an institutional entity, while at the same time maintaining its ability to issue independent ethics review decisions.
2. When appointing members, the institution shall consider the following:
  - 2.1. Membership shall be multidisciplinary and multi-sectoral, with adequate age and gender representation.
  - 2.2. Members shall have relevant scientific expertise, such as medical (in case of RECs reviewing clinical trials), social, or behavioral science; or qualifications relevant to the areas of research the REC is most likely to review. Members with expertise in ethics, law, environment, public health shall also be considered to reflect social and cultural diversity in research.
  - 2.3. The REC shall include an individual (non-medical, non-scientist) who will represent the interests and concerns of the community, as well as serve as the voice of patients, persons living with challenging health conditions, and their families.

- 2.3.1. The primary role of the non-medical, non-scientist member shall be to share his or her insights about the communities from which participants will be drawn and about the informed consent process and form.
  - 2.3.2. In RECs that review clinical studies (especially clinical trials), it is recommended that the community representative be drawn from either a patient or family support organization or a patient advocacy organization.
- 2.4. At least one member shall be independent of the institution or research site (non-affiliated member) to ensure the independence of the REC.
- 2.5. The number of REC members shall be adequate to ensure that the review can be done efficiently and effectively following international and national standards.
3. In addition to the REC members, the institution shall support the REC with adequate resources including staff, adequate and equipped office and facilities, and financial resources to enable it to carry out its responsibilities.

## **Appointment**

4. The officers and members of the REC shall be officially appointed by the administrative head of the institution.
5. The appointing official shall indicate their functions, terms of office, scope of work, conditions of appointment, and compensation, if any.
6. The appointment document shall mention the responsibilities of members with special roles (e.g., officers, non-medical/non-scientist member, non-affiliated member).
7. Procedures for renewal of appointment, resignation, replacement; grounds for disqualification; and procedures with regard to COI due to

financial gains shall be included in the SOP manual.

8. Prior to serving as a regular member, each member of the REC shall sign both a confidentiality agreement, as well as a disclosure agreement that states that he or she has no COI (e.g., financial interests in a pharmaceutical company or connection with the funding agency) as a reviewer.
9. 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).
10. The senior decision-makers of the entity creating the REC or of any organization that sponsors or conducts research reviewed by the REC (such as director of the institution or his or her agent) shall not serve as members of the REC or as its Chair (WHO, 2011).

### **External or independent consultants**

11. The REC shall establish a list of external or independent consultants who can provide specific expertise regarding ethical, scientific, psychological or social aspects of research for review. They are not considered REC members; therefore, they shall not take part in REC decision making (no voting privilege).
12. In deliberations on research involving special participant groups or concerns (e.g., HIV, AIDS, the physically challenged), best efforts shall be exerted to include participation of advocates.
13. External or independent consultants shall be qualified individuals with the needed expertise and training. They shall also be appointed by the institutional authority, stating the terms of their appointment.

### **Functions and responsibilities**

14. The REC shall act 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, 2000 and 2011). In the Philippines, the regulatory agencies include the PNHRS-PHREB, DOH-FDA, CHED, the National Committee on Biosafety of the Philippines (NCBP), National Commission on Indigenous Peoples (NCIP), and others. The REC should be updated with regards to Philippine laws and policies of regulatory agencies about possible areas or groups for research.

15. The REC's functions shall be as follows:

- 15.1. Review the scientific merit and ethical acceptability of the research involving human participants;
- 15.2. Undertake the same review process for foreign research protocols even if they have been ethically cleared by a foreign institution, applying ethical standards that are no less stringent than they would be if the research were to be carried out in the country of the sponsoring agency;
- 15.3. Ensure that the proposed research is responsive to the priorities and health needs of the country and that it meets the requisite ethical standards;
- 15.4. Issue the ethical approval required for the implementation of any research it has reviewed and approved;
- 15.5. Promote research integrity by identifying and resolving conflicts of interest;
- 15.6. Establish appropriate mechanisms in all stages of the research to:
  - 15.6.1. Ensure the safety, protect the rights, and promote the welfare and well-being of research participants;
  - 15.6.2. Provide counsel to research participants, including proponents and researcher;

- 15.6.3. Ensure prompt reporting of changes in the protocol and unanticipated problems;
  - 15.6.4. Ensure the proper documentation of and adherence to the confidentiality rule and policy on informed consent; and
  - 15.6.5. Monitor the progress of ongoing research until its completion.
- 15.7. 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;
  - 15.8. Keep a systematic and organized record of all proposals reviewed, including actions taken and other pertinent information;
  - 15.9. Submit an annual report to the PHREB (within the first quarter of the year ending on March 31), which shall contain the following:
    - 15.9.1. The composition of the REC, including a short curriculum vita (name of the person, educational attainment, most recent ethics training/seminars attended), and term of office of each member;
    - 15.9.2. Members of the REC secretariat, office and email addresses, and contact numbers;
    - 15.9.3. Number of meetings (regular and special) held during the year, including the date and venue;
    - 15.9.4. Number of research reviewed by the REC during the year, classified by the types of research, REC decision or action (approval, minor or major modifications, disapproval), and other information required by PHREB.



## **Meetings and deliberations**

16. The REC 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.
17. For RECs with five to nine members, quorum requires at least five members present, otherwise, quorum shall follow the 50%+1 rule. Quorum also requires the presence of at least one non-medical or non-scientist and one non-affiliated member(s) to make decisions about the proposed research (WHO, 2011). In the absence of these required members, there is no quorum.
18. Deliberations of the REC shall be characterized by transparency and collegiality. A member who is involved in whatever capacity in the study or project under consideration shall inform the committee of this potential COI, and his or her further participation in the deliberations shall be determined accordingly. Those with COI shall not be present during the deliberations and decision making. A member who is the principal investigator or researcher may remain during the REC meeting to answer questions for clarification with regards to his or her research, but shall leave the room during the REC deliberation and decision making.
19. The REC shall make clear in its SOP how the committee arrives at a final decision. There shall be a special effort to consider the opinion of the non-scientist (especially with regards to the informed consent process and form) and/or the non-affiliated member. Strong objections shall be addressed and reasonably resolved.

## **Training and continuing education of REC members**

20. Members of the REC shall undergo initial and continuing training on the ethics and science of health-related research.

20.1. Initial training shall be required of new members. In case, there

is no basic ethics training available at the time there are newly appointed members, the REC Chair shall ensure that proper orientation of new members is done on basic ethical principles, international and national ethical guidelines, and REC SOP, before they serve in the REC.

- 20.2. Members shall be encouraged and given support to attend regular continuing educational activities on research ethics, such as advanced training on ethical issues and concerns. Additionally, the REC shall include similar activities at least once a year. These may be linked with those of RECs within the province or region.

### **Review fees**

21. Review fees are intended to support the operations of the REC, training activities, and continuing education of its members. Charging review fees for other purposes puts the REC in a COI situation, from which it may not be easy to extricate itself.

### **Accreditation by PHREB**

22. All RECs shall apply for PHREB accreditation that shall indicate the nature of research that it can review (See PHREB Policies and Requirements for Accreditation, page 189)

## ***The Research Ethics Review Process***

The ethical review of research proposals involving human participants is conducted by an REC based on an evaluation of the research activities described in the protocol and protocol-related documents. These are submitted to the REC for approval before study implementation.

Since quality of the ethical review is an important concern, the REC shall have a manual of SOPs which shall clearly describe all areas of its work. For the initial and continuing review of protocols, the REC shall 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.

The ethical review of protocols involving several sites may be done as a joint review of a group of PHREB accredited RECs, provided that the review is conducted in accordance with SOPs approved by PHREB.

### **Required documents for REC review of an initial protocol submission**

1. The researcher shall be required to submit to the REC the following documents before REC reviews his or her research proposal:
  - 1.1. Application for review addressed to the REC which may be a formal letter or part of an application form as described in the REC's SOP;
  - 1.2. Clearance from technical/ethical review(s) from other committees (if applicable);
  - 1.3. Research protocol which must include the title, significance of the study, literature review, objectives of the study, methodology and procedures, description of the study population, exclusion and inclusion criteria, data analysis, and ethical considerations;

The Section on Ethical Considerations shall 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.

- 1.4. Informed consent and assent documents (see Informed Consent on page 11, Research among Minors on page 131; and Template of Informed Consent and Assent Forms on pages 221 to 234). The informed consent and assent documents must be both in English and in a language appropriate to the level of understanding of the research participant (see General Guidelines, page 10). A sample template of statements to be written in an ICF is found in page 221;
- 1.5. Study tools (questionnaires, case report form, posters, advertisements for recruitment, etc.);
- 1.6. Study drug or medical device information like researcher brochures, published literature, and medical device manufacturer's design, if relevant;
- 1.7. Curriculum vitae (CV) of researcher and co-researchers, which will also include relevant training and proof of their GCP training (in case of a clinical drug trial);
- 1.8. Statement of on presence or absence of COI of the researcher;
- 1.9. Information regarding funding, sponsors, institutional affiliations, other potential conflicts of interest;
- 1.10. Contracts and approval of relevant offices (Memorandum of Agreement (MOA) if study is collaborative in nature; Material Transfer Agreement (MTA), Intellectual Property approval, Investigational Device Exemption (IDE), when relevant;

- 1.11. Study/protocol budget; and
- 1.12. The researcher shall submit to REC the number of copies of the protocol package that is required by REC for its review.

### **Initial review procedure**

2. After receipt of the application form and protocol package, the REC office shall check the submitted documents for completeness. The submitted protocol shall be officially recorded in a log book or an electronic database noting the date of submission, protocol title, researcher or principal investigator, funding agency or sponsors, and other relevant fields.
3. The REC Chair, or his or her representative, shall determine the proposal's exemption from review or the kind of review required – full or expedited review.
  - 3.1. **Exempt from Review** is the term used to denote that a protocol does not need to undergo either full or expedited review after a preliminary assessment by a designated member of the REC. “Exempt from Review” is a decision made by the REC.
    - 3.1.1. Protocols that neither involve human participants nor identifiable human tissue, biological samples, and data (e.g., meta-analysis protocols) shall be exempted from ethical review.
    - 3.1.2. Provided that the following do not involve more than minimal risks or harms, these protocols may be considered by the REC for exemption from review:
      - 3.1.2.1. Protocols for institutional quality assurance purposes, evaluation of public service programs, public health surveillance, educational evaluation activities, and consumer acceptability tests;

3.1.2.2. Research that only includes interactions involving survey procedures, interview procedures, or observation of public behavior (including visual or auditory recording) if the following criteria are met:

3.1.2.2.1. There will be no disclosure of the human participants' responses outside the research that could reasonably place the participants at risk of criminal or civil liability or be damaging to their financial standing, employability, or reputation; and

3.1.2.2.2. The information obtained is recorded by the investigator in such a manner that the identity of the human participant cannot readily be ascertained, directly or through identifiers linked to the participant.

3.1.2.3. Protocols that involve the use of publicly available data or information.

The decision to exempt from review may be delegated by the REC to an office or group of individuals for efficiency and in the interest of time. There must be assurance, however, that the delegated individuals or office have been properly oriented and trained to make such decisions with due diligence. Subsequently, these decisions shall be documented and submitted to the institutional REC for review.

The REC, in its annual report submitted to the PHREB,

shall include a list of all proposals or protocols that were exempted from review.

- 3.2. The Chair or the designated officer of the REC shall assign the reviewers for full or expedited review. The proposal shall be distributed to these designated reviewers accordingly.
- 3.3. **Full Review** shall be required for protocols that entail more than minimal risk to participants or those that involve vulnerability issues.

In a full review, the proposal is assigned for primary review to all REC members or to at least two reviewers (a scientific and a non-scientific/non-medical member) prior to the REC meeting. The reviewers shall present their findings during the REC meeting for discussion and final action.

- 3.4. **Expedited Review** can be done by the REC for proposals that do not need a full review such as the following:
  - 3.4.1. chart review
  - 3.4.2. survey of non-sensitive nature
  - 3.4.3. use of anonymous or anonymized laboratory/pathology samples or stored tissues or data

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

- 3.5. Submissions after the approval (e.g., protocol or informed consent amendments, progress or final reports, monitoring reports) shall be subject to either full or expedited review.

## Protocol review

4. Research protocols are evaluated relative to the elements of research ethics (see Elements of Research Ethics, page 11) and other considerations as follows:
  - 4.1. Social value: scientific validity, relevance to community and national needs, suitability of the dissemination plan and recipients;
  - 4.2. Informed consent: voluntariness (absence of coercion and undue influence), comprehensibility of information (use of native and non-technical language), and capacity to decide (of legal age and sound mind);
  - 4.3. Risks, benefits, and safety: assessment of risks, favorable risk-benefit ratio, and access to favorable research outcomes;
  - 4.4. Privacy and confidentiality of information: respect for right to privacy, and mechanisms to protect confidentiality;
  - 4.5. Justice: Fairness of selection process, appropriate care, compensation and reimbursement, and access to benefits;
  - 4.6. Transparency: Management of COI, sharing of relevant information to participants, honesty in participation, and disclosure of research results;
  - 4.7. Qualification of researcher: appropriate education, training, and experience;
  - 4.8. Adequacy of facilities: supportive of protocol procedures and well-being of participants; and
  - 4.9. Community involvement: respect for local traditions and culture, community empowerment, acknowledgement of participation.



## Action on proposals

5. The action of the REC shall be one of the following:
  - 5.1. **Approval**, in which case, the REC shall inform the researcher, in writing, of the REC's requirements for approved research that must be complied with during the conduct of the research, with definite timelines such as:
    - 5.1.1. Progress Report, at least once a year or as requested by the REC;
    - 5.1.2. Final Report;
    - 5.1.3. Amendments;
    - 5.1.4. SAEs and SUSARs;
    - 5.1.5. Termination of the research before its anticipated completion date, and the reason for it; and
    - 5.1.6. Protocol deviations and violations.
  - 5.2. **Modifications (Minor or Major) Required**, in which case, the REC shall clearly communicate to the researcher, in writing, a clear description of required modifications to the protocol and protocol-related documents.
  - 5.3. **Disapproval**, in which case, the REC shall clearly state the reason(s) for disapproval.
  - 5.4. **Deferred**, if clarifications are necessary, before a decision of the REC can be made.
  - 5.5. Ethical clearance is usually for a period of one year which may be renewed if an application for continuing review is submitted before the expiration of the earlier ethics clearance.

## **Appeal for reconsideration**

6. In case of an unfavorable decision, the researcher may make oral or written representation to the REC for reconsideration.

## **Withdrawal of prior approval**

7. Prior approval may be withdrawn for the following reasons:
  - 7.1. Noncompliance with reportorial requirements;
  - 7.2. Undue or significant number of SUSARs directly or indirectly attributed to the research;
  - 7.3. Protocol violation(s);
  - 7.4. Valid serious complaints from participants;
  - 7.5. Scientific misconduct

## **Review of post approval submissions**

8. As part of its function, the REC shall monitor the conduct of a research that it has approved. The process includes review of amendments, revisions, protocol deviations, and their approval before implementation. The process also includes review and approval/acceptance of reports (progress, termination, end of study, and final reports). The reviews may be expedited or full.

## **Site monitoring visit**

9. The REC or designated representative may also do an onsite visit of 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.
  - 9.1. REC shall inform the researchers of the visit at a date agreeable to both.

- 9.2. The REC shall 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.
- 9.3. After the site visit, a report is given to the principal researcher and to the REC.
- 9.4. The REC may recommend corrective actions for observations made.

### **Review of SAE and SUSAR reports**

10. The REC shall have SAE/SUSAR report forms available which may be used for reporting by the researchers. The form should include the determination of the expectedness and relatedness of the SAE/SUSAR and relationship to the study drug, health product or device used in the research. If deemed trial-related, the REC shall determine what action to take.
11. SAE reports shall be evaluated by the REC with special attention on the SAEs from the site with an approval from the REC.

### **Early termination/suspension of study**

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

### **Completion of the research**

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

## Documentation and archiving

14. All documentation and communication of the REC shall be dated, filed, and archived according to the committee's written procedures (WHO, 2011). Agenda and minutes of REC meetings shall have templates to facilitate their preparation and filing.

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

14.2. The study files shall include protocol and current version, informed consent documents, amendments, all communications regarding application, decision, follow-up, safety reports, continuing progress reports.

14.2.1. Completed study files include all of the above and the final report. They are usually archived for a minimum of three years.

14.2.2. Active and completed studies shall be identified and filed in a secure place.

14.2.3. The REC shall maintain a file of the following:

- REC SOPs;
- International, national and local guidelines;
- Annual REC reports;
- Curriculum vitae of REC members including initial and continuing training in ethics review, GCP, among others, which shall be updated, signed and dated;
- Log books and electronic database to facilitate

checking and follow-up of approved protocols;

- Log book for inquiries and complaints (dated) especially from study participants with their contact numbers;
- Log book for SAEs from local study site; files of reports of SAEs from international sites are kept in another file;
- Flow charts of REC procedures which shall be clearly visible to guests; and
- Templates of various forms to be used in ethics review available electronically or in print.

## **Responsibilities of the Research Adviser**

All research conducted in academic institutions by students/trainees, including postdoctoral fellows, shall be under the supervision and guidance of a senior research or faculty adviser.

The senior research or faculty adviser shall:

1. Guide the student or trainee in the development of a scientifically and ethically sound research protocol;
2. Assist the student or trainee in the addressing ethical and scientific concerns raised by reviewing bodies;
3. Serve as a model in intellectual humility and refer the student to other persons with expertise in social, legal, and other considerations affecting the research;
4. Supervise the student or trainee in the proper collection and recording of data including the duty to maintain the confidentiality of information and the privacy of human participants for all the phases of the research processes including the disposal or archival of data;
5. Review interim and final reports for accuracy and consistency;
6. Share responsibility and accountability with the student/trainee for the ethical conduct of the research; and
7. Ensure that the research to be undertaken by undergraduate students involves only minimal risk (See Roles and Responsibilities of the Investigator or Researcher, page 50)

## Responsibilities of Research Institutions

All institutions that are mandated to conduct research or those who allow or require its faculty, staff, students, or trainees to do research are considered in this guideline as “research institutions”.

The research institutions shall:

1. Provide a supportive environment for ethical research;
  - 1.1. Ensure the ethical conduct and monitoring of research being undertaken in the institution given the institutions available resources by taking reasonable steps, to comply with CHED Memorandum Order No. 52 Series of 2016 (p.20) which requires higher education institutions to adhere to the National Ethical Guidelines for Health Research. In the absence of an REC, the institution shall refer researchers to other authoritative bodies with expertise in ethics review.
  - 1.2. Establish an independent and competent REC and provide adequate administrative support for it, including fair compensation to REC members for protocol review and attendance in meetings.
2. Maintain an efficient recording system of research studies being done and their status and researchers involved in the study;
3. Establish SOPs regarding the review of research studies to be done in the institution including fees to be charged;
4. Establish safety monitoring and management systems (for researchers and participants);
5. Put in place systems, subject to the available resources of the institution, to enable researchers to maintain the privacy and confidentiality of information pertaining to human participants including secure processes for the sharing of data by the research community, as well as the disposal and/or archiving of data;

6. Provide opportunities for dissemination of results in collaboration with other stakeholders;
7. Update itself and systematically disseminate information to its community of researchers and administrative staff, regarding national and international policies and regulations and comply with them; and
8. Ensure that a system for the education and protection of human participants is in place in the institution.



## Roles and Responsibilities of the Investigator or Researcher

For the purposes of this set of guidelines, the term “researcher” refers to an individual or group of individuals who conceptualizes, initiates, and conducts a study. On the other hand, the term “investigator” refers to an individual or group of individuals who are responsible in the conduct of clinical trials involving investigational new drugs or devices, usually commissioned and sponsored by pharmaceutical companies or manufacturers. The “Principal Investigator” is the lead implementer of the clinical trial protocol. “Co-Investigators” (Co-Is) are a subset of key personnel who have special responsibilities in clinical trials. “Sub-investigator” is a term used to identify study team members who make critical clinical trial-related procedures and/or to make important trial-related decisions. Generally, these are also study Co-Is but may also include study team members with critical and important trial-related roles. All investigators have the same responsibilities pertinent to protection of human participants and ensuring credibility of data, but they perform their tasks based on clear delegation of responsibility emanating from the principal investigator.

Eligibility requirements for conducting research on human participants vary depending on the role of the researcher or investigator. Research personnel shall be appropriately qualified by training and experience to perform their research responsibilities.

Investigators or researchers shall be responsible for the protocol and the conduct of study. These responsibilities are particularized as follows:

1. Preparing the research protocol and ensuring its ethical acceptability by submission to the REC for review.
2. Obtaining ethical approval of the protocol, and for cooperation with the REC in the conduct of the clinical trial.
3. Bearing ultimate accountability for all activities associated with the protocol, including compliance with adopted international guidelines, national and local laws, institutional policies, and ethical principles.
4. Consulting or collaborating with colleagues in the scientific or academic

community to which he or she belongs and seeking advice from authoritative bodies possessing expertise in ethical, legal, social and other issues that the researcher may encounter throughout the research process; from the crafting of the proposal up to the disposal or archiving of data.

5. Performing or delegating to qualified co-investigators or research staff all the necessary tasks to carry out their studies; while remaining ultimately responsible for proper conduct of the study and fulfillment of all associated obligations.
6. Providing members of the research team with sufficient oversight, training, and information to facilitate appropriate safety procedures and protocol adherence.
7. Ensuring that adequate resources (facilities, equipment, supplies, and personnel) exist to:
  - 7.1. Conduct the research (e.g., through internal or external funding for staff, facilities and equipment);
  - 7.2. Protect subjects; and
  - 7.3. Ensure the integrity of the research.
8. Evaluating the resources available at each site where the research will be conducted, in multicenter/sited studies.
9. Applying for ethical review and approval before the conduct of a research/clinical trial. Thus, the researcher shall factor in the period for ethical review in the research timeline.
10. Providing evidence of Good Clinical Practice (GCP) training for clinical trials (NOTE: A GCP training certificate is valid for three years, and a local GCP training is preferred to ensure that the investigators are informed of the local regulatory requirements of the clinical trials).
11. Obtaining informed consent from each prospective research participant

(or the participant's legally authorized representative) before the participant begins to participate in the research (including any related eligibility testing not conducted solely for clinical purposes), unless the appropriate REC has approved a waiver of consent, or waiver of documentation (See Informed Consent, page 11).

12. Having adequate time to enlist the necessary number of participants to the research.
13. Providing a copy of the signed informed consent form to the research participant, and retaining a copy in both the research record and regular medical record (as applicable).
14. Informing the REC if a researcher or investigator can no longer fulfill his or her duties for any reason including, but not limited to, traveling for a prolonged period of time.
15. Cooperating, at all times, with the REC in fulfilling its responsibilities, and shall provide all information required by the REC as part of the review process such as all key personnel who contribute to the scientific development or execution of a study in a substantive, measurable way.
16. Bearing accountability for the content of all submissions (e.g., initial review, continuing review, adverse event reporting, reportable negative events, progress reports) to the REC and other review units and for ensuring that those documents are submitted in a timely manner, as required by the REC and other review units (e.g., audit teams).
17. Conducting the research as specified in the REC-approved protocol and complying with all REC decisions pertinent to the REC-approved protocol.
18. Submitting to the REC an amendment application for prospective changes in the approved protocol before the change is implemented, unless urgently necessary to eliminate apparent immediate hazards to subjects.
19. Reporting promptly to the REC any additional risks that are identified

during the course of the research project.

20. Monitoring the effective period of the ethical approval of the protocol and submitting a continuing review application in a timely manner to the REC, for renewal of approval (NOTE: If REC approval for a study lapses for any reason, even if the researcher or investigator has submitted an application for continuing review in a timely manner and has promptly responded to any requests for clarifications or changes, the recruitment of participants shall stop until the REC issues its formal approval, or determines that it is in the best interest of individual participants to continue participating in the research interventions or interactions).

21. Reporting promptly to the REC any of the following:

21.1. Unanticipated problems involving risks to participants or others, such as an adverse event or exposure of member(s) of the research team to harm;

21.2. Noncompliance with applicable laws or regulations or REC requirements, whether by the researcher or investigator, research staff, or others, even if the noncompliance was unintentional or was discovered in the course of quality assurance or quality improvement activities; and

21.3. Disapprovals, suspensions, or terminations of the project by any University or non-University review units or agencies.

22. Cooperating with:

22.1. Internal evaluations, inspections, and audits performed by authorized internal oversight authorities, including the RECs.

22.2. External reviews (e.g., by industry sponsors or government agencies such as the FDA).

22.3. Any external investigation, inspection, or other external review and its outcome must be reported to the REC responsible for

the research in question. Researchers should consult with their administrators, the RECs, and as appropriate, the legal counsel for assistance and representation.

23. The researcher or investigator shall disclose all financial and non-financial COI.
24. Complying with all applicable FDA regulations and fulfilling all investigator responsibilities, and in some cases, sponsor-investigator responsibilities, as applicable when conducting research involving FDA-regulated products.
25. Complying with the ICH-GCP guidelines in fulfilling all other duties in clinical trials that require FDA regulation.

## Responsibilities of Foreign Researchers

A foreign researcher is (1) a non-Filipino doing research in the Philippines, or (2) a Filipino conducting research in the Philippines on behalf of a foreign research institution or in compliance of requirements of a foreign institution.

### Requirements

1. Familiarity with the General Guidelines in the National Ethical Guidelines for Health and Health-Related Research 2017 (page 10) and the national governance structure for human protection in research.
2. Submission of required documents to the concerned institutional REC which, in general, include the following:
  - 2.1. Letter requesting for ethics review;
  - 2.2. Accomplished application for ethical review;
  - 2.3. Latest version of the research protocol;
  - 2.4. Informed consent form;
  - 2.5. Data collection forms;
  - 2.6. Letter of endorsement from the foreign institution where researcher is affiliated (if applicable);
  - 2.7. Technical review approval;
  - 2.8. Ethical review clearance from the concerned foreign institutional REC; and
  - 2.9. Curriculum vitae of researcher.
3. Ethical approval of the protocol shall be based on:
  - 3.1. Relevance of the study to Philippine research priorities;
  - 3.2. Acceptability of justification for choosing the Philippines as research-site;
  - 3.3. Identification of a qualified and appropriate local researcher and/or adviser;
  - 3.4. Scientific soundness;
  - 3.5. Ethical soundness;
  - 3.6. Familiarity of the researcher with the culture of the community

- research site;
- 3.7. Appropriate expertise of the researcher; and
  - 3.8. Appropriate reporting and dissemination plan.
4. Ethical clearance is usually for a period of one year, which may be renewed if an application for continuing review is submitted before the expiration of the earlier ethics clearance.
  5. Ensuring compliance with international, foreign, and local laws and regulations shall be the responsibility of the entire research team. For this purpose, however, the local research collaborators shall be accountable to local authorities, in cases of violations of local laws and regulations.
  6. Transfer of biological materials overseas shall be covered by a Material Transfer Agreement (MTA) through an institution-to-institution arrangement, and shall comply with all applicable international, foreign and local laws and regulations. Examples of said norms include the Convention on Biological Diversity, CITES, the Wildlife Resources Conservation and Protection Act (RA 9147), the issuances of the DENR and DA on scientific studies on wildlife, the bioprospecting regulations, IPRA (RA 8371), and the Technology Transfer Act of 2009 (RA 10055).
  7. Safeguards shall be in place to ensure protection of sensitive and personal information that will be transmitted outside the country.
  8. Compliance with local regulations shall be ensured by the foreign researcher.

## Responsibilities of the Funding Agency and Sponsor

Sponsor is defined as an individual, company, institution, or organization which takes responsibility for the initiation, management, and/or financing of a clinical trial (ICH-GCP, 1997). This definition describes the role of the sponsor in initiating the research, including protocol development. This definition also differentiates the sponsor from an agency that is mainly responsible for financing or funding of the research. The latter is what this guideline refers to as the “Funding Agency”.

1. The funding agency shall:
  - 1.1. Ensure competent technical and ethical review of all research projects receiving its support;
  - 1.2. Ensure regular and timely release of funds to support research;
  - 1.3. Monitor the proper implementation of the protocol;
  - 1.4. Promote research integrity;
  - 1.5. Provide remedial support in case of incident problems;
  - 1.6. Ensure satisfactory completion of the project within a reasonable time; and
  - 1.7. Provide opportunities for dissemination of results.
2. The sponsor is expected to fulfill responsibilities specifically provided in the ICH-GCP Guidelines.



## Gabay para sa mga Kalahok sa Isang Pananaliksik

Kalahok ang tawag sa mga taong sumasali sa isang pananaliksik kung saan sila mismo ang pinag-aaralan. Kasama sa pananaliksik ang pagtatala at pagsusuri ng kanilang personal na impormasyon, lagay ng kalusugan, mga reaksyon, damdamin, pag-uugali, kaalaman, at mga palagay. Ang kredibilidad ng mga resulta ng isang pananaliksik ay nakasalalay sa pagiging wasto ng mga impormasyong nabanggit.

Kadalasan ang mga kalahok nagkakaroon ng kaalaman tungkol sa layunin at mga pamamaraang gagamitin sa pag-aaral sa pamamagitan ng proseso ng *pahintulot (informed consent)*.

### Pagsali sa isang pananaliksik

1. Ang isang pananaliksik ay isinasagawa ayon sa isang dokumento na ang tawag ay “Protokol”. Ang protokol ay ginagamit na gabay ng mga mananaliksik para sa kanilang pag-aaral.
2. Ang protokol din ang pinagmumulan ng lahat ng impormasyon tungkol sa pag-aaral na kinakailangan upang makapagpasya ang mga maaaring maging kalahok kung sila ay sasali o hindi.

### Pahintulot

3. Ang bawat pananaliksik ay dapat may dokumentong pinapipirmahan sa mga kalahok, tanda ng kanilang pagsang-ayon na sumali. Ang tawag sa dokumentong ito ay “*Informed Consent Form*” o sa Filipino, “Pahintulot”. Ang “**Pahintulot**” ay isang prosesong nagpapatunay ng boluntaryong pagsali ng isang taong may kakayahang pumirma, matapos maintindihan ang karampatang impormasyon ukol sa mga iba’t ibang aspeto ng pag-aaral na makakaimpluwensya sa pagpapasya.
4. Kasama sa prosesong ito ang pagbibigay-alam sa kalahok ng kaukulang impormasyon tungkol sa pananaliksik bago magpasyang sumali.
5. Ang pagsali sa isang pananaliksik ay hindi dapat sapilitan (boluntaryong pagsali), kung kaya ang mga kalahok ay:

- 5.1. Maaaring kumonsulta ng ka-pamilya o kaibigan kung may agam-agam;
  - 5.2. Huwag mahiyang tumanggi sa mananaliksik; at
  - 5.3. Maaaring tumiwalag anumang oras habang isinasagawa ang pananaliksik nang walang mawawalang dati nang tinatanggap na pribelehiyo.
6. Ang maalam na pahintulot ay dapat na naglalaman ng mga sumusunod na impormasyon:
- 6.1. Sino ang nagpopondo o sponsor ng pag-aaral?
  - 6.2. Ano na ang kaalaman o karanasan tungkol sa pinag-aaralan? Saang mga bansa ginawa o ginagawa ang pag-aaral na ito?
  - 6.3. Sinu-sino ang at anu-ano ang responsibilidad ng mga mananaliksik?
  - 6.4. Anu-ano ang mga responsibilidad ng mga kalahok?
  - 6.5. Anu-ano ang mga hakbang na pagdadaan ng mga kalahok?
  - 6.6. Ilalagay ba ang mga kalahok sa iba't ibang grupo o pamamaraan ng pag-aaral kung saan ang pagtatakda ay *random* o ala swerte?
  - 6.7. Ano ang mga panganib na maaring idulot ng mga pamamaraan sa pag-aaral?
  - 6.8. Gaano katagal ang pakikilahok?
  - 6.9. Mayroon bang gastos ang pagsali?
  - 6.10. Mayroon bang matatanggap na kabayaran ang mga kalahok?
  - 6.11. Sino ang mananagot kung sakaling ang kalahok ay mapahamak

o magkaroon ng pinsala?

- 6.12. Mayroon bang ibibigay ang mananaliksik na mga benepisyo pagkatapos ng pag-aaral? Halimbawa ay:
- Gamutan
  - Pagsama sa mga *support groups*
  - Impormasyon tungkol sa resulta ng pagaaral
- 6.13. Ang pag-aaral ba ay aprubado ng isang research ethics committee (REC) na awtorisado ng Philippine Health Research Ethics Board (PHREB)?
7. Ang mga kalahok ay dapat na may kakayahang maunawaan ang mga impormasyon tungkol sa pagsali.
- 7.1. Anong wika ang ginamit sa maalam na pahintulot?
- 7.2. Madali ba itong maunawaan ng mga kasali?
8. Maaaring magbigay ng maalam na pahintulot ang mga sumusunod:
- 8.1. Ang mga kasali mismo, kung sila ay:
- Nasa hustong edad na (18 pataas);
  - May malinaw at tamang pag-iisip;
  - May kakayahang intindihin ang pagsali sa pag-aaral; at
  - May kakayahang bumasa at pumirma sa wika ng maalam na pahintulot
- 8.2. Ang mga kinatawan ng kasali, kung walang kakayanan ang mga kasali na magbigay ng maalam na pahintulot, tulad ng:
- Magulang (kung bata);
  - Asawa; o
  - Kinatawan ayon sa batas
9. Ang mga kasali ay maaaring humingi ng karagdagang impormasyon mula sa mga sumusunod kung sila ay may agam-agam ukol sa nilalaman ng pahintulot:
- Sa kanilang doktor (kung ang pananaliksik ay clinical trial);

- Sa mananaliksik;
- Sa REC na nag-apruba ng pag-aaral (ang numero ay dapat nakasulat sa dokumento ng pahintulot).

## Guidance for Research Participants

Research participants are the primary subjects of a study. The research may involve recording and analysis of their personal information, health status, reactions, feelings, attitudes, knowledge, and opinions. The credibility of the study results is largely dependent on the correctness of this information.

Participants normally get to understand the research objectives and procedures through the informed consent process.

### Participation in a research

1. A research is conducted in accordance with a document called the *Protocol*. It is the principal reference for the implementation of the research.
2. The protocol is also the source of information to be given to potential participants for their consideration when they are recruited in to the research.

### Informed consent

3. Every research involving humans shall have a document which is intended for participants to sign as evidence of their consent to participate in the study.

This document is called the Informed Consent Form. Informed consent is a process by which a participant confirms his or her willingness to participate in a study, after having been informed of all aspects of the study that are relevant to the participant's decision to participate. Informed consent is documented by means of a written, signed, and dated informed consent form.

4. The informed consent process requires communicating relevant information about the study to the participant before he or she decides to participate.
5. Willingness to participate is emphasized, such that joining a particular

study shall not be obligatory, hence, prospective participants:

- 5.1. May consult family members or friends if they have issues about participation;
  - 5.2. Should not be ashamed to turn down participation; and
  - 5.3. May refuse to participate or withdraw from the study, at any time, without penalty or loss of benefits to which the subject is otherwise entitled.
6. The informed consent form shall contain the following information:
- 6.1. Who sponsors or funds the study?
  - 6.2. Is there prior research about the subject of the study? In which countries was the study conducted or will be conducted?
  - 6.3. Who are the researchers and what are their responsibilities?
  - 6.4. What are the responsibilities of the participants?
  - 6.5. What procedures will participants undertake?
  - 6.6. Will there be a probability for random assignment of participants into groups which will undergo different procedures?
  - 6.7. What are the reasonably foreseeable risks or inconveniences to the participants?
  - 6.8. How long will the participation take?
  - 6.9. Are there anticipated expenses to the participant for participating in the study?
  - 6.10. Will there be payment or any form of compensation to the participant for participating in the study?

- 6.11. Who will be accountable in case participants are harmed?
  - 6.12. Will there be post-study benefits? For example:
    - Treatment
    - Membership in support groups
    - Information regarding the results of the study
  - 6.13. Was the study given approval by a PHREB-accredited REC?
7. Research participants must have the capacity to understand information regarding study participation.
    - 7.1. In what language was the informed consent document written?
    - 7.2. Can participants easily understand the information about the study?
  8. The following can give informed consent:
    - 8.1. The participant, if he or she is:
      - Of legal age (18 years or above);
      - Of sound mind;
      - Capable of understanding the nature of his or her participation; and
      - Capable of reading and signing the informed consent form.
    - 8.2. Representatives of the participant, if the participant does not have the capacity to give informed consent, such as:
      - Parent (if minor);
      - Spouse; or
      - Legally authorized representative
  9. Participants may request additional information from the following if there are issues regarding the contents of the informed consent form:
    - Doctor (if the study is a clinical trial);
    - Researcher or Investigator; and/or

- The REC who gave ethical clearance for the study (the contact number of the REC shall be written in the informed consent form)



## Community Participation

Community participation is not only an ethical consideration but it also 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, right of dissent, and community involvement in the actual conduct of research, and in the sharing of benefits (Wendler & Emanuel, 2000). Community participation provides a proactive character in the research, and establishes a symbiotic relationship in knowledge production.

1. Researchers shall actively engage with communities in decision-making about the design and conduct of research (including the informed consent process), while being sensitive to and respecting the communities' cultural, traditional, and religious practices (WHO, 2011).
2. Community consultation shall be seriously taken into consideration when:
  - 2.1. The study involves established community practices;
  - 2.2. The results of the study may impact on the health and welfare of the community constituents; or
  - 2.3. The study outcome may bring economic benefit to the community.
3. Involvement of a community representative in the study team may be required when:
  - 3.1. There is risk that the study procedures may be disrespectful of community traditions and practices; or
  - 3.2. The community itself requests for representation in the ownership and outputs of the study.
4. The REC may invite a representative from the community during deliberations.

## **OTHER CONSIDERATIONS**

### **National Research Agenda**

1. In general, all research shall support and contribute to the achievement of the current Philippine Development Plan as formulated by the National Economic Development Authority (NEDA).
2. Health research shall adhere to the National Unified Health Research Agenda (NUHRA) and Regional Unified Health Research Agenda (RUHRA) must be firmly grounded through a process of priority-setting.
3. Government funding agencies shall seriously consider conformity of the proposal with their respective research priorities.

### **Externally-funded collaborative research**

4. Sponsors and researchers involved in externally-funded collaborative research, have the ethical obligation to ensure that the research project shall contribute effectively to capacity building.

### **Protection of the environment and biosafety**

5. The conduct of biomedical or behavioral research shall be in a manner that minimizes possible harm to the environment.
6. Research 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 of Biosafety of the Philippines (NCBP) before implementation.

### **Welfare of animals**

7. The use of animals for research shall adhere with Animal Welfare Act of 1998 (RA 8485), amendments on its certain sections (RA 10631), and its Implementing Rules and Regulations through the Department of Agriculture AO No. 40 series of 1998 and the Code of Practice for the

Care and Use of Laboratory Animals in the Philippines, 2<sup>nd</sup> edition, 2002 developed by the Philippine Association for Laboratory Animal Science (PALAS).

# **SPECIAL GUIDELINES**

## ETHICAL GUIDELINES FOR CLINICAL RESEARCH

Clinical research encompasses studies involving human participants; designed and intended to add to medical knowledge related to the treatment, diagnosis, and prevention of disease or illness. The term “clinical” indicates that the study has moved up the development cycle from basic research (e.g., laboratory or animal research) to one that can be done in humans, inclusive of interventional and observational studies. Clinical trials may be investigator-initiated or sponsor-initiated (pharmaceutical companies). Interventional studies that involve food and agricultural products are not addressed in this section.

In the Philippines, clinical trials for marketing authorizations on drugs, devices, biologics, and other cellular products are regulated by the Food and Drug Administration (FDA) through various administrative orders and circulars derived from the FDA Act of 2009 (RA 9711), as well as international guidelines, such as the International Council on Harmonization Guidelines for Good Clinical Practice (ICH-GCP) and common requirements from regulatory agencies of reference countries (EU, Japan, and the US). The FDA law empowers the FDA to “conduct, supervise, monitor, and audit research studies on health and safety issues of health products” produced or marketed by entities under its regulatory oversight.

Clinical trials on drugs are “investigations involving human subjects intended to discover the clinical and pharmacological effects of and adverse reactions to an investigational product, and/or its pharmacodynamics and pharmacokinetic properties, with the object of ascertaining its safety and efficacy” (ICH-GCP, 1997). Drug trials generally consist of phases I, II, III, and IV.

Clinical trials on medical device include those in rehabilitation medicine (e.g., transcutaneous electrical nerve stimulation, ultra sound therapy, short wave diathermy, traction devices, use of wax), in ophthalmology (e.g., lenses, ophthalmic products), or in orthopedics (e.g., implants, prosthetics, orthotics). Clinical investigation of medical devices aims to demonstrate safety and performance rather than efficacy. Thus, clinical trials on a medical device shall show that the device performs safely and in accordance with its intended purpose, as claimed by the sponsor/manufacturer. Medical

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

Clinical trials on diagnostic procedures and preventive measures, including vaccines, raise similar ethical concerns, especially on the informed consent process, and potential COI. In contrast to drug 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, while benefits accrue mainly to the community. Direct benefit from the investigational vaccine is provisional, that is, if the vaccine is successful and that the participant who received the trial vaccine gets exposed to the infectious agent at some future time. It must be noted that a significant number of vaccine trials are done on children, who belong to a vulnerable population group (see Guidelines on Research among Minors or Children, page 131).

Clinical research may be conducted in an emergency room or intensive care unit (ICU) setting, which involves a highly diverse and critically ill research population. Such studies generate unique ethical issues because of the vulnerability of the research participants and the demand for exigency.

All clinical studies, both researcher-initiated and those sponsored by commercial companies, shall be conducted in accordance with these Guidelines.

1. All clinical studies must be adequately justified by reference to the priority health needs of the country.
2. Investigators involved in clinical trials shall be governed by clinical equipoise. A state of clinical equipoise means that, based on 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 research participants/clients pursue any of the treatment strategies being tested, since none of them have been clearly established as preferable.

3. Careful consideration of the different phases of clinical trials shall be made as they present different ethical issues (ICH-GCP E8, 1997). These include heightened risks because of product toxicities in Phase I, the use of placebo in Phases II and III, and the COI situation in post-marketing activities in Phase IV.

### **Contents of the clinical research protocol**

4. The protocol shall at least contain the following:
  - 4.1. Administrative information about the study such as researcher(s) or investigator(s), sponsor(s), monitor(s), other qualified medical expert(s), diagnostic laboratories, and research institutions involved;
  - 4.2. Background information regarding the study, relevant past and current research findings and references to such information and data, and potential risks and benefits;
  - 4.3. Background information on the drug under investigation, reason for the indicated route of administration, dosage, periods of treatment, population to be studied, a declaration regarding compliance with GCP, and regulatory requirements (in case of clinical trials under FDA oversight);
  - 4.4. Objectives and purpose;
  - 4.5. Study design, which substantially determines the scientific integrity of the study and reliability of the data, and includes the following:
    - 4.5.1. Description of the type of design, diagram of procedures and stages, and for clinical trials, the trial plan (e.g., double-blind, placebo controlled, parallel design);
    - 4.5.2. Primary and secondary endpoints to be measured;

- 4.5.3. Measures to minimize or avoid bias (e.g., randomization and blinding);
- 4.5.4. Trial treatments and investigational product's dosage, packaging, labeling, and storage (for clinical trials);
- 4.5.5. Nature of the placebo (if applicable);
- 4.5.6. Estimated duration of individuals' participation in the study;
- 4.5.7. Discontinuation rules for the participants and the study;
- 4.5.8. Treatment randomization codes maintenance and rules on breaking the code;
- 4.5.9. Procedures for accountability for product being investigated, placebos, and comparators, if applicable; and
- 4.5.10. Other sources of data;
- 4.6. Selection and withdrawal of research participants, inclusive of criteria for inclusion, exclusion, and withdrawal;
- 4.7. Informed consent of adult study participants or their minor children, and assent of adolescent participants with their parents' or legally authorized representative's (LAR) informed consent;
- 4.8. Research participants' therapy or treatment and respective monitoring procedures;
- 4.9. Efficacy parameters, methods, and timing;



- 4.10. Safety parameters, methods, timing, and procedures for recording and reporting, as well as monitoring adverse reactions;
- 4.11. Safety measures for research participants when they withdraw or are withdrawn from the study;
- 4.12. Plan for data and statistical analysis;
- 4.13. Information describing direct access to study data and documents for monitoring, audit, ethical review, and regulatory inspections;
- 4.14. Ethical considerations;
- 4.15. Data management and record keeping;
- 4.16. Financing and insurance;
- 4.17. Dissemination and publication plans and procedures; and
- 4.18. Clinical trial participants' information sheet or brochure, if applicable.

### **Use of placebo**

5. Use of placebo is generally not acceptable when there are standard treatments available to a research participant population. Thus, a placebo control may be used only if all the following conditions are present:
  - 5.1. There is compelling and scientifically sound methodological reason to use placebo;
  - 5.2. Research participants who receive placebo shall not be subject to additional risks or serious or irreversible harm as a result of not receiving the best proven intervention (Declaration of Helsinki, 2013);

- 5.3. Research participants give free and prior informed consent; and
- 5.4. In addition to the above, any of the following:
  - 5.4.1. Standard therapy is unavailable and other existing interventions are of unproven efficacy;
  - 5.4.2. Standard therapy is available but:
    - 5.4.2.1. Existing treatment is unacceptable for different reasons except for economic reasons; or
    - 5.4.2.2. Testing an add-on treatment to a standard therapy when all research participants get all treatments that would normally be given.

### **Protocol amendments**

- 6. Any amendment(s) to the protocol shall be resubmitted to the REC and FDA.

### **Therapy versus research**

- 7. Strong justification shall be presented by the principal investigator or researcher when combining medical research with medical care, and that participation in the study will not adversely affect the health of the research participant.
- 8. The difference between therapy and research shall be clarified throughout a clinical study. The research participants should be made to understand that, in a clinical trial, the drug is experimental and that its benefits are currently being proven.
- 9. It shall be clearly defined in the informed consent document which components are standard care and which are components of the study.

10. It shall be clearly explained to participants that participating in the research will neither provide nor entitle them to better therapy (therapeutic misconception).

### **Agreements in sponsor-initiated clinical trials**

11. The investigator(s) shall establish with the sponsor an agreement on the protocol, SOPs, monitoring, and auditing of the trial and allocation of trial-related responsibilities, including publication and authorship.
12. The institution, investigator, and sponsor must take the responsibility to define and mutually agree on the process for immediate management of study related injuries such as medical expense reimbursement or hospitalization expenses, inclusive of timelines and payment options.

### **Compliance with regulatory requirements in clinical trials**

13. A clinical research shall comply with the necessary regulatory requirements for the conduct of the clinical trial. The FDA has several AOs and circulars that define processes and criteria for the approval and conduct of clinical trials (e.g., DOH AO 47-A series of 2001 and FDA Circular 2012-007).
14. The investigator(s) and sponsor shall be responsible for complying with all applicable regulatory requirements of FDA.
15. Investigational and comparator products, whether produced locally or abroad, shall be prepared in accordance with the principles of good manufacturing practice and other quality standards. The products should be 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.
16. Good laboratory practice shall be strictly observed when a clinical trial requires laboratory tests and assays.

## **Considerations in recruitment of women of reproductive age in clinical trials**

17. A pregnancy test shall be done and access to effective contraceptive methods shall be ensured before the research commences, if participation in the research is potentially hazardous to a fetus, or a woman, if she becomes pregnant.
18. Researchers and RECs 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.
19. Research in this population shall be performed only if it is relevant to the specific 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, the risks of teratogenicity and mutagenicity.

## **Research on medical devices, diagnostic procedures, and preventive interventions**

20. Randomized trials for medical devices are not usually indicated.
21. Review of clinical study protocols on medical devices shall include an expert consultant, such as a bioengineer who shall look into the material and design, as well as the electrical safety of the device.
22. The research participant information sheet shall contain information on procedures to be adopted should the research participant decide to withdraw from the study.
23. Safety procedures in the introduction of a medical device in the research participant shall be followed.
24. 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.

25. Safety precautions regarding the implants, like effect of magnetic fields, allergic reactions, etc., should be clearly described in the protocol.
26. Follow-up period for medical device trials is longer than drug trials, and may last for several years, especially for implantable devices.
27. In the case of contraceptive implant trials, adequate monitoring and counseling for removal of the implant shall be done when the study ends, or when the participant withdraws (or is withdrawn) from the study. 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 on the use of diagnostic procedures**

28. Clinical trials involving diagnostic agents using radioactive materials and x-ray shall not unnecessarily expose participants to more radiation than normal, and shall be undertaken only on research participants needing the procedure for diagnostic or therapeutic purposes.
29. Clearance from the Philippine Nuclear Research Institute (PNRI) that the level of radiation from the radio-pharmaceutical product is within the allowable limits for human use, shall be secured and submitted to the REC for consideration.
30. Measures to safeguard research participants and others who may be exposed to radiation shall be described in the protocol.
31. Adequate provisions shall be ensured for detecting pregnancies to avoid risks of exposure to the embryo.
32. RECs shall require that the informed consent document includes the information that participation will involve exposure to radiation, which may have impact on significant others and possible genetic damage to their offspring.

## **Vaccine trials**

33. Child bearing women who participate in vaccine trials shall be properly advised on the use of acceptable contraception. Should pregnancy ensue, adequate provision for prenatal care shall be provided. Pregnancies as a result of failure of contraception shall be reported and monitored for abnormalities during a follow up a period determined as appropriate by the REC.
34. For vaccine trials using active or live attenuated microorganisms, the researcher shall:
  - 34.1. Inform the participants and/or legal guardians about exposure to the specific infection for which the vaccine is being tested; and
  - 34.2. Ensure provision of the necessary care for the affected participants.
35. DNA vaccines and vaccines developed using recombinant DNA technology shall have a prior clearance from the Biosafety Committee of the institution where research will be done, or if none, such shall be referred to the National Committee on Biosafety of the Philippines (NCBP).
36. Informed consent shall be obtained from third parties who may be exposed to study-related infections or treatments through contact with participants (e.g., parents, siblings, spouse, etc.).

## **Research in an emergency room or ICU setting**

37. The well-being or safety of the critically ill patient shall be the paramount consideration in the emergency room or ICU setting. No research shall stand in the way of the standard of care that should accrue to the critically ill patient.
38. In cases where the research participant, by the virtue of the nature of

his disease, is unable to give consent (e.g., research participant has delirium or the sensorium is impaired), consent must be obtained from the research participant's LAR prior to enrollment in the clinical study.

39. When the LAR is not available at the time the research participant is brought to the hospital, the principal investigator must exhaust all means to locate the research participant's LAR and document this process, within the therapeutic window.
40. The protocol shall describe appropriate procedures to inform the LAR, at the earliest feasible opportunity, of the participant's inclusion in the study and his or her right to discontinue participation in the research.
41. Once the research participant's sensorium improves during the course of management, and is able to give informed consent, the researcher or investigator should seek consent from the research participant himself or herself on whether to continue or not with the study. If the research participant decides not to continue, he or she shall receive the standard treatment due him or her.
42. In rare instances, the REC may grant exemption or waiver of the informed consent requirement, provided all the following conditions exist:
  - 42.1. Research participant has a life-threatening condition for which available treatments are unproven, lacking, or unsatisfactory;
  - 42.2. Prospect of direct benefit to the research participants;
  - 42.3. When research participants are unable to give consent (e.g., impaired sensorium), and no LAR is present or cannot be located;
  - 42.4. The risks associated with the investigation are reasonable in relation to what is known about the emergent condition; and
  - 42.5. Where to be effective, the intervention under investigation must be given right away upon admission to the emergency

room or ICU or within the specified therapeutic window.

### **Referral fees**

43. Payment of fees for referral of potential research participants is not allowed. Such practice taints the clinical research process, and provides the wrong motivation for those involved in the activity.
44. The recruitment process and possible payment of fees shall be subject to approval by the REC.

### **Publication of results of clinical studies**

45. Results of clinical studies shall be published regardless of whether they are positive, negative, or inconclusive. Findings shall be released in the public domain, and generally made known through scientific and other publications. Special effort must be exerted to share the results with the participants.
46. Preliminary reports that raise false hopes and expectations of product safety, efficacy, and immediate use shall not be made public.
47. 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, imperil their privacy as individuals, family, or community, or breach the confidentiality of their personal and health information.



## ETHICAL GUIDELINES FOR HERBAL RESEARCH

The Traditional and Alternative Medicine Act (TAMA) of 1997 (RA 8423), 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 enhanced research activities on herbal remedies, or preparations to evaluate safety and effectiveness. Necessarily, these research activities involve human participants for which ethical review is mandated.

There are traditional healing practices in many Philippine communities, which are rich in oral and unpublished written reports on the use of plants and their derivatives in addressing ailments. Whereas a significant component of drug discovery (such as that of PCHRD) is the screening of plant parts and of insect symbionts for biological and pharmacological activity, the aforementioned traditional healing practices are areas of research that aim to record and preserve the healing tradition amongst our people, to validate the safety and efficacy of the practice, and subsequently, to deconstruct the plant parts and attempt to isolate the active components singly, or in combination. It is in the latter step that studies on indigenous herbal medicines and drug discovery programs come together.

Both drug discovery and herbal medicine studies involve the collection of plant samples in communities, especially in indigenous cultural communities (See Guidelines on Research involving IPs, page 124). Researchers must consider the impact of these activities on the environment and biodiversity, as well as community proprietary claims. Thus, in this context, the individual is not the only participant, but a complex network of family and community is involved.

Some advocates of traditional and 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.

However, despite all the arguments against treating research on indigenous herbal medicines 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. The formulation of these ethical guidelines is guided by the TAMA as its policy framework, and the ICH-GCP Guidelines for its scientific and quality underpinnings.

1. In a research that aims to validate the therapeutic or diagnostic value of a traditional herbal preparation,
  - 1.1. There shall be proof of a long history of use of the herbal plant or 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 its use may be both in the written, oral, or video form. Evidence regarding usage of the herbal preparation shall be validated with the National Commission on Indigenous Peoples (NCIP), the National Museum, or by an expert opinion, should the need arise.
  - 1.2. The original herbal preparations and manner of use by people in the community shall be similar to the intended form and use in the proposed research. For example, if the herbal plant is applied as a poultice for a condition to be studied, then it shall be given in the same form to the research participants.
  - 1.3. The geographic area, maturity of collection of the plant, and

the method of its preparation must be clearly described.

2. Research in herbal remedies shall include standardization of the preparation and identification of markers to ensure that the ingredients being studied and assessed are the same. This method must be followed all throughout the conduct of research.
3. When the traditional herbal preparation is modified in some way—either shape or form—including dose, dosage form, mode of administration, herbal medicinal ingredients, methods of preparation and medical indications, it is classified as a herbal product.
4. Herbal product research shall undergo Phases I and II studies prior to Phase III.
  - 4.1. Phase I/II studies shall require the inclusion of the following information in the protocol:
    - Amount of herbal component;
    - List of excipients/diluents;
    - Type of product (tablet, capsule, etc.) and its method of manufacture;
    - Analysis of putative active ingredient(s) via chemical or biological parameters;
    - Analysis of a sizeable chemical constituent (analytical marker compound);
    - Analysis via chemical fingerprint (analytical markers);
    - Analysis for absence or lack of contamination by pesticides, herbicides, heavy metals;
    - Presence of synthetic drug adulterants, microbials, toxins, etc.;
    - Results of dissolution studies; and
    - Storage conditions and stability over the length of the trial.
  - 4.2. Phase III studies shall require the same information in Phase I/II clinical trials and an environmental impact statement.

5. 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 ICH-GCP and Good Manufacturing Practice (GMP) Guidelines.

### **Informed consent**

6. Uncertainty regarding the herbal preparation or product 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 Traditional Medicine Strategy 2002-2005).

### **Recruitment of volunteers**

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

### **Participation of traditional healers**

8. 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 REC. The traditional healer is the community's steward of indigenous knowledge.

### **Research design**

9. Placebo-controlled trials may be accommodated in consonance with the guidelines on the use of placebo as indicated in Guidelines for Clinical Research (page 70).
10. 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 shall be objectively measured.

11. Although efficacy of herbal preparations is a major objective of herbal research, adverse reactions such as side effects, tolerance profile, and interaction with other administered preparations shall always be part of herbal research.
12. Blinding in herbal research may be challenging because of the difficulty in preparing control galenicals/concoctions indistinguishable from the herbal preparation being tested. In this case, it is acceptable to “blind” the health status assessor or evaluator in support of objectivity.

### **Transport**

13. 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 (MTA).
14. Researchers shall comply with the MTA if plant products or herbal preparations will be tested outside the country. (See International Collaborative Research, Guideline 15)

### **Benefit sharing**

15. When possible, the community from where the herbal preparation/product originates shall be consulted during the course of the research, and the results and benefits of the research shall be shared with this community (WHO, 2005).
16. A memorandum of agreement regarding benefit sharing and patenting conditions, especially for indigenous plant products, shall be set as early as the planning stage of the research.

### **Commercialization of herbal preparations**

17. Researchers shall include provisions for conditions when the herbal preparation or product may likely be commercialized. They shall be guided by existing laws and regulations of the Intellectual Property

Office of the Philippines (IPOP HL).

### **Safeguarding indigenous knowledge**

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

## ETHICAL GUIDELINES FOR RESEARCH IN COMPLEMENTARY AND ALTERNATIVE MEDICINE

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 the Traditional and Alternative Medicine Act of 1997 (RA 8423), 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 (WHO) 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 rigor 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 or alternative or 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) in 2011, CAM therapies include the following:

- Biologically-based therapies such as dietary supplements, herbal

products, animal products, and aromatherapy;

- Manipulative body-based methods such as massage, acupuncture, 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; and
- 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, such as whether these therapies are safe and whether they work for the diseases or medical conditions for which they are used.

### **Background information**

1. There should be adequate documentation of the use of the therapy in the community in, at least, one generation.

### **Involvement of an external resource person in the review**

2. The REC shall include an expert or practitioner in the specific traditional medicine modality being considered in the research protocol.
3. The REC shall also include a member of the community where the specific traditional medicine is being or will be used.



## **Use of randomized controlled trial design**

4. 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.
5. Assignment of treatments may use geographic separation of groups to avoid contamination of data.

## **Blinding**

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

## **Safety**

7. The study shall ensure that there is evidence of safety and that the experimental arm will not worsen the patient's condition by the delay in administering conventional medicine.
8. The protocol must identify and describe the rescue medication, which shall be available to the research participants who may require such an intervention.

## **ETHICAL GUIDELINES FOR RESEARCH INVOLVING 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 psycho-socio-cultural aspects of reproductive technology. Research in the reproductive health field, in general, is studded with gender issues.

Research in ART is ethically complex because the research participants in ART research, in contrast to other health research, 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 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 2011, and the Philippine Society of Reproductive Endocrinology and Infertility (PSREI) have set requirements that must be satisfied in medical hospitals, clinics, centers, and other facilities where assisted reproductive techniques or technologies and related research are conducted. Additionally, it is emphasized that clinical and biological research in 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.

The following are considerations that are specific to Reproductive Health Research:

1. All research participants must be accorded due respect. The ethics of Assisted Reproductive Technology research must take into consideration not only respect for the adults involved in the research, but also a special consideration for the ensuing product of the reproductive process.

2. The research protocol must not include any prohibited or unacceptable practices (see Practice Guidelines for ART, Sections 1-6, Philippine Society of Reproductive Endocrinology and Infertility, Inc., Guidelines on the Ethics and Practice of ART and IUI, 2011).
3. Obtaining the informed consent from the potential participants must take into consideration, separation of the research activities from the usual clinical care, gender equity and equality, information regarding the future disposition of the resulting embryo/s, and any COI.
  - 3.1. Information sheets for research projects must be completely separate from, and capable of being read independently of, written information provided to a patient in the course of routine clinical care.
  - 3.2. The consent process must include an opportunity to discuss the protocol with the male and female partners, individually.
  - 3.3. The possibility of multiple embryos must be discussed with the partners; with decisions settled in the light of institutional practice and religious considerations.
  - 3.4. Consent for the use of excess human gametes or human genetic material must be obtained from all concerned persons.
  - 3.5. The participants in research are entitled to know about any financial benefits that the researcher or clinic may gain from the research. For example, when researchers intend to use embryos for research that may ultimately yield commercial profit, such intention must be made clear to the donors from whom these are collected, during the informed consent process.
4. Researchers must keep accurate records of all gametes and embryos in their care, subject to appropriate requirements for privacy and confidentiality.
5. The Protocol should include long-term follow-up procedures to monitor

outcomes of the ART.

6. Researchers must disclose in the protocol to be submitted to the REC, any financial interests they have in the research.
7. Conscientious objections must be appropriately recognized.
  - 7.1. If any personnel or trainee expresses a conscientious objection to the research conducted by an ART clinic or a research facility, they must be allowed to withdraw from involvement in the research to which he or she objects.
  - 7.2. Clinics or research facilities must also ensure that such personnel or trainee are not disadvantaged because of a conscientious objection.

## **ETHICAL GUIDELINES FOR RESEARCH ON COSMETICS**

These guidelines shall be applicable to research on "Cosmetics" as defined by the Consumer Act of the Philippines (RA 7394), as follows: (1) articles intended to be rubbed, poured, sprinkled or sprayed on, introduced into or otherwise applied to the human body or any part thereof for cleansing, beautifying, promoting attractiveness, or altering the appearance, and (2) articles intended for use as a component of any such article, except that such term shall not include soap.

### **Social value**

1. Cosmetic research shall not promote a specific ideology of "beauty" that disparages the characteristics of the Filipino.
2. In consideration of vulnerability issues, cosmetic research shall not be conducted among populations and in communities with limited resources. Neither shall it involve individuals who are not capable of giving informed consent.

### **Quality and safety of the cosmetic product**

3. A certificate of compliance with Good Manufacturing Practice (GMP) shall be obtained for the cosmetic product.
4. Before any participant is exposed to the test product, all safety information regarding the product and its individual ingredients shall have been assessed. Prior to human testing, proof must be presented that each component of the cosmetic article has been tested for safety, respectively, and as compounded.
5. Clinical testing must be preceded by a safety assessment by adequate laboratory experimentation (when applicable), or screening tests (e.g., patch testing) to demonstrate a reasonable probability of success without undue risk.

## **Inclusion and exclusion criteria**

6. Inclusion and exclusion criteria shall take into consideration different skin conditions, allergic reactions, occupation of the participant, and past experiences with cosmetics.

## **Avoidance of risks**

7. The protocol shall include all precautions to be taken to avoid occurrence of adverse skin reactions, (e.g., exposure to sunlight, wetting and drying, interaction with other common skin products, etc.)
8. Cosmetics to be tested on the face, neck, or scalp should be most carefully evaluated for risk of serious adverse reactions.

## **Withdrawal from the study**

9. A participant who withdraws from research for reasons related to the study, such as unacceptable side-effects of the tested product (as defined in the protocol), or who is withdrawn on health grounds, shall be recompensed for lost wages for unfulfilled visits and provided with the appropriate medical care in accordance with REC-approved procedures.

## **Clinical care and compensation of participants**

10. In case of occurrence of unexpected/adverse skin reaction, the investigator shall assess the severity of the reaction, complete the required safety report (e.g., SAE, SUSAR), and start the appropriate therapy promptly.
11. Investigators shall ensure that research participants who suffer an injury as a result of their participation are entitled to free medical treatment for such injury, and to such financial or other forms of assistance that would compensate them equitably for any resultant impairment.

# ETHICAL GUIDELINES FOR ENVIRONMENTAL HEALTH RESEARCH

Environmental health focuses on the physical, chemical, and biological aspects peripheral to individuals, as well as the interconnected factors influencing a person’s behavior. It incorporates all environmentally related attributes that are capable of negatively affecting human health. Additionally, it also delves on the impact of individuals on the environment (WHO, 2011).

The Stockholm Declaration Principle 1, which states that “man has the fundamental right to freedom, equality, and adequate conditions of life, in an environment of quality that permits a life of dignity and wellbeing, and he bears a solemn responsibility to protect and improve the environment for present and future generations.” This shall be the basis of all activities related to environmental health.

The matrix below indicates the core areas of concern in environmental health and are the topics of inquiry in environmental health research.

|                      |                        |                                       |
|----------------------|------------------------|---------------------------------------|
| Air                  | Emergency Preparedness | Food Safety                           |
| Healthy Housing      | Injury Prevention      | Infectious Disease and Vector Control |
| Radiation            | Toxicology             | Vector Control                        |
| Waste and Sanitation | Water                  | Weather and Climate Change            |

Thus, environmental health research is an arm of public health, concerned with understanding the health effects of environments in which humans live and work. It is a diversified field encompassing a range of objectives,

research methodologies, and study designs (Sharp, 2013).

The common objectives of environmental health research include:

- Identification of ecologic hazards and environmental toxicants;
- Assessment of biological mechanisms through which environmental toxicants affect human health;
- Evaluation of interventions designed to mitigate harms associated with environmental hazards; and
- Identification of susceptible populations at increased risk of developing occupational and environmental diseases

The importance of environmental health is emphasized in its inclusion in the global thrusts listed in the post 2015 Sustainable Development Goals. The document enjoins everyone to ensure the attainment of goal number 3, that is, that the number of deaths and illnesses from hazardous chemicals and air, water, and soil pollution and contamination will be substantially reduced by 2030.

A major issue in environmental health research is the existence of potential COI that would put into question research results and recommendations. The 'polluter pays' principle should guide researchers in avoiding COI. It requires that those who produce pollution should bear the costs of managing it to prevent damage to human health or the environment.

### **Study design**

1. The study design shall not include a withholding of effective environmental health interventions from research participants.
2. Environmental health research involving children shall take into consideration their unique susceptibility to certain toxicants that is different from adults. Children shall not be treated like they are little adults.
3. Adequate relocation shall be the goal when there is possibility of contamination in environmental monitoring.



## **Community participation**

4. The participation of the community shall be encouraged in the preparation of the research agenda.
5. Community empowerment and local government action shall be ensured prior to community based environmental monitoring or health research.
6. The research protocol shall describe the communication strategy that ensures cultural setting and community expectations are better understood.
7. Researchers shall first obtain approval from community leaders or whoever is the traditional gatekeeper of the community (e.g., church leaders) before the study begins.

## **Research involving housing-related health hazards and pesticide exposure**

8. The protocol shall ensure that intrusion into the privacy of residents are minimized.
9. The vulnerability of communities in poor-quality housing shall be recognized and protected.
10. In poor housing communities, undue influence to participate because of financial and material incentives shall not be allowed.
11. Mechanisms shall be in place to address the persistence of environmental concerns after the study is completed.

## **Sharing of results with community**

12. Research results, including levels of biomarkers, shall be shared with the community unless results are not definitive and are ambiguous.
13. Results of environmental health studies shall inform policy makers to take appropriate action.

## **Use of biobanks in environmental health research**

14. Environmental health research concerning biobanks shall include a mechanism in its protocol to address the following:
  - 14.1. Respect for the decision of subjects from whom specimen were collected, who participated as children or through their parents and have now become adults, to withdraw their specimen from the biobank;
  - 14.2. Management of incidental findings, especially false positives with putative psychological implications; and
  - 14.3. Transparency in the handling of the financial aspects of the biobank.

## **Management of conflict of interest**

15. Presence of any of the following indicators shall require a declaration of COI by the researcher or expert (adapted from the National Academy of Sciences, 2009).
  - 15.1. Employment and consulting within the past four years, such as being employed by an interested party or provided professional opinion on an environmental issue in court or to a government agency;
  - 15.2. Research support, which additionally, requires a submission of an account of support for the expert's own research and that of his or her unit, including supplies and equipment; or
  - 15.3. Financial interest such as ownership of stock, and other securities, business interest, and patents or intellectual property related to environmental health concerns.

## ETHICAL GUIDELINES FOR EPIDEMIOLOGIC RESEARCH

Epidemiology is the “study of the occurrence and distribution of health-related diseases or events in specified populations, including the study of the determinants influencing such states, and the application of this knowledge to control the health problem” (Porta, 2014).

Epidemiologic research is used to elucidate the causes of diseases and other health-related states as well as to provide information that are utilized for the development and evaluation of interventions for disease prevention and control.

A major part of epidemiologic research involves collection of data from individuals who will not gain any personal benefit and often may not have a disease that needs treatment. There must be assurance that research risks are minimal and that the benefits to society are worthwhile.

Although epidemiologic research does not usually involve interventions that may cause physical 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 may be psychological harms such as embarrassment, strong emotional reactions, and social risks that need to be considered.

Consent procedures in epidemiologic studies need not be as stringent as those for experimental study designs. However, when the researcher proposes selective disclosure of information to the participants, the REC takes a closer look at the protocol and decides whether such non-disclosure is justified.

Oftentimes, genetic and other biological materials are collected in an epidemiologic study. RECs and other appropriate authorities shall set the conditions for the use of these materials beyond the epidemiologic objectives.

Conflicts of interest in epidemiologic studies may not be as obvious as in intervention research like clinical trials, but they do exist. Financial interests and a researcher's ideological advocacy may affect scientific judgment and

influence study results. For example, marketing of vaccines in developing countries may be based on the prevalence of a disease established in an epidemiologic study or public health programs, and may be influenced by ideologically driven epidemiology data.

### **Requirement for ethical review**

1. Epidemiologic studies that aim to contribute to generalizable knowledge shall undergo ethics review prior to start of the study. Exemption from review is a decision made by an REC. (See The Research Ethics Review Process, page 36)
2. The ethical review of an epidemiologic study shall consist of the same elements of review for other studies, namely: social value, scientific soundness, fair selection of participants, favorable balance of risks and benefits, validity of the informed consent process, protection of privacy and confidentiality, respect for participants and protection of vulnerable populations, and appropriateness of the qualifications of the researcher.
3. Collection of data by questionable means, such as deception, shall not be condoned.

### **Scientific validity**

4. The nature of the data and biological samples to be collected, the method of collection, the population from whom the data shall be collected, the method of data analysis shall all be as dictated by the objectives of the study and basic statistical principles.
5. Explicit and detailed research protocols shall fully account for the requirements for scientific validity.
6. Human participant protection, through adherence to ethical principles, precedes that of science and society.

## Informed consent

7. Researchers, in principle, shall obtain written informed consent from all research participants prior to conducting any epidemiological study. Researchers 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.
8. In cases where written informed consent is impracticable, alternative methods of obtaining consent (e.g., verbal consent) shall be employed as discussed in Guidelines for Health-Related Social Research (page 108).
9. Informed consent shall be obtained from parents or in their absence, a legal guardian or legally authorized representative (LAR), for collection of data among children. The informed consent process shall ensure that there is no basis to think that the participant would have dissented.
10. For individuals who are temporarily or permanently incapable of giving a valid consent (as determined by an appropriate assessment method) for themselves, the LAR can sign the ICF, provided that the research does not involve more than minimal risks to the participants.
11. Researchers may request for waiver of the informed consent process if the process is impractical and the research procedures entail not more than minimal risk, for example:
  - 11.1. Collection of information in the public domain. However, it should be noted that communities differ in their definition of what type of information about individuals is regarded as public.
  - 11.2. Review of medical records, if anonymity can be maintained and if information sought is considered non-sensitive (Data Privacy Act of 2012). This means if a data set is successfully anonymized—and therefore, it no longer permits the identification of the individual whom the data set pertains to—it is taken out of the scope of the Data Privacy Act, and the

latter's provisions will no longer be made to apply to the processing (e.g., review) of such data set (e.g., anonymized medical records).

- 11.3. Exemption from the use of the standard form for informed consent (e.g., non-disclosure of all the study objectives) may be permissible if full disclosure of the study hypothesis could bias the investigation. (For other criteria for exemption from the use of standard informed consent form, see Guidelines on Health-Related Social Research, page 108)
12. When feasible, debriefing of research participants shall 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.
13. In general, 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 (waiver of informed consent documentation), since answering the questionnaire implies consent.
14. Appropriate consent for storing biological material for research must be obtained from the research participants. If the samples are to be used for research are not covered by the original consent, an REC shall 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 Genetic and Genomic Research (page 157).

### **Risks and benefits**

15. The protocol shall clearly describe identified risks and ensure that these are minimized by, for example, proper timing of interviews and appropriate design of questionnaires.
16. Since individual participants are not always benefited by epidemiologic studies, benefits to the community and society should be carefully weighed against possible harms to individuals.

## **Privacy and confidentiality**

17. 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.
18. Researchers shall properly manage and protect the personal data of all research participants in compliance with the Data Privacy Act of 2012 and its 2016 IRR. A working standard for data protection that secures as little risk of disclosure as possible shall be developed.
19. Data regarding income, personal habits, preferences, personal opinions, political and religious inclinations, among others, may be considered sensitive and will require consent prior to collection.
20. Researchers shall 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.
21. Whereas, the general population can benefit from information required for timely control or prevention, in no case, however, shall protection of privacy and respect for confidentiality be waived. Removal of identifiers or keeping to the minimum data that could identify groups shall be done to avoid labeling or stigmatizing them. In cases where populations at risk have to be notified, researchers have to ensure that risks of harm outweigh the benefits.

## **Sharing of study results with participants**

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

## **Compensation for participants**

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

## **Management of conflict of interest**

24. Researchers shall disclose all potential and actual COI including involvement in an ideological advocacy related to the research, all forms of financial interests, and sources of funding when applying for ethical clearance, obtaining informed consent from participants, and when publishing or disseminating research results.
25. Potential or actual financial conflicts of interest shall also be disclosed when obtaining informed consent from research participants.
26. Researchers shall avoid entering into contractual agreements that prevent them from publishing results in a timely manner.



## ETHICAL GUIDELINES FOR RESEARCH USING ONLINE AND DIGITAL TOOLS

Online and digital tools provide a relatively new platform for health-related research. They present several opportunities, but also raise ethical issues, especially in the informed consent process. Ambiguity in the determination of risk arises from the minimal interaction between the researcher and the participant. In Internet research, there is little means of gauging participant characteristics (e.g., age), and how participants are responding to the study. In addition, there are issues that are associated with data and personal privacy, and access that are inherent in most Internet activities. While ethical guidelines and standards have yet to be established for Internet-based research, researchers shall be mindful of these issues, and consider current best practices to safeguard the rights of participants and protect them from harm.

1. Researchers utilizing online and digital tools shall be guided by the following questions to ensure that respondents' right to privacy and confidentiality is upheld:
  - How will participants be recruited?
  - How can the requirements for informed consent be fulfilled?
  - Are the individuals identifiable or anonymous? (note that "online identity", even if a pseudonym, may already be attached to an individual's real identity)
  - Is the online behavior "public" or do respondents have reasonable expectations of privacy?
  - Did individuals know or expect that records were being kept (versus ephemeral or impermanent data)?
2. If individuals have reasonable expectations of privacy and impermanence of their online activities, then researchers may need to take specific measures to inform the respondents and obtain their consent to use their data for research, with the attendant protections to their rights to privacy.
3. Soliciting the participation of minors shall be done with extreme care, given that the researcher is unable to verify the age of the respondent,

and shall include strategies for checking and ensuring parental consent. Internet research involving minors should be limited to minimal risk research.

4. Research in the Internet shall be limited to those that entail minimal risk. Moreover, data collection via the Internet shall be justified (versus other means).
5. Additional safeguards for maintaining privacy and confidentiality of information shall be used (e.g., pseudonyms, modified quotes to prevent immediate retrieval through search engines, encryption, separation of data files for identifiers and responses).
6. The study team shall include a member who is familiar with technical issues concerning Internet security, including additional safeguards.

## ETHICAL GUIDELINES FOR HEALTH-RELATED SOCIAL RESEARCH

The relationship between health research and social realities is a symbiotic and complex one. First, all health research involving human participants are conducted within a social context. Second, while health and health-related research encompass a broad range of academic disciplines and concerns, social research not only covers a wide of social science disciplines but also a host of interrelated but possibly conflicting theoretical and methodological approaches, albeit even within a particular academic discipline. Not surprisingly, these differences may in turn lead to divergences in ethical considerations and requirements. Third, there are also such subfields in the social sciences, such as health social science and the sociology of health, where the intricate relationship between health and society are more closely examined. Fourth, overlaps and divergences in the social sciences notwithstanding, all social research involving human participants have possible health and health-related implications. Under these circumstances, it is the responsibility of social researchers to anticipate these possible health-related ethical concerns and make the necessary referrals to relevant organizations and agencies, if the need arises.

Notwithstanding differences, health or health-related social research must adhere to the General Guidelines which are founded upon the principles in the Belmont Report (1979). The aim of these guidelines is to encourage researchers to think through the ethical issues that may arise during the entire research process and to see how they can in utmost good faith, uphold the requirements of respect for persons, beneficence, and justice given the particular theoretical and methodological underpinnings of the research from the preparation of a research proposal until the archiving and destruction or disposal of raw research data. To enable researchers to further critically reflect on the above principles, the guidelines contain references to ethics codes and legal norms relied upon as their basis.

Some theoretical perspectives and research methods make use of inductive logic in order to produce or develop theories and hypothesis in the course of fieldwork. It will not be immediately possible for researchers using such methods to provide RECs specifically formulated research questions, as well as instruments, and to identify all possible participants whom the researcher

may encounter during the course of fieldwork. RECs shall recognize that using such perspectives and methods means allowing for flexibilities in research design that allows modifications of topic focus as the research is carried out. Researchers using said perspectives and methods have to periodically deal with ethical issues throughout the research process and respond to different circumstances.

## **General Issues**

While most ethical concerns in social research are basically the same as in other categories of research, there are certain unique issues given that the context of the research and the role of the researcher are different compared to clinical or controlled studies. Ethical issues concern the role the research plays in addressing social inequities, or power relations between the researcher and the participants which may impact the informed consent process. Moreover, the nature of the risks to participants and the strategies to mitigate them may not be as easily apparent, as they go beyond physical or health risks.

The relationship between the researchers and the people they study involves an inherent imbalance in power in favor of the researcher. The researcher is more knowledgeable and has greater access to resources than the people they are studying, especially if the sample population is a marginalized group. There are opportunities to take advantage of this imbalance when seeking to enter communities, households, and the personal and social lives of participants.

The burden is therefore on the researcher to undertake measures to clarify and balance the personal and political power of all stakeholders involved in the study. An example of these measures would be to increase the level of participation of the people being studied in designing the study or validating the results of the study. Researchers shall likewise exercise care that their research does not exacerbate existing inequities, including gender-based and class-based inequities, and shall ensure that no group is inequitably burdened with risks in research.

## Consent process

1. A prospective participant is given a voluntary choice to participate in a study after being fully informed about the nature, purpose, and procedures of the study, and potential risks and benefits of participation.
2. The researcher shall fully disclose 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 specific details about the research procedures (e.g., the number of interview sessions and the length of time involved), foreseeable risks and benefits, and how privacy will be safeguarded.
3. Obtaining informed consent needs to be seen as a process, not a single event occurring at the beginning of the research. The burden is on researchers to see to it that participants are aware that they can withdraw at any time from the research. Researchers must be sensitive to the cues given by participants who may not always verbalize that they wish to withdraw from the research but who show through their actions that they are thinking twice about being participants.
4. Where there is a psychological or social intervention that is being tested that is, as yet, of uncertain benefit (e.g., pilot studies), researchers shall indicate this and its foreseeable risks and outcomes (whether positive, negative, or no effects) in the informed consent form. This is to forestall any unwarranted assumptions of benefits of the social intervention, which may induce individuals or communities to participate.

### *Undue coercion and influence*

5. The researcher must be mindful of implicit undue coercion to participate in studies, and address this in the informed consent process, such as in the following situations:
  - 5.1. *When students are “required” to participate in faculty research; to be part of the subject pool; and other contexts wherein participation in studies is graded.* In such cases, students shall

be presented with alternative requirements or projects that are equivalent in effort and merit to participation in studies. The benefit of research participation shall not be so large as to remove students' freedom to voluntarily decide to participate.

- 5.2. *When students are enjoined or required to collect data for faculty or for a class; to recruit a certain number of participants for a grade.* In such cases, students may be pressured to circumvent the informed consent process to obtain a grade or benefit in their classes. Students shall be trained and supervised by faculty or senior researchers in the necessity of the informed consent process, and the number of participants recruited must not be the basis of a grade or class benefit.
- 5.3. *Soliciting the participation of prisoners and other institutionalized persons, or of indigent groups.* The marginalized status of these samples, and their restricted autonomy, make them vulnerable to coercion. Researchers shall take more care to uphold their autonomous right to decide to participate in a study.
- 5.4. *When consent or permission is initially sought from individual gatekeepers, such as community leaders and officials, or from collective decision-making bodies.* In addition to negotiating access to the field through such "gatekeepers", the researcher shall supplement the permission of collective bodies with that of individuals, particularly where substantial sectors of the local society are excluded from collective decision-making but are also research participants (Association of Social Anthropologists, 2011).

### *Research with Indigenous Peoples*

6. The researcher must be aware of the special requirements and considerations in conducting research with and obtaining informed consent from indigenous peoples (IPs). Best practices in research with IPs ensure that the rights of IPs are upheld, and that the research purpose, design, and methods are culturally sensitive, empowering, and

beneficial to the IP community. (See Guidelines for Research among Indigenous Peoples, page 124)

*Waiver of informed consent*

7. The informed consent process may be waived in specific research contexts, such as:
  - 7.1. Archival research involving publicly available documents;
  - 7.2. Research that uses the method of naturalistic observation (often described as “covert” method) in data collection. Naturalistic observation does not necessitate informed consent if the activities or behaviors observed are public in nature such that any person can observe them without violating principles of confidentiality or privacy;

However, if observations are recorded in such a way that the individuals involved are identifiable, then informed consent may be necessary depending on the nature of the study (i.e., if risks to participants are likely). Moreover, use of this method requires that the researcher provide:

- 7.2.1. A thorough justification for the use of naturalistic observation;
- 7.2.2. A plan for how the data collected will be used; and
- 7.2.3. A mechanism to ensure confidentiality and anonymity of observed individuals and their data.

*Waiver of signed informed consent*

8. Under the General Guidelines (page 10) informed consent is documented through a signature of the participant or his or her legally authorized representative (LAR) on the informed consent form (ICF). Documented informed consent may be waived (with the approval of the REC) if:

- 8.1. The research presents no more than minimal risk and does not involve procedures (e.g., medical interventions) for which informed consent is normally required; or
  - 8.2. The only record linking the participant to the research would be the informed consent document, and the principal risk to participants would be the potential harm resulting from the disclosure of the informed consent document; and
  - 8.3. In cases where the documentation requirement is waived, the REC may require the researcher to provide participants with a written statement regarding the research.
9. Under certain circumstances, it is appropriate to obtain informed verbal consent. Participants can be highly suspicious of formal bureaucratic procedures. Requests for signatures on printed forms can render standard procedures for obtaining written consent problematic. However, the process must still be documented and witnessed.

*Waiver of some elements of the informed consent.*

10. Some or all of the elements in the informed consent may be waived or altered (with the approval of the REC) if all these conditions are met (see Informed Consent Form, page 11):
- 10.1. The research presents no more than minimal risk; and
  - 10.2. The alteration will not adversely affect the rights and welfare of the participants; and
  - 10.3. The research cannot be practicably carried out without the waiver or alteration; and
  - 10.4. The participants will be provided with additional pertinent information after their participation (whenever appropriate).



### *Withholding of information*

11. Withholding information in the informed consent process may be necessary in order to control biased responses of participants (i.e., demand characteristics; good subject phenomenon). This may be done if:
  - 11.1. It is justified by the prospective scientific, educational, or applied value of the study;
  - 11.2. The risk is minimal and the potential harm is reversible;
  - 11.3. No equally effective design or method can be used; and
  - 11.4. Debriefing is performed as soon as appropriate.

### *Consent of minors and mentally incapacitated persons*

12. In the case of 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 witnessed. (See Guidelines for Research among Minors or Children, page 131)

In the case of potential research participants who are elderly, demented persons, or other mentally incapacitated persons, there shall be independent screening of their capacity to make decisions on their involvement in the study. (See General Guidelines, page 10).

### **Community research**

13. In community-based research (e.g., studies involving social action or participatory action research [PAR], community or multi-component interventions), community consent or permission shall be sought alongside individual consent.
14. The researcher shall conduct proper consultation with community leaders and stakeholders prior to initiation of the research. If relevant, there shall be disclosure to the community during consultations prior to

data collection that observations 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 shall not be divulged, the researcher shall explain to the community why such prior disclosure could not be done.

15. In no case shall the researcher collect data through naturalistic observation if the community forbids it. There are communities (e.g., indigenous communities) who consider certain public activities (as defined above) to be sacred, and certain behaviors of outsiders as taboo.
16. The researcher shall consider the customary or culturally-valued practice of decision-making in the community while noting permissible waivers or modifications of the informed consent process.

### **Management of risks and harms**

17. Researchers shall ensure that risks of harm to the research participants in their study are minimized.
18. In research protocols where risk is not completely eliminated or mitigated, the benefits of conducting the study must clearly outweigh these potential risks.
19. The researcher shall consider the overall benefit of conducting the study as well as the specific need and benefit of asking each question or item in the research instruments. The need to know or ask the questions or items (i.e., the researchers' priorities) must be balanced with the welfare of the participants and their right to privacy.
20. The protocol shall include referral and reparation strategies where there is potential or actual harm. These must be concrete, specific, and realistic, and not general statements.
21. The researcher shall have the necessary expertise and competency to undertake the study (e.g., training and/or experience in the use of the specific method and on the subject matter). Competency shall also

include sociocultural sensitivity to the population and community under study, and awareness of the ethical issues involved.

22. When the research causes psychological stress to the research participants, there shall be provision for debriefing or counseling.
23. In case unforeseen situations arise during the study that require its temporary or permanent cessation, researchers shall discontinue the study completely or resume it when the risk of harm is at a reasonable level. Researchers shall undertake appropriate measures to prepare the research participants or community for exit of the study.
24. The researcher shall report to the REC any increased levels of risks or harms, and await the REC's advice prior to continuing or making changes in their procedures, unless such changes are necessary to prevent immediate harm to the participants.
25. The table below shows examples of risks and corresponding protection strategies that may be incorporated in a social science research protocol:

| <b>RISK CATEGORY</b> | <b>EXAMPLE OF RISKS</b>        | <b>EXAMPLES OF PROTECTION STRATEGIES</b>  |
|----------------------|--------------------------------|---|
| Physical             | Fatigue                        | Inclusion of rest breaks in the protocol; supervision of a physical trainer                                       |
| Social               | Stigma                         | Procedures to safeguard confidentiality of data; de-identification of materials and data at soonest possible time |
| Psychological        | Emotional Distress             | Friend or spouse can accompany respondent; referral protocol for follow-up psychological support if needed        |
| Legal                | Disclosure of illegal drug use | Obtain legal safeguards to protect confidentiality of data; referral protocol                                     |
| Economic             | Loss of job or advancement     | Confidentiality of data (non-disclosure to employer)  |

26. Risks to researchers shall be identified in the protocol and the proposed

management of such shall be a consideration for ethical approval. The researcher shall include a report on negative events (e.g., sexual harassment, physical threats, stalking), in its progress and final reports, to the REC.

27. The institution shall compile a list of reportable negative events (RNEs) as part of its research safety monitoring and management program.

### **Access to services or benefits**

28. Researchers shall endeavor to protect and promote the safety and interests of the individual or community participants. Researchers shall include in the proposal a description of how the benefits of the study will be shared with the study population.
29. In carrying out experimental or quasi-experimental research, access to services or benefits provided to the experimental group shall also be provided to the control group (if such services or interventions were found to be positive). If the intervention is a benefit at the same time the experimental variable, the withholding of the intervention to the control group shall only be for the duration of the experiment.
30. In 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.
31. In the matter of possible commercial use of output, benefit sharing shall be discussed with the participants during the solicitation of consent, and shall be based on current good and legal practices.
32. Researchers shall include in the proposal how the research findings or report will be shared with the people being studied after data collection. Researchers shall endeavor to inform the research participants or community they studied about their research findings. The findings shall be presented in a language and style that is understandable to them.
33. Potential legal repercussions in the research, for both or either the researcher and research participants, shall be carefully identified in the

study proposal, and steps undertaken to mitigate or eliminate such repercussions.

## ETHICAL GUIDELINES FOR RESEARCH IN MENTAL HEALTH

A quick survey of current research in mental health revealed a rich variety of research projects like anthropological studies on mental illness, an inquiry into the common language for mental health symptoms and manifestations, clinical drug trials including pharmacogenomics, the determination of effectiveness of psychosocial interventions in drug abuse and post-traumatic or aftermath of violent experiences, establishment of a national clinical registry for mental illness, the derivation of a of a Filipino diagnostic manual for mental illness, various association and causative genetic studies, and development of programs that support mental health. Mental health research involves the young and older persons, for the whole range of normality and illness, and different sexual orientations.

Mental health research may be described as positivistic or phenomenological in approach and includes both clinical and non-clinical studies that involve different disciplines (e.g., anthropology, psychology, sociology, psychiatry, genetics, pharmacology, philosophy, and the like). It is conducted in various settings including health care facilities, free-standing clinics, schools, and in communities where mental health interventions are planned or done.

While most ethical concerns in research involving human participants are similar to those recognized in other research areas, there are unique issues challenging mental health research, with particular issues found in the Philippines. Foremost is the usual exclusion of persons with poor insight, thus creating a selection bias and introducing a limiting factor in the study conclusion. There are certain difficulties in clinical drug trial protocols like when the inclusion criteria require the selection of patients who are actively psychotic, who need immediate medical attention and cannot undergo the usual washout period, and the risk of suicide among patients who are recovering from depression, as an effect of an investigative new drug. There is also conflict between giving the current acceptable standard of care, when the drug trial excludes psychotherapy. There are certain interventions in mental health research where blinding is not feasible, like when psychotherapy is in one of the research arms. Further, there can be legal issues when dealing with reportable crimes (e.g., illegal drug use, domestic violence, etc.).

Fundamental to mental health research is the use of mental health status or behavioral scales. These are clinical or behavioral scales that have been developed, validated, established, and licensed in Western countries. There is a perceived lack of validated translations, both conceptually and culturally, for Filipino participants. Mental health organizations are thus urged to translate and validate internationally-sourced clinical/behavioral scales such that they are conceptually and culturally applicable for Filipinos and, thereby, be able to contribute to global mental health knowledge and policies.

## **Methodology**

1. The researcher shall develop ways and means, other than blinding, to promote objectivity of data collection. One way is for the observer or assessor to be uninformed (assessor-blind) about the intervention. Another is for the control and experimental groups to be geographically separate so that there is no contamination of data observations.

## **Selection of participants**

2. All persons, regardless of mental health status and place of care, who will potentially benefit from the knowledge generated in the proposed mental health research, shall be considered as possible participants.
3. Exclusion of certain groups of individuals because of their lack of capacity (e.g., poor insight) to provide a valid informed consent is not fair especially if the study can generate benefits to the individual or group. This incapacity is addressed by a proxy consent (LARs), while continuing to exert effort to obtain the individual's informed consent when the individual's insight improves.

## **Informed consent**

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

5. Informed consent is a continuing process and the mental health researcher must base his or her assessment of the decisional-capacity of the potential subject on established tools or instruments.
6. Proxy consent based on best interest shall be obtained from LARs whenever there is doubt. The involvement of LARs in the informed consent must be properly documented as required by law, such as, The Family Code of the Philippines (EO 209).
7. In cases where the decisional capacity is not a permanent disability, the researcher shall endeavor to obtain the informed consent during moments of rationality.
8. Researchers must take care to clarify the purpose of the study in order to address participants' desires for therapeutic outcome, social contact, or practical help.

### **Confidentiality**

9. Confidentiality is the responsibility of the person with whom this private information was given. However, when the right to safety of another individual is infringed, the policy of right to privacy may be breached. This happens, for example, when the plan to harm another individual is unearthed during an interview, or in the data interpretation and analysis. The researcher shall exercise due diligence in determining whether such findings justifies breaching of the privacy of the participants.

### **Special guidelines in clinical trials**

10. In clinical trials, the protocol shall include a rescue strategy or rescue medication, including a close monitoring strategy (that may include hospitalization) in order to look after the safety of the subject patient during a wash-out period, where there is a risk of exacerbation of symptoms and heightened risk of adverse events. This requires that the clinical trial site has the capability to manage serious adverse events.
11. Investigators involved in clinical drug trials for management of



depression shall include the risk of suicide among the enrolled patients in the orientation and training of the research staff, and in the arrangements regarding patient care. For example, the investigator shall weigh his or her options for outpatient or inpatient observations and the need for round-the-clock monitoring and observation.

12. Clinical trials of drugs for mental illness where standard care includes psychotherapy shall be designed, such that a psychotherapy regimen is clearly described and is included in the protocol for both the control and the experimental. Non-inclusion of the psychotherapy regimen must be justified, and clear clinical metrics be put in place to monitor early signs of deterioration.
13. The investigator and the REC shall clarify the nature and extent of care for clinical trial participants at the end of the trial period. Arrangements for continuing care shall reflect fairness, as an important ethical principle in research.
14. Pharmacogenetic studies that usually ride on clinical drug trials shall have a separate informed consent process and a separate form for signature of the patient or the LAR.
15. Studies on genetic causation of and susceptibility to mental illness shall be carefully conceptualized, and the limits in the interpretation of data seriously considered and analyzed. Genetic counseling must be in place before embarking on these endeavors.

### **Community-based research**

16. Research conducted in specific communities that have implications on the general mental health of the constituents and their possible stigmatization must be avoided, unless there is a strong justification for it. The justification must be weighed against the risk of harm for the present and future members of the community.

## **Research where illegal activities may be encountered**

17. As much as possible, unless the objectives of the study significantly address problems related to illegal activities, such studies shall be avoided by researchers. However, if the benefits to society are commensurate with the risks, proper and adequate consultation with the law and police authorities shall be done prior to its implementation to protect both the researcher and the participant.

## ETHICAL GUIDELINES FOR RESEARCH INVOLVING INDIGENOUS PEOPLES

There are challenges in the use of mainstream standards or guidelines when indigenous peoples/indigenous cultural communities (IPs/ICCs) are involved as research participants. The composition, standards, and procedures of RECs pose problems when IP/ICC ethics are not represented because there may be norms and practices that could be inconsistent with existing research ethics guidelines.

The PHREB and the National Commission on Indigenous Peoples (NCIP) agreed on a Memorandum of Understanding in 2016 (page 186) that described the level of coordination about the ethical review of research conducted in IPs/ICCs. It specified that the research protocol must first undergo a preliminary evaluation by an REC, and if found acceptable, the REC shall endorse the same to the local or provincial NCIP authority which, in turn, will evaluate the protocol using NCIP requirements and processes. If found compliant and satisfactory, the protocol will be given an NCIP clearance. The clearance is to be used by the REC as basis for issuing the final ethical approval.

### Oversight considerations

1. In deliberations on research involving special populations by an REC, the following considerations shall be included:
  - 1.1. Social and cultural needs of the IPs/ICCs;
  - 1.2. Clarification of the various roles of different stakeholders such as the sponsors, researchers, and volunteer workers and identification of potential conflicts of interest;
  - 1.3. Compliance with existing national and local regulations and international guidelines relevant to the protection of rights of IP populations and establishment of a monitoring mechanism to ensure that the guidelines are complied with such as the:
    - Indigenous Peoples' Rights Act (IPRA) of 1997 (RA 8371);

- United Nations Declaration on the Rights of Indigenous Peoples (UNDRIP);
  - Convention on Biological Diversity (CBD)
- 1.4. Access to a member, advocate, or representative of IPs/ICCs who has a good understanding of the nature of indigenous knowledge and its means of expression;
  - 1.5. Recognition of the right to self-determination of the IP; and
  - 1.6. Recognition of the members of IPs/ICCs as partners with equal rights in the research process.

### **Informed consent**

2. Research involving IPs/ICCs must comply with standard elements of free and prior informed consent (FPIC), such as capacity to consent, disclosure, comprehension of information disclosed, voluntariness, and signification of consent, both oral and written, including a memorandum of agreement with the community, as needed; with special consideration for IP values and concepts.
3. Obtaining informed consent involves two interrelated processes: (a) obtaining the FPIC of the community for the study to proceed, and (b) individual consent to participate. The first is required by IPs/ICCs for the second to proceed.
4. Whereas balance must be sought between community approval and individual informed consent, the former cannot override the latter. If a member of the community feels compelled to consent because the community has already approved the study, then such autonomy may be regarded as compromised. However, if community approval was arrived at after several community meetings, discussions, consensus taking, where members freely participated, the community approval may be regarded as the representation of the members' decision. In this case, the group's decision strengthens individual decision rather than violates individual autonomy.

5. 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.
6. Securing free and prior informed consent shall be in adherence to the processes specified under the IPRA and if possible, with the presence of NCIP members.
7. Other documents may be required in addition to the standard informed consent form (e.g., IPRA documentary requirements such as a memorandum of agreement with the community).

### **Competence of researcher**

8. The researcher must be familiar with the culture and preferably with the language of the indigenous people being studied. The researcher shall approach the IPs/ICCs, seek informed consent, develop a culturally-sensitive research design, and conduct a study that does not violate its tradition, while respecting individual autonomy.
9. The researcher shall identify the appropriate community members to consult for specific research problems.
10. Competence of researchers to conduct the study shall be assessed as part of the ethical review process. The researcher may be requested to appear before the REC that is processing the application for ethical clearance, and manifest required competence.
11. The researcher shall ensure the protection of confidentiality of research materials and results, including those that may be deemed proprietary by the community.
12. Researchers shall familiarize themselves with the procedures for pre-termination. A researcher shall pre-terminate a research project when

the welfare and rights of the IPs/ICCs are compromised.

### **Respect for traditions**

13. The researcher must demonstrate knowledge and appreciation of the traditions of IPs/ICCs through the inclusion of an appropriate social preparation phase of the study.
14. The researcher shall acknowledge and maintain respect for elders, which is a highly-valued tradition in IPs/ICCs. The tradition underscores the rationale why communities would not participate in a study without the approval from elders for the study to commence. Ignoring or bypassing the elders disrespects the tradition of IPs/ICCs. (See informed consent above)
15. The researcher shall respect sacred places and rituals, including request of communities to conduct rituals, as part of the decision-making process of IPs/ICCs whether to allow the study or not.
16. The research design shall 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**

17. Risks and harms to normal populations shall be included in the risk-benefit assessment.
18. Special attention shall be given to the vulnerability of IPs/ICCs. It is essential that procedures for informed consent taking and arrangements for benefit sharing consider this vulnerability.
19. Care shall be exercised in disseminating information that could be used by vested interests in exploiting IP resources or violating their traditions. The community should consent to the dissemination plan and the information to be disseminated.

20. 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.
21. The study shall take into consideration requirements for the protection of biodiversity already contained in the Guidelines for Herbal Research (page 82), as well as other pertinent legislation.

### **Benefit Sharing and Ownership**

22. The research plan shall include explicit description of access and benefit sharing 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.
23. Information about access and benefit sharing shall be disclosed during community consultations and solicitation of individual consent.
24. Access and benefit sharing agreements shall be formalized as stipulations in a contract or memorandum of agreement between the IPs/ICCs and other parties.
25. Research shall comply with Philippine laws on the transport and protection of indigenous materials.
26. Results of the research project shall respond to the needs of the IP/ICC and presented in a manner that is useful and accessible to its members, and in a language fully understandable to the community. The research results shall be presented to the community members prior to publication or presentation in various research forums; with their comments taken into consideration in the development of the final report.
27. In case communities, or parties other than the study community, make an ownership claim on the knowledge (and on the benefits) from the study, the researcher shall undertake separate consultations and negotiations with these parties or communities.

28. Sponsors or funders of the research shall comply with all access and benefit sharing agreements, and this compliance should be made part of the researcher’s stakeholder responsibility. Additionally, the researcher shall 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.
29. Dissemination and communication plans of the research shall 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.
30. IP/ICC ownership of traditional knowledge shall be acknowledged in any report in any medium.

### **Role of the Research Ethics Committee**

31. An REC that processes the ethical clearance of research involving IPs must have adequate understanding of the application of the instruments cited in the “Oversight considerations” section of this guideline (see 1 above). If necessary, the REC shall invite an expert to assist in the review of the study.
32. Expertise of the REC could be enhanced by the presence of articulate and empowered IP/ICC representatives who genuinely embody the interest of the indigenous peoples to be studied. Empowerment is key because without it, the IP/ICC representative could be awed and inhibited in the presence of professionals in the REC.
33. If an indigenous expert is available, there shall be a preference for this person to inform the decision of the REC, in which case, the REC should consider using language that is familiar to the indigenous expert during its deliberations.



## **Approval of Protocol Amendments**

34. Any change in the approved protocol shall undergo the approval process of the REC and the ICC.

# ETHICAL GUIDELINES FOR RESEARCH INVOLVING MINORS OR CHILDREN

“Minors” are persons under 18 years of age and the term may be used interchangeably with the term “children.”

Republic Act No. 6809 places the age of majority at 18 years 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 enter into contracts on their own, or sign the ICF.

Pediatric practice, on the other hand, includes patients who are more than 18 years though under 19 years old. The practice means that pediatric research may include patients who can already sign the ICF on their own, without requiring parental consent.

Assent is the manifestation of the agreement of a minor to participate in a research or clinical trial. The assent may be in the oral or written form.

Minors are considered as belonging to a vulnerable population.

1. Research involving minors is justified when:
  - 1.1. 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 such that research among adults who had these illnesses in their childhood will not elicit accurate results.
  - 1.2. The purpose of the research is to obtain knowledge relevant to the health needs of children.

## **Requirement for permission from a legally authorized representative**

2. A parent or legally authorized representative (LAR) of each child shall provide the necessary consent for participation of the minor. In default of parents or judicially declared guardians, this order of authority shall

be followed:

- 2.1. Grandparents;
  - 2.2. Oldest sibling over 21 years of age, unless unfit or disqualified;
  - 2.3. Actual custodian over 21 years of age, unless unfit or disqualified.
3. Where the parents are both of minor age or themselves incapacitated to enter contracts, or give consent to their child's participation in research, the guidelines on medical treatment of such a child may be followed whereby a third party may give the consent (i.e., the child's grandparents, physician, or the hospital administrator, as in emergency cases).

### **Requirement for assent**

4. Aside from the informed consent being required from LARs, assent from minors must also be obtained. Thus, the protocol must include the procedure for obtaining the minor's assent. The minor's assent to participate in the study shall be obtained without coercion.
5. At any age, any sign of dissent shall be observed, and children who dissent must not be recruited to the study.
6. The manner and form by which a minor provides his or her assent shall be as follows:
  - 6.1. If the minor is under 7 years-old, no formal assent, whether verbal or written, is needed as long as there is no manifestation of dissent.
  - 6.2. If the minor is 7 to under 12 years-old a verbal assent is acceptable. Documentation of the verbal assent is required. Documentation may be in the form of a written description of the process and witnessed.

- 6.3. If the minor is 12 to under 15 years-old, he or she shall sign a simplified Assent Form that is different from the Informed Consent Form which the parents or guardians sign. The Assent Form shall have been reviewed and approved by the REC. The decision to have an Assent Form for participants below 12 years-old rests on the REC. (See Appendix L: Informed Assent Template)
- 6.4. If the minor is 15 to under 18 years-old, he or she can sign on the same informed consent document signed by the parents.
7. A minor's refusal to participate or continue in the research shall be respected.
8. Information on the study to which the child's participation is sought, and terms such as "research," "study design," "procedures," "adverse effect," "voluntary" shall be explained in a manner and language the child understands for purposes of assent and dissent.

#### **Determining the age of the child**

9. The age of the child shall be determined by documentary evidence as follows:
  - 9.1. Child's birth certificate;
  - 9.2. Child's baptismal certificate;
  - 9.3. Any other pertinent documents such as, but not limited to, the child's school records, dental records, or travel papers;
  - 9.4. In the absence of all of the above, competent testimonial evidence may be used.
10. 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 the best interest of the child.

11. Assent presupposes that the child is mentally and physically capable of understanding what study participation entails. However, a competency examination of a child, *motu proprio* or by request of a party, shall be conducted when there exists substantial doubt regarding the ability of the child to understand the nature and consequences of giving assent.

## ETHICAL GUIDELINES FOR RESEARCH INVOLVING OLDER PERSONS

The Philippines needs to prepare for the burgeoning population of older persons. The population of those who are 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 research 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 research.

There is a need to differentiate between legal competency and the capacity to make research-related decisions.

Ethical challenges in research on older persons include the following:

1. Variability of health status and functional capacity among the young old (60 to 69 years), middle old (70 to 79 years), and the oldest old (80 years and above). This implies that researchers will need to design protocols to take into consideration such variability and to disaggregate data during the stage of data analysis. In 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-research participant interactions, leading to adverse drug events.
2. Physical and sensorial disabilities such as blindness, deafness, and mobility problems may inappropriately exclude such persons from needed participation in research.
3. Neurological and psychiatric illnesses that affect mood, movement, and cognition are accompanied by challenges in obtaining informed consent.

4. Research participants' 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.
5. An increasing number of older persons living in long-term care institutions, or home-bound, may be inadvertently excluded from participating in research, leading to recruitment bias.
6. Socio-economic demographic characteristics may render the older persons more vulnerable, and may affect their participation in research.

### **Inclusion of older persons in research**

7. 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 shall be represented in research.

### **Informed consent**

8. Researchers must be careful to clarify the purpose of the study to address participants' desires for therapeutic outcome, social contact, or practical help.
9. 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.
10. 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. But these shall not necessarily exclude them from participation in the research.
11. In the event that capacity for an informed consent is doubtful, a

cognitive assessment shall be done. There are several tools that may be used to determine decisional capacity. To assess cognition, the Alzheimer’s Disease Association of the Philippines (ADAP) 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 the use of the Adapted-Functional Activities Questionnaire (A-FAQ). The researcher may also use the following guide to determine competency:

- LS1: the research participant knows that he or she is faced with a choice;
- LS2: the research participant has the capacity to make a reasonable choice comparable to that of a normal person;
- LS3: the research participant is aware of the emotional consequences of his or her positive or negative choice;
- LS4: the research participant is able to provide reasons for his or her choice;
- LS5: the research participant 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 researcher’s clinical judgment, based on history and assessment, is of utmost importance.

12. In the absence of capacity or competency to provide informed consent, a legally authorized representatives (LAR) may provide consent on 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**

13. It is recommended that the research design consider representing the various subgroups such as age, gender, socio-economic, and functional status.
14. A thorough list of chronic diseases, prescription drugs, over the counter drugs, and supplements will help determine potential for adverse drug events, which is especially relevant in clinical trials.
15. The protocol shall include safeguards that are proportionate to impairment and experimental risk and benefit.

## **Conduct of the research**

16. Involve LARs and primary caregivers in all phases of the research. This may entail regular, weekly communication between the study staff and the primary caregiver.
17. The research participant has the right to withdraw from the research, at any time, during the conduct of the research. The LAR and researcher must be sensitive to signs of dissent from the research participant, especially those with communication problems. Dissent must be respected.
18. The researcher shall ensure that the study compensation will directly benefit the research participants.

## **Dissemination of research output**

19. The researcher 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 results of the study.
20. Reports of study results that are communicated to older persons must be in the form that is easily understandable to the participant.

## **ETHICAL GUIDELINES FOR RESEARCH INVOLVING MILITARY PERSONNEL**

Military organizations have their own culture and tradition that is rooted on discipline, obedience, and value for training. In this context, research may be expected to accord substantial consideration for the nature of the hierarchical or superior-subordinate relationship in the military, based on the “obey first before you complain” principle. Thus, soldiers are rendered vulnerable in the context of health research.

1. Involvement of soldiers in a research framed within the above military tradition must be justified by any of the following reasons:
  - 1.1. The study pertains to a special concern of military personnel;
  - 1.2. The study will provide direct benefit to military personnel; or
  - 1.3. The risk entailed is minimal.

### **Recruitment and enrollment**

2. Officers shall not influence the decision of their subordinates.
3. Officers and senior non-commissioned officers shall not be present at the time of recruitment of the subordinates.
4. Officers and senior non-commissioned officers shall be recruited separate from the subordinates.

### **Informed consent**

5. Special protection must be accorded to military personnel to ensure that the informed consent process is truly voluntary, free from undue influence or a coercive presence or intimidation from superior officers.
6. Researcher-officers shall not to be in military uniforms when obtaining informed consent.

## **ETHICAL GUIDELINES FOR RESEARCH INVOLVING PEOPLE WITH DISABILITIES**

Any research involving human participants is ethically bound to be done in a manner that respects the human rights of the concerned individuals. With respect to persons with disabilities (PWDs), the UN Convention on the Rights of Persons with Disability has made it clear that these human rights include the respect for the inherent dignity, individual autonomy, and independence of persons. In ethical review of research involving PWDs, other core principles in Article 3 of the UN Convention, such as equality, full and effective participation and inclusion in society, respect for difference, and accessibility must be addressed.

Under the Magna Carta for Disabled Persons (RA 7277), disabled persons are those persons suffering from restriction or different abilities, as a result of a mental, physical, or sensory impairment, to perform an activity in the manner or within the range considered normal for a human being. Impairment may be any loss, diminution or aberration of psychological, physiological, or anatomical structure or function. Any research protocol would therefore have to address and accommodate the nature and type of disabilities of the intended research participants.

The general principles in research involving persons with disabilities, as enumerated, are not any different from those involving persons without disabilities. However, it is the depth of sensitivity to the PWD situation, and the representation of this population in the collection of data that spells the difference. PWDs are classified as vulnerable participants, and the informed consent process shall ensure freedom from manipulation and coercion; with special consideration to this population's special needs.

1. The well-being of the PWDs participating in research, involved in or affected by the research process shall be promoted at all times.
2. The dignity, autonomy, equality, and diversity of all the persons involved in the research process shall be respected.
3. The researcher shall respect the PWDs freedom to choose to participate or not, and protect their privacy and the confidentiality of their personal

information.

4. Respecting autonomy means that PWDs who participate in a research have the right to make their own decisions regarding participation in the research process.

### **Participation of PWDs in research**

5. If research involving humans is to be truly representative, PWDs should be equally eligible to participate as research participants, and the protocol shall describe the necessary steps to facilitate such participation.
6. The diverse nature of research means that the various ways of including PWDs need to be assessed in order to decide which one is appropriate for a particular study.
7. The researcher shall consult with PWDs or their representative groups regarding the research topic, research questions, and research design.

### **Disability awareness and sensitivity training**

8. Researchers and the research staff shall have disability awareness training (or equivalent qualifications) in preparation for the implementation of any research conducted with this population.

### **Facilitating participation in research of PWDs**

9. The researcher shall endeavor to address the needs of research participants with visual, hearing, speech, cognitive, or other physical impairments in order to facilitate participation in research as follows:
  - 9.1. Use of large print materials or audio tape for people with vision impairments;
  - 9.2. Provision of easy-to-read materials or interpreters for people with cognitive impairments;

- 9.3. Facilitation of interviews through lip-reading, written materials, or sign language interpretation for people who have hearing impairments; and
- 9.4. Use of physically accessible venues during interviews or focus group discussions (FGDs).

### **Dissemination of research findings**

10. The researcher shall ensure that research participants and disability groups are included in the dissemination of the research findings.

## **ETHICAL GUIDELINES FOR RESEARCH INVOLVING PEOPLE LIVING WITH HIV AND AIDS**

HIV and AIDS research encompasses a wide range of research activities that include basic research on the infectious agent and its effect on individuals, clinical trials on vaccines and other therapeutic protocols, and investigations on the psycho-socio-cultural 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, RECs, researchers, and funding agencies shall 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 sensitivity of reproductive health issues.

In the preparation of the protocol, the researcher shall employ measures that increase the level of participation of the PLHIV being studied.

Recruitment of participants in the research usually involves members of the most-at-risk-population (MARP) (e.g., commercial sex workers and men having sex with men) who may be difficult to identify because of social marginalization. The accuracy of epidemiologic data is very much dependent on the integrity of recruitment and the resulting estimation of denominators in prevalence and incidence reports.

Nevertheless, the recruitment process shall be sensitive to the social implications of being identified as a person that is possibly HIV positive or with AIDS. Specific mechanisms to protect the privacy of individuals shall be described and put in place in accordance with the provisions of the Philippine AIDS Prevention and Control Act of 1998 (RA 8504).

### **Recruitment process and informed consent**

1. The protocol shall describe the recruitment process, in detail, including mechanisms to avoid double counting through interlocking of area groupings.
2. In non-intervention or observational studies, where the written consent may serve to increase the possibility of identifying the person with HIV

and become a permanent record, verbal informed consent can be done, as long as it is witnessed and properly documented with appropriate and specific codes.

3. Special attention shall be given to the potentially sensitive nature of the information to be extracted from the research participants and, if applicable, the necessity of undergoing an HIV test.
4. It is important to determine the participant's willingness to be informed of the test result, the test's reportability, and the implication on his or her sexual partners and life style, if found positive.
5. The research participant must also be informed that he or she is free to withdraw from the study anytime.

#### **Pre- and post-test counseling**

6. Pre- and post-test counseling shall be put in place as part of the research protocol; conducted in private by well-trained, culture- and gender-sensitive research personnel.

#### **Standard of care**

7. In an interventional study, the control group shall receive the standard of care accepted by the larger community. It is not acceptable 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**

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

## **Use of research data**

9. 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.



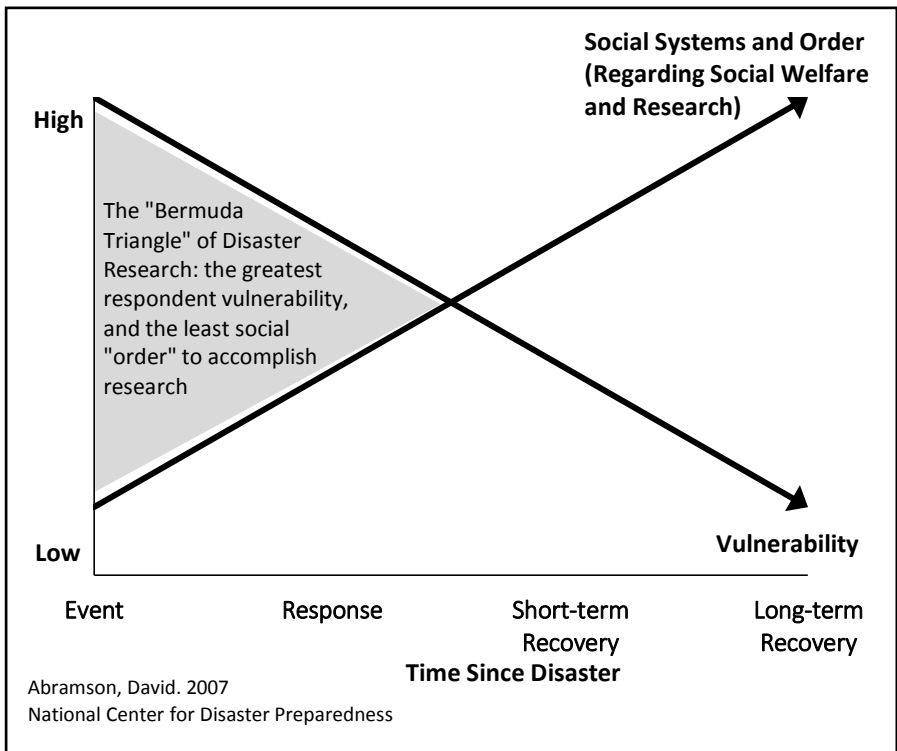
## ETHICAL GUIDELINES FOR RESEARCH INVOLVING POPULATIONS IN DISASTER SITUATIONS

Disasters may have lingering physical, social, and psychological consequences, including chronic poverty, deprivation of basic needs, violation of basic rights, vulnerabilities, and a pervasive sense of hopelessness and disempowerment. These guidelines refer to research conducted among populations that have experienced extreme forms of stress due to natural calamities (e.g., floods, earthquake, fire, etc.), armed conflict, or other forms of violence.

Research involving populations in the aftermath of emergencies and disasters must be guided by principles in consonance with 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.

Research in post-disaster areas shall promote the following norms:

- Allowing for stability in the aftermath of the disaster, such that basic physical and safety needs are met
- Sensitivity to heightened vulnerabilities of the participants:
  - Heightened psychological and physical risks against potential benefits (refer to the diagram below for the period of highest vulnerability),
  - Vulnerability to undue influence (especially if research is linked to service),
  - Diminished capacity to make decisions about participation due to stress.
- Prioritizing welfare of participants or community versus scientific goals (i.e., utilitarianism and social justice)



Proper assessment of benefits and risks requires that the following questions are addressed first by the researcher, and later by the REC during the ethical review: Are there known potential harms and risks to individuals and the participant population, overall, by their involvement in the proposed research? How can the risks be mitigated, and how much will it cost?

These guidelines address several issues related to risks, benefits (i.e., contribution to the healing of the affected community), COI, recruitment and informed consent, and gender and cultural sensitivity. The potential for harm resulting from the research process itself and its sociopolitical implications, implies an equal potential for exploitation of participants.

The ideal situation would be that government or academic institutions in the community have RECs that can undertake the ethical review of the proposed studies. In their absence, however, concerned agencies (e.g.,

DOH, DSWD, CHED, or the DOST) may refer such studies for review to the NEC.

### **Ethics committee review**

1. Research in emergencies and disasters shall give special attention to the unique needs and special concerns of victims and their specific cultural, religious, racial, and ethnic affiliations, so that pursuit of answers to the study questions may also bring about services and opportunities that are appropriate and acceptable to these individuals.
2. During the deliberations of the review committee on research involving populations in emergencies and disasters, a community representative or an accepted and established advocate for similarly situated populations must be present.
3. The ethical review process shall address the following considerations related to the care of the study population:
  - 3.1. Is the research necessary? Justified in a post-disaster context?
  - 3.2. Where does the research fall along the disaster-time continuum?
  - 3.3. How ephemeral (time-bound) are the data?
  - 3.4. What is the nature of exposure to the disaster?
  - 3.5. Who are the research participants? How vulnerable? How will they be selected?
  - 3.6. What are the risks and benefits to participants?
  - 3.7. Can one obtain local support or endorsement (e.g., barangay or municipal endorsement)?
  - 3.8. How should the informed consent process be conducted?

- 3.9. How will referrals for help be handled?
- 3.10. Are the research design, tools, methods, valid, and appropriate to the research questions?

### **Roles and responsibilities**

4. The different roles of the researchers, health providers and volunteer workers shall be clarified and the actual and potential conflicts of interest identified.
5. The researchers shall 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.
6. Researchers must demonstrate familiarity with the community's situation and their cultural beliefs and practices.
  - 6.1. The research team may include a local community counterpart (e.g., barangay or municipal officials).
  - 6.2. The research team must describe a preliminary community mapping or scoping exercise to ensure familiarity with the situation of the community, as well as identify local resources that will support the faithful implementation of the project.
  - 6.3. The research team must demonstrate ability to anticipate potential negative events (e.g., post-disaster trauma) and facilitate appropriate interventions.

### **Justification for the study**

7. Research in disaster areas shall be justified if it can demonstrate that the objectives of the study cannot, otherwise, be achieved if done in a more stable setting
8. The research proposal must explain how its objectives relate to the priorities of the interests of the community.

## **Research design and methodology**

9. Collecting personal data on traumatic experiences shall 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.
10. Group methods shall be used with much caution because confidentiality and anonymity cannot be guaranteed (in all types of research among this population); and in security sensitive situations, this takes greater importance. For example, when recruiting Focus Group Discussion (FGD) participants, people with history of conflict shall 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.
11. The protocol shall include provisions for proper intervention, or referral mechanisms, to address the health needs and security of research participants and the study team; and exit strategies, including closure activities and associated costs, throughout the proposed duration of the project.
12. In research involving people in emergencies or disasters, the involvement of participants is of prime importance. The study design shall provide the highest possible degree of participation and involvement of research participants.
13. Procedures shall be established for a course of action in the event that a criminal act is disclosed or discovered through data collection, such as interviews.

## **Recruitment and the informed consent process**

14. The researchers shall consult the community and secure its permission before approaching individuals for their informed consent. Further, there shall be close coordination with the local government in the conduct of the research.

15. The research team shall identify factors that serve as a barrier to the freedom of individual members of the participant population to give consent, and provide effective mechanisms to address them.
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 Guidelines for Health-Related Social Research (page 108), and with the approval of the REC.

### **Risks and benefits**

17. Direct benefits to the participants and to the community shall be a primary consideration in the conduct of the research.
2. The research activity shall contribute to or enhance the development of intervention programs and shall not impede the healing or recovery of the community.
18. Possible repeat traumatization and potential risks (e.g., stigmatization and reprisals) for the study population shall be anticipated and planned for in the proposal.
19. The security risks for studies on population in an armed conflict situation shall be clearly identified and included in the ethical considerations section, specifically in the risk- benefit assessment, recruitment and informed consent process, and contents of the informed consent form
20. Data security shall be accorded top priority.
  - 20.1. The protocol shall anticipate potential misuse of seemingly “innocent” demographic or family data (e.g., number of males, females in the family) that may put individuals at risk (e.g., forced recruitment of male members by any of the combatant groups).
  - 20.2. Protection of sensitive information that can escalate violence

shall be guaranteed to prevent potential misuse (e.g., information on delivery of supplies could lead to an ambush).

### **Conduct of the research**

21. Researchers shall provide professional help (or at least a referral) during the conduct of the research to take care of the psychosocial needs of the community.

## **ETHICAL GUIDELINES FOR RESEARCH ON EMERGING TECHNOLOGIES: NANOTECHNOLOGY, NANOMEDICINE, AND BIOSIMILAR DEVELOPMENT**

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, of these two things:

- (1) Incredibly advanced and extremely capable nanoscale and microscale 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. In research involving emerging technologies, there shall be assurance that product, if found effective and safe, will be available and affordable to the population where the participants were chosen.



A biosimilar is a biopharmaceutical product that is similar to a licensed biologic product in terms of quality, safety and efficacy. Development of biosimilars involves emerging technologies especially recombinant DNA technology and requires compliance with Good Manufacturing Practice (GMP) and stringent drug development requirements.

1. Guidelines for GMP shall be clearly set for specific emerging technologies.
2. Data on pre-clinical and all phases of a clinical trial shall be provided prior to full-blown application of emerging technologies for research participant treatment.
3. Public education programs, with particular emphasis on research participant and family education, shall 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 shall 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 shall be required.

### **Ethics in nanotechnology**

7. Nanotechnology research shall be conducted with the least possible risk to human beings and public welfare.
8. Experimental work on nanomaterials shall be done in contained and regulated facilities. Biosafety precautions specific to the handling and processing of nanomaterials shall be strictly observed at all times in the research facility.

9. Safety standards shall be set for all stages of research involving nanomaterials.
10. A nanotechnology researcher shall provide a credible account of the benefits, costs, and risks of the technology.

### **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 shall be reasonable in relation to the potential benefits to the participants and society and these risks shall 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 shall 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, SOPs, follow-up with participants after they complete the study, and creation of a data and safety monitoring board.
16. The researcher shall 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, researchers shall inform research participants that there may be some risks that cannot be anticipated.
18. Researchers shall 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 shall 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 shall 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 research participant populations (e.g., stem cell donors) than for others, thus, extrapolation shall 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 research participant population.
23. Owing to the limited clinical database available during the approval of a biosimilar, it is important to collect post-approval safety data for these products. This means conducting post-marketing surveillance studies to monitor the efficacy and safety of biosimilar products.

## ETHICAL GUIDELINES FOR GENETICS AND GENOMIC 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, and gene cloning. These types of research can be either therapeutic or non-therapeutic in nature. The primary aim of therapeutic research is essentially to treat and/or cure a disease. 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 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. 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 participants cannot be identified.

Many ethical considerations in genetic research are similar to those that arise in other types of research. However, 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. There is potential harm to research participants arising from the use of genetic information, such as stigmatization or discrimination. Researchers shall take special care to protect the privacy of participants and confidentiality of such

information. Confidentiality, privacy, and security are important considerations in the ethics of a genetic study, given the hereditary nature of genetic traits.

These guidelines are intended to assist research institutions, scientists, pharmaceutical companies, health researchers, and RECs in the ethical pursuit of genetic studies so that the expected benefits in the improvement of health and healthcare can be attained with minimal harm.

### **Collection of samples from humans**

1. Human biological samples shall be collected, processed, used, and stored only for the following purposes:
  - 1.1. Therapeutic and non-therapeutic genetic research (i.e., epidemiological, prognostic, population-based genetic studies, anthropological or archeological studies);
  - 1.2. Forensic medicine, in which case, use of samples shall be in accordance with domestic laws and consistent with laws on human rights;
  - 1.3. Development of drugs, biomedical devices, molecular diagnostics, and medical technologies; and
  - 1.4. Other reasons of public interest.

### **Informed consent**

2. Prior, voluntary, informed, and expressed consent, shall be obtained for the collection of biological samples, human genetic and proteomic data, and for their subsequent processing, use, and storage; without inducement relating to the offer of financial or personal gain.
3. Research participants shall be provided with proper and full, but comprehensible information that explains the basics of genetics, the research in its various steps, and the potential benefits and risks to the participants.

4. Potential research participants shall be adequately informed about what will happen to any genetic material or information obtained as part of the study including where (local or foreign institutions) they will be stored and kept.
5. The informed consent shall include statements on the disclosure and sharing of the results and findings of the study, that is, to whom the information be revealed, among others.
6. Research participants shall be recruited as individuals in their own right, rather than as a family group, and shall consent as individuals.
7. In cases where identities of groups or communities can be linked with genetic traits under study, permission or endorsement may be obtained from an elected or recognized leader who will be responsible for giving the permission for the participation of the group in the study.
8. If genetic markers are yet to be determined at some future date, this information shall also be included in the consent form.
9. Informed consent shall 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. All second and third party uses of biological samples shall be restricted to anonymized or anonymous samples, as above. Such use shall require ethical approval. Limited, non-identifying, demographic information may be retained on the sample.
11. Stored biological samples collected for purposes, other than those stated 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 shall be

irreversibly unlinked from their source through the destruction of all identifiers. Non-anonymized human biological materials shall also be destroyed.

### **Genetic studies among indigenous peoples**

13. Genetic studies involving indigenous groups shall be guided by international and national laws and regulations on respect for human rights and privacy, and protection from exploitation. (See Guidelines on Research among Indigenous Peoples, page 124)

### **Requirement for genetic counseling**

14. Genetic counseling shall be provided before and after the test when there may be a need to disclose the findings of the genetic testing.

### **Privacy, confidentiality, and security**

15. Researchers must ensure the confidentiality of stored genetic information or research results relating to identified or potentially identifiable participants in accordance with the national (Data Privacy Act of 2012) and international laws on human rights. Researchers shall also ensure that safeguards are in place to avoid accidental disclosure of sensitive personal information.
16. In general, no individual results shall be disclosed to research participants; neither shall result of genetic research go into the individual's medical record. Nevertheless, the potential for disclosure shall be declared in the initial process of seeking consent.
17. In case the disclosure of genetic information becomes impossible to avoid, such information shall be dealt with sensitively and with proper counseling.
18. Researchers shall ensure that the results of genetic testing and genetic counseling records are protected from access by third parties.
19. Identifying genetic information shall not be released to others, including

family members, without the written consent of the individual to whom the information relates, or to a person or institution which may legally provide consent for that person.

20. 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**

21. The researcher shall ensure that handling and preservation of biological samples shall be in accordance with standard scientific procedures and local laws and policies, for example, Guidelines on the Use, Retention, and Storage of Residual Dried Blood Spots from Newborn Screening (DOH AO 2012-017).
22. Disposal of stored biological specimens shall be done in accordance with standards for handling biohazardous and infectious materials.
23. Documents pertaining to the transport, transfer, use, and disposal of all stored biological samples shall be properly archived in accordance with national and international guidelines. Transfer of custody of biological samples to foreign institutions shall be covered by a Material Transfer Agreement (MTA) that shall be concluded at institutional levels. The terms of the MTA must include compliance with applicable Philippine laws.
24. Retention time for stored biological samples shall be determined by the respective institutions, in accordance with the applicable provisions of the Data Privacy Act of 2012 (RA 10173), and must be declared in the informed consent form signed by the participant or subject.
25. All specimens in a tissue bank must be accompanied by a copy of the consent agreement signed by the donor.



26. No specimen shall be removed from a tissue bank for research purposes without an approved research protocol.
27. A researcher must not transfer genetic material or related information to another research group, unless:
  - 27.1. The researcher and the other research groups are collaborating on research which has been approved by their respective RECs;
  - 27.2. The genetic material and information are provided in a form that ensures participants cannot be identified.

### **International collaborative genetic research**

28. An approved MTA or Limited Use Agreement (LUA) shall accompany genetic research of collaborative nature. The terms of reference of these documents must comply with applicable Philippine laws.

## ETHICAL GUIDELINES FOR STEM CELL RESEARCH

Human stem cell research holds enormous potential for contributing to an understanding of fundamental human biology. Research in this area may lead to potential novel treatment, and ultimately, a cure for many diseases.

Stem cells are primordial cells that have the potential to develop into many different cell types in the body during early development and growth. In many tissues (gut and bone marrow), stem cells serve as an internal repair system, by dividing to replace damaged cells.

Stem cells are found in embryos and in adult tissues. The use of human embryonic stem cells from the pre-implantation embryo (from the inner cell mass of the blastocyst) results into the destruction of the embryo. This is fraught with ethical issues because of differing perspectives on the moral status of the embryo.

The discovery of adult stem cells, including the development of human induced pluripotent stem cells (iPSCs), has greatly improved acceptance of translational stem cell research. However, 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. Mechanisms for the management of COI situations that promote transparency and accountability must be established.

The National Ethical Guidelines on Stem Cell Research has adopted several provisions in the 2016 Guidelines for Stem Cell Research and Clinical Translation prepared by the International Society for Stem Cell Research, that were deemed applicable to the local research environment.

### Securing stem cells from donors

1. Securing stem cells for research, whether from children, adults, or naturally aborted fetuses, shall be done under conditions of utmost integrity. The process shall:
  - 1.1. Protect the interests of the donors;

- 1.2. Guarantee that important boundaries are not being overstepped;
  - 1.3. Encourage participation of the donors to the greatest extent possible; and
  - 1.4. Ensure highest quality of research and outcomes.
2. Obtaining adult stem cells shall require 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.
  3. Stem cells that are retrieved from the umbilical cord blood after delivery shall require informed consent from the donor (the woman or the couple concerned, as applicable), including information possible present and future use of the cells for research.

#### **Use of aborted fetuses and preimplantation embryos**

4. The Rules and Regulations Governing Accreditation of Health Facilities Engaging in Human Stem Cell and Cell Based Therapies in the Philippines (DOH AO 2013-12) categorizes aborted human fetal cells and their derivatives for human treatment and research as prohibited.

#### **Disclosure of source of stem cells**

5. Research participants and collaborating researchers shall be informed of the source of the stem cells in the study, to allow them the option of not participating in the study if stem cells were derived in a way they consider unethical.
6. Documentation of the original source of the stem cells shall be made readily available to researchers and potential recipients of stem cell-based experimental therapies.
7. Appropriate steps must be taken to protect and preserve the identity of

both the donor and the recipient in stem cell research and use.

### **Risks**

8. In clinical applications of stem cell research, the risk of harmful outcomes that may be deemed irreversible shall be minimized.
9. The protocol shall clearly describe quality control systems in the identification, harvesting, and expansion of stem cells to ensure that reagents and culture media are free of animal cells and protein that may induce strong immune reactions in the recipient.
10. The protocol shall also include biomarkers, surrogate markers, and other indicators of viability and functionality of the infused stem cells in the recipient target tissue.

### **Fees**

11. In cases where patients are invited to participate in a clinical translation of stem cell experimental therapy, professional fees and other fees related to clinical care shall be carefully disclosed, such that there is no confusion, on the part of the patient, which component is research and which component is clinical care.

### **Vulnerability of patients**

12. The vulnerability of terminally-ill patients, or those with chronic disease without effective treatment, shall be seriously addressed. Such patients shall be accorded special protection to prevent exploitation and abuse.

### **Conflict of interest**

13. COI exists when the researcher has financial investment in the production of stem cells, or in the equipment used in the extraction and expansion of stem cells. Such conflicts of interest may influence the reporting of clinical outcome data. COI shall be declared and managed with utmost care, transparency, and accountability.

14. Institutional COI exists when stem cell experimental therapy is promoted by the institution as an iconic project that defines the aspirations of the institution for public recognition. The REC must avoid the coercive influence of administrative officials, and insist on its independence in decision-making.
15. The REC shall clearly define COI situations and provide the necessary steps to manage them in its official documents (e.g., SOPs).

## **ETHICAL GUIDELINES FOR RESEARCH USING HUMAN DATA AND SAMPLES FROM BIOBANKS, REGISTRIES, AND DATABASES**

A biobank is a physical repository of biological samples (usually human) for use in research. Biobanks are an important resource in biomedical research, especially in genomics, transcriptomics, and proteomics. Through biobanks, researchers are able to access biological samples and data from a large number of people that ordinarily would have needed much more time and resources to collect. Genome-wide association studies that require thousands of individuals can very well be done using biobanks. However, use of biobanks have raised issues of privacy, validity of informed consent processes, and ownership of information.

Clinical registries and databases are set up to collect data about specific groups of patients from different treatment centers for analysis and descriptive reporting. Registries are a practical solution to information needs that cannot be met from simple hospital administrative data. They are especially useful for information about diseases with low prevalence, and for describing outcomes for groups of patients undergoing specific medical procedures. The use of clinical registries and databases in a clinical research without prior consent from a patient has raised similar ethical questions, as in the use of biobanks.

### **Establishment of biobanks and registries**

1. The purpose, both current and for the foreseeable future, of Human Biobanks, Registries, and Databases (HBRD) shall be clearly formulated and communicated to all involved contributors of human biological materials and data, investigators, research staff, RECs, and others who are involved in their establishment.
2. The governance and custodianship of the HBRD shall ensure its long-term security and sustainability especially when funding support is terminated, or its nature changed.
3. The HBRD custodian shall perform the following functions:

- 3.1. Clearly formulate HBRD governance structure and the responsibilities of its management, and make such information publicly available;
- 3.2. Ensure that sufficient professional staff and resources are available to operate effectively; and
- 3.3. Create guidelines on who will have access and how access to samples or data can be granted.

### **Data Privacy Act of 2012**

4. The use of human data from biobanks, registries, and databases shall comply with the Data Privacy Act of 2012 and its IRR of 2016.

### **Informed consent**

5. During the consent process for the collection and storage of specimens or data, participants shall be informed of specific terms of future, secondary, or third party uses of their samples or data.
6. If subsequent use of specimen or data is not consistent with the original informed consent, new consent shall be obtained from the participant or from an appropriate legally authorized representative (LAR), or a waiver of consent shall be obtained from an REC.
7. The informed consent shall include information on whether specimens or data will be made available for allowable non-research purposes.
8. The participant shall be informed during the consent process whether the HBRD custodian is required by law to make available human biological materials or data to third parties such as insurers, employers, law enforcement agencies, or other civil-law agencies, for non-research purposes.

### **Collection and storage of biological samples and information**

9. Stored human biological materials or data shall be coded or

anonymized, such that the study participant cannot be identified.

10. Duration of specimen or data storage is subject to the capability of the custodian to support the sustainability of the HBRD facility.

### **Access to data and transfer of materials**

11. Access to HBRD shall be justified by a scientifically and ethically appropriate research protocol. This implies review and approval by a technical review committee and an REC.
12. Access to human biological materials and data shall be based on objective and clearly articulated criteria in the protocol, and should be consistent with the participants' informed consent.
13. Human biological materials and data shall only be transferred when the recipient has adequate standards in place regarding privacy and confidentiality. Use of information and materials for marketing purposes is not allowed.
14. A Material Transfer Agreement (MTA) shall be made between institutions involved in a collaborative project that will make use of the stored human samples or data.
15. Researchers shall only have access to human biological materials or data that are coded or anonymized, and they shall be required not to attempt to re-identify participants. Only coded or anonymized samples or data in HBRD may be used in new research.
16. Except when required by law or for purposes of public safety and national security, the custodian of HBRD shall not make accessible or disclose participants' human biological materials or data to third parties (e.g., law enforcement agencies, employers, insurance providers) for non-research purposes. The restriction shall be guaranteed by an institution beyond the term of office of the custodian, such that the protection of information is guaranteed even when the custodian is no longer employed in the institution that houses the databank or biobank.



## ETHICAL GUIDELINES FOR INTERNATIONAL COLLABORATIVE RESEARCH

International collaborative research may be of different forms where each form presents unique issues. The different forms are as follows:

**Type 1:** An International Study Group working on a global phenomenon or disease problem. The Study Group is composed of country representatives, each of whom contributes local data toward better understanding of a global phenomenon. The International Study may have a common international funder, several local funders, or mixed funding providing financial support. Here, the Filipino member generates local data and includes these to the global data pool.

**Type 2:** A multi-country research group (an international collaboration) working on a specific disease that is endemic in the Philippines. Different aspects of the disease are addressed jointly, or separately by different research groups based in different countries. In this arrangement, patient clinical data and biological samples are sourced in the Philippines and shared with foreign collaborators identified in different countries.

**Type 3:** Clinical drug trials is the most common international collaborative research. In the usual setup, a foreign pharmaceutical company sponsors the clinical trial of an investigational new drug, such that the same protocol is implemented in different countries by different investigators. Reporting of clinical data follows the standards of the ICH-GCP Guidelines.

Some major ethical issues when developing countries are involved have constantly been raised like:

- The standard of care that shall be used in research in developing countries;
- The “reasonable availability” of interventions that are proven to be beneficial during the conduct of research;
- The quality of the informed consent.

The persistence of these issues has been partly due to 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.

One other major issue is that of inequitable funding—only 10 percent of global research funding goes to diseases that make up 90 percent of the global burden. We can address the inequity by identifying the national priorities that are going to be the basis for setting the research agenda.

Whereas, scientific advances are the usual yardstick used to measure success in international collaboration, priorities such as areas of work, the sustainability of the studied interventions outside the research setting, and the investment in local research capacity should be equally regarded as indicators of success.

Relevant and meaningful health research in developing countries must focus on promoting health equity and developing local capacity in bioethics. Involvement of patients in international research collaboration raises hope, thus implying greater disappointment and frustration in research failure.

In 2008 and 2010, the KFPE (Commission for Research Partnerships with Developing Countries) adopted 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. These were just recently updated to include the following:

- Set agenda together
- Be accountable
- Create transparency
- Clarify responsibilities
- Promote mutual learning
- Enhance capacities
- Share data and networks
- Disseminate results
- Pool profit and merits
- Apply results
- Secure outcomes

The above practical measures are adopted in addressing ethical issues in international collaborations, most especially in Types 1 and 2 arrangements. (Type 3 Multi-country clinical trials is taken up in the Guidelines for Clinical Research, page 70)

### **Setting the agenda together**

1. Filipino researchers shall take into account local capacities and needs in developing the agenda in Type 1 collaboration.
2. Filipino researchers shall be deeply involved in setting the research agenda especially in Type 2 arrangements.

### **Being mutually accountable**

3. Collegial decision-making and respect for one another's opinions shall be promoted, such that group decisions are respected and finger-pointing is avoided. An openness to constructive criticism shall be an important indicator of maturity in the collaborative interaction.
4. Technical review shall be the responsibility of an international panel, but ethical review must be done at the local level. In the case of Type 2 arrangements, the involvement of Filipino patients requires ethical review by a Filipino REC.

### **Creating transparency**

5. The partnership shall develop comprehensive SOPs that shall guide processes and indicative activities, to promote transparency in all transactions and decisions.
6. The informed consent obtained from patients must indicate the specific research protocol, the name of the proponent, source of funding, procedures involved, and the site of research data collection.

### **Clarifying responsibilities**

7. A set of terms of reference shall be developed and agreed upon by the collaborators, in order to clearly delineate responsibilities and accountabilities of experts, clinicians, lead researchers, funders/sponsors/research managers, and the like.
8. Each study shall have separate terms of reference with regard to funding

support on the basis of scientific merit and ethical soundness.

9. Deficiencies in the performance of agreed upon responsibilities shall be addressed in such a manner that attainment of objectives is still ensured.
10. Responsibilities shall be set proportionately based on capacities in relation to the overall research agenda.
11. In case of conflict, there shall be initial attempts for resolution internally at the level of the collaboration group, before it is allowed to escalate beyond the group (e.g., involvement of disciplinary and legal authorities).

### **Promoting mutual learning**

12. Research is a continuing search for knowledge. Each member of the research team is benefited by his or her participation in the form of new knowledge and insights from both good and bad decisions, or right and wrong techniques. There shall be periodic meetings to assess developments and consolidate learnings derived from the different research experiences.

### **Enhancing capacities**

13. The collaboration shall include workshops and seminars toward enhancing technical and research skills.

### **Sharing data and networks**

14. Data sharing as a strategy for ensuring data integrity and promoting geometric growth of knowledge shall be part of the basic agreements in research collaboration. This is not to say that authorship rights must be set aside, but only to emphasize that a very important advantage of research collaboration is the presence of many minds.
15. Transfer of materials and data shall be covered by a memorandum of agreement and shall comply with existing Philippine laws and

regulations (e.g., Intellectual Property Code [RA 8293], Data Privacy Act [RA 10173]).

16. Sensitive and personal information that will be transmitted outside the country shall be covered by the Data Privacy Act of 2012.
17. Despite an agreement on transfer of patient data and biological samples in Type 2 collaboration, ownership of data and biological samples remains with the Filipino collaborators, and further use of remaining samples shall be subject to Philippine approval.

### **Dissemination of results**

18. International collaboration shall disseminate results that impact on the improvement of the health of the patients in the collaborating countries. The social value of research is best appreciated when results are disseminated.

### **Pooling profit and recognition**

19. Basic agreements among the collaborators shall be forged in the beginning of the collaboration that shall describe how profits and recognitions shall be enjoyed and shared.

### **Applying results**

20. All collaborators shall endeavor to translate research results into better outcomes in the care of Filipinos suffering from the disease or condition under study.

### **Securing outcomes**

21. Sustainability of good outcomes shall be part of the strategic plan from day 1 of the collaboration. Without sustainability, the impact will be small and narrow.

## **Further use of clinical data and biological materials**

22. At the end of the collaborative project, further use of clinical data and biological materials shall require approval of the source-country researchers. The request for approval shall include an offer for further collaboration.

## ETHICAL GUIDELINES FOR AUTHORSHIP AND PUBLICATION

Authorship implies ownership of an idea or product, and confers privileges and responsibilities to the author. Guidelines emphasize the proper assignment of credit to, and the corresponding accountability of those identified as authors of a scientific or creative work.

The Committee on Publication Ethics (COPE) Council (2014) stipulated that whereas various disciplines and institutions have norms and practices, those who want to be identified as author should, at the very least, provide assurance that they have actually done the work as presented and that they have not violated any other author's copyright.

1. The PHREB endorses the guidelines issued by the International Committee of Medical Journal Editors (ICMJE) that define authorship as fulfillment of all four of the following criteria:
  - 1.1. Substantial contribution to the conception or design of the work; or the acquisition, analysis, or interpretation of data for the work;
  - 1.2. Drafting the work or revising it critically for important intellectual content;
  - 1.3. Final approval of the version to be published; and
  - 1.4. Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

In applying the above criteria, all individuals who have participated in criterion 1.1 should be given the opportunity to be part (or to decline to be part) of criteria 1.2, 1.3, and 1.4.

2. The following activities shall not be regarded as sufficient grounds for attributing authorship:

- 2.1. Acquisition of grant money;
  - 2.2. General supervision;
  - 2.3. Collection of data; and
  - 2.4. Involvement in the technical writing and editing.
3. Authors shall obtain the informed consent of research participants as a condition for the publication of photographs or identifiable information.
  4. In submitting articles for publication, the authors shall provide the following information to the editors:
    - 4.1. The specific contribution of each author to the scientific paper;
    - 4.2. An acknowledgment of the contributions made by people other than the authors; and
    - 4.3. A statement that the authors complied with ethical review requirements.
  5. The basis for listing of authors shall be transparent, and may follow any of, but not limited to, the following norms depending on prior agreements:
    - 5.1. Alphabetical listing;
    - 5.2. Listing based on level of contribution; or
    - 5.3. First author is the one who did most of the work, the last author is the most senior in the group.
  6. The student shall be listed as principal author of a publication that substantially derives from the student's dissertation or thesis.
  7. In collaborative groups, the important consideration shall be the



identification of the responsible individual for the integrity of the work and the corresponding author.

# APPENDICES

## **APPENDIX A: EXCERPTS FROM THE PHILIPPINE NATIONAL HEALTH RESEARCH SYSTEM ACT (RA 10532)**

### **SEC. 10** Creation and Functions of the Steering Committee.

(a) The Governing Council (GC) shall create a Steering Committee to be headed by the PCHRD Executive Director. It shall be composed of the following:

- (1) The Executive Director, DOST-PCHRD;
- (2) The Director, Department of Health – Health Policy Development and Planning Bureau (DOH-HPDPB);
- (3) The Director, Commission on Higher Education, Office of Policy, Planning, Research, and Information (CHED-OPPRI);
- (4) The Executive Director, University of the Philippines Manila – National Institutes of Health;
- (5) The Director of the Social Development Services of the National Economic and Development Authority (NEDA);
- (6) The Chair of the Philippine Health Research Ethics Board (PHREB);
- (7) A representative from the Philippine Health Insurance Corporation (PHIC);
- (8) A representative from the National Statistics Office (NSO);
- (9) A representative from the Professional Regulation Commission (PRC);
- (10) A representative from the Department of Transportation and Communication – Land Transportation Office (DOTC-LTO);
- (11) A representative from the Department of Environment and Natural Resources – Environment Management Bureau (DENR-EMB);
- (12) A representative from the local government units (LGUs); and
- (13) The Chairpersons of relevant PNHRs TWC.

(b) The Steering Committee shall perform the following functions:

- (1) Recommend policies to the GC;
- (2) Perform oversight function on the implementation and harmonization of the PNHRs activities and the allocation of the PNHRs fund;

- (3) Coordinate and harmonize the activities of the six (6) PNHRS TWC; and
- (4) Monitor and report to the GC the progress of the PNHRS programs.

**SEC. 12.** *The Philippine Health Research Ethics Board (PHREB).* – The PHREB, created under DOST Special Order No. 091 s. 2006, shall ensure adherence to the universal principles for the protection of human participants in research. It shall, among other things:

- (a) Formulate and update guidelines for the ethical conduct of human health research;
- (b) Develop guidelines for the establishment and management of RECs and standardization of research ethics review;
- (c) Monitor and evaluate the performance of institutional RECs in accordance with procedures outlined in a prior agreement;
- (d) Promote the establishment of functional and effective RECs;
- (e) Provide advice and make recommendations to the PNHRS GC and other appropriate entities regarding programs, policies and regulations as they relate to ethical issues in human health research;
- (f) Initiate and contribute to discourses and discussions on ethical issues in human health research; and
- (g) Network with relevant local, national, and international organizations.

## **APPENDIX B: EXCERPTS FROM THE IMPLEMENTING RULES AND REGULATIONS OF THE PNHR ACT (RA 10532)**

**Rule 23.** *The Philippine Health Research Ethics Board (PHREB).* – The PHREB, created under DOST Special Order No. 091 s. 2006, shall ensure adherence to the universal principles for the protection of human participants in research.

The constitution of PHREB shall be governed by the same terms of reference contained in the above DOST Special Order.

The PHREB shall, among other things:

- (a) Formulate and update guidelines for the ethical conduct of human health research;

The National Ethical Guidelines for Health Research shall be regularly updated every five years or whenever necessary. For this purpose, PHREB shall constitute a committee which shall be responsible for this undertaking;

- (b) Develop guidelines for the establishment and management of RECs and standardization of research ethics review;

All research involving human subjects must undergo ethical review and clearance before implementation to ensure the safety, dignity, and well-being of research participants. The research ethics review shall be facilitated by a Research Ethics Committee (REC) duly registered with and/or accredited by PHREB as provided for in the Joint Memorandum Order 2012-001 of the Department of Science and Technology (DOST), Department of Health (DOH), Commission on Higher Education (CHED), and the University of the Philippines Manila (UPM).

The National Ethical Guidelines for Health Research shall include the standards for the establishment and management of RECs and the standards for research ethics review.

PHREB may conduct the necessary training activities for researchers, REC members, and administrators, which may function at the national, regional, or local levels; or as cluster or individual committees

- (c) Monitor and evaluate the performance of institutional RECs in accordance with procedures outlined in a prior agreement;

In carrying out its monitoring and evaluation function, PHREB shall establish or designate Regional Ethics Monitoring Boards (REMBs). These Regional Ethics Monitoring Boards may be located within existing regional DOH, DOST, CHED offices, or designated institutions; and shall directly supervise the RECs established in their regional area of responsibility.

PHREB and the REMBs, in consultation with RECs shall develop and agree on indicators of good performance which shall be used in ensuring and monitoring quality ethics review in health research.

- (d) Promote the establishment of functional and effective RECs;

The standards for the establishment of functional and effective RECs shall be included in the National Ethical Guidelines for Health Research for reference of institutions and organizations.

RECs shall be categorized as follows:

- (a) Institution-based RECs like those in hospitals, academic, and research institutions
- (b) Government Agency-based RECs
- (c) Organization-based RECs
- (d) Cluster-based RECs
- (e) Research site-based RECs

PHREB shall oversee and recognize functional and effective RECs through the mechanisms of registration and accreditation as provided for in the Joint Memorandum Order 2012-001 of the DOST, DOH, CHED, and the UPM. Registration procedures must be described in the National Ethical Guidelines for Health Research and in the website of PHREB.

In coordination with the CHED and DOH-Food and Drug Administration, accreditation shall be made mandatory such that RECs can be classified into different levels based on a set of criteria that shall determine the type and nature of research the REC is qualified to review.

- (e) Provide advice and make recommendations to the PNHRS Governing Council and other appropriate entities regarding programs, policies, and regulations as they relate to ethical issues in human health research;
- (f) Initiate and contribute to discourses and discussions on ethical issues in human health research; and

PHREB shall institutionalize a Forum for RECs that shall meet at least annually during the PNHRS week, for discussions of ethical issues in human health research and other concerns.

- (g) Network with relevant local, national, and international organizations.

PHREB shall link and cooperate with local, national, and international organizations in furtherance of its goals and objectives to foster ethical health research for the protection of human participants and promotion of the integrity of research data.

## APPENDIX C: DOST, DOH, CHED, UPM JOINT MEMORANDUM ORDER NO. 2012-001

SUBJECT: Requirement for Ethical Review of Health Research Involving Human Participants

Pursuant to national commitment to the protection of the rights of individuals, the four core agencies of the Philippine National Health Research System (PNHRS) namely the Department of Science and Technology (DOST), Department of Health (DOH), Commission on Higher Education (CHED), and the University of the Philippines Manila (UPM), hereby require that all health research involving human subjects must undergo ethical review and clearance before implementation to ensure the safety, dignity, and well-being of research participants.

The research ethics review and approval shall be facilitated by a Research Ethics Committee (REC) duly registered with and/or accredited by the Philippine Health Research Ethics Board (PHREB). To ensure efficient, transparent, and timely review, the REC should have a manual of SOPs which must clearly describe all areas of its work. The REC 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 six weeks after receipt of the submitted documents.

A reasonable review fee may be charged after proper consultation with and notice to concerned individuals and agencies.

Institutions must show support for their RECs with proper funding for office maintenance, administrative staff, and honoraria of members.

For immediate dissemination and compliance of all concerned,

Done this 28<sup>th</sup> of December 2012 in Metro Manila.

/s/

**MARIO G. MONTEJO**

Secretary

Department of Science and Technology

/s/

**ENRIQUE T. ONA, MD**

Secretary

Department of Health

/s/

**PATRICIA B. LICUANAN, PhD**

Chairperson

Commission on Higher Education

/s/

**MANUEL B. AGULTO, MD**

Chancellor

University of the Philippines Manila



## APPENDIX D: PHREB-NCIP MEMORANDUM OF UNDERSTANDING

### KNOW ALL MEN BY THESE PRESENTS:

This Memorandum of Understanding is made and entered into by and between:

The **PHILIPPINE HEALTH RESEARCH ETHICS BOARD (PHREB)** represented by its Chair, **LEONARDO D. DE CASTRO**, with principal office at the DOST Main Building, General Santos Avenue, Bicutan, Taguig City, hereinafter referred to as **PHREB**, and

The **NATIONAL COMMISSION ON INDIGENOUS PEOPLES (NCIP)** represented by its Chairperson, **LEONOR T. ORALDE-QUINTAYO**, with principal office at N. Dela Merced Building, West Avenue corner Quezon Avenue, Quezon City, hereinafter referred to as **NCIP**.

**HEREIN** referred to as the Parties in this Memorandum of Understanding;

### WITNESSETH:

**WHEREAS**, there are 110 identified major indigenous people groups in the Philippines representing 14% of the total Philippine population;

**WHEREAS**, there are challenges in using mainstream guidelines in researches involving indigenous cultural communities (ICCs)/indigenous peoples (IPs) as participants;

**WHEREAS**, **NCIP** is the primary government agency that formulates and implements policies, plans, and programs for the recognition, promotion, and protection of the rights and well-being of ICCs/IPs with due regard to their ancestral domains and lands, self-governance and empowerment, social justice and human rights, and cultural integrity;

**WHEREAS**, **NCIP** ensures the integrity of the free and prior informed consent (FPIC) process for research projects involving ICCs/IPs as participants in line with the NCIP Administrative Order No. 3 Series of 2012 or the “The Revised Guidelines on Free and Prior Informed Consent (FPIC) and Related Processes of 2012”;

**WHEREAS**, **PHREB** is the national policy making body on health research ethics, created under DOST Special Order No. 091 and mandated to ensure that all phases

of health-related research shall adhere to the universal ethical principles that value protection and promotion of the dignity of research participants;

**WHEREAS, PHREB** among other things, is mandated to monitor and evaluate the performance of research ethics committees (RECs) in order to promote and establish an effective research human protection;

**WHEREAS**, the Parties recognize the need for coordination in approving researches involving ICCs/IPs.

**NOW THEREFORE**, for and in consideration of the foregoing premises, the Parties to this Understanding hereby agree to the following:

1. The NCIP, as the lead agency in protecting and promoting rights of ICCs/IPs, shall ensure the integrity of the FPIC process for health research projects involving ICCs/IPs which are endorsed by PHREB or its accredited RECs.
2. The NCIP will facilitate the participation of authorized individuals (e.g., IP experts) during deliberation of RECs in reviewing protocols of health research projects involving ICCs/IPs.
3. The NCIP shall endeavor to update PHREB regularly or as the need arises regarding the status of proposals for health research projects which are endorsed by PHREB or by its accredited RECs.
4. The NCIP shall inform PHREB and concerned REC/s regarding any violations, non-compliance to guidelines, and deviations from approved protocol which occurred during the conduct of research to ICCs/IPs.
5. The NCIP shall advise researchers, investigators, and all concerned stakeholders to secure from PHREB or its accredited RECs, ethical clearance and endorsement of proposals for health research projects involving ICCs/IPs.
6. The PHREB, as the national policy making body on health research ethics, or its accredited RECs, will provide approval and endorsement for proposals of health research projects adhering to the National Ethical Guidelines and which have secured the free and prior informed consent of the concerned ICCs/IPs following existing NCIP guidelines.
7. The PHREB shall regularly update NCIP of project proposals that have been endorsed by its accredited RECs.

8. The PHREB shall consult NCIP for issues that may arise in the review and conduct of research involving ICCs/IPs for prompt resolution of actual and potential problems.
9. The Parties will promote exchange of information about their respective processes in the review of health research projects involving ICCs/IPs.
10. The Parties will explore and facilitate collaborations to ensure efficient review of health research projects involving ICCs/IPs and to monitor faithful compliance of these projects to the guidelines set by the Parties.
11. The Parties, may formalize specific partnerships or initiatives through specific Agreements, separate from this Memorandum of Understanding, each clarifying the scope of work and responsibilities of the parties specific to the agreements.

This **Memorandum of Understanding** shall take effect upon signing of all the herein parties and shall remain in full force and effect unless otherwise terminated by operation of law or by a written mutual agreement of the parties for termination/cancellation of this Understanding.

**AND WITNESS WHEREOF** the duly authorized signatories of the Parties signed this Memorandum of Understanding on 13 May 2016 in Quezon City, in two originals, both in English language, both having the same validity.

/s/  
**LEONARDO D. DE CASTRO, PHD**  
Chair, PHREB

/s/  
**LEONOR T. ORALDE-QUINTAYO**  
Chairperson, NCIP

**WITNESSES**

/s/  
**JAIME C. MONTOYA, MD, MSC, PHD, CESO III**  
Executive Director, PCHRD

/s/  
**LEE T. ARROYO**  
Officer-in-Charge – Executive Director, NCIP

# **APPENDIX E: PHREB POLICIES AND REQUIREMENTS FOR ACCREDITATION OF RESEARCH ETHICS COMMITTEES**

*(Version Date: 07 September 2016)*

## **RATIONALE**

An REC is a body, constituted by a duly recognized authority that makes independent decisions regarding the review, approval, and implementation of research protocols/proposals, in order to ensure the protection of the rights, safety, and well-being of human participants. It promotes integrity of research data.

Section 12 of the PNHR Act of 2013 on the constitution of PHREB states that "The PHREB, created under DOST Special Order No. 091 s. 2006, shall ensure adherence to the universal principles for the protection of human participants in research." In order to promote and establish an effective health research protection system, the PHREB, among other things, shall:

- Formulate and update guidelines for the ethical conduct of human health research;
- Develop guidelines for the establishment and management of RECs and standardization of research ethics review; and
- Monitor and evaluate the performance of RECs in accordance with PHREB approved procedures outlined in a prior agreement including requiring an annual report.

PHREB has set requirements for accreditation of RECs in the Philippines in order to guide them in the conduct of quality scientific and ethical review of research protocols.

To this end, PHREB accreditation is a requirement for all RECs.

## **COVERAGE**

The requirements for PHREB accreditation shall cover all RECs in the Philippines, which may be any of the following:

1. Academic Institution-based RECs (AI-RECs). These RECs are under a

university, college, medical school, or other professional school or institution. An AI-REC which functions independently of others under the same academic institution must apply for PHREB accreditation separately;

2. Hospital-based RECs (H-RECs). These RECs are under a hospital. A H-REC that functions independently of others under a hospital must apply for PHREB accreditation separately;
3. Government-based RECs (G-RECs). These RECs are under an office, department, bureau, or agency in the government. A G-REC that functions independently of other RECs under a government office, department, bureau, or agency must apply for PHREB accreditation separately.
4. Consortia for regional health and development RECs (CHRD RECs) will be considered as G-RECs for funding purposes but if the different institutions establish their own REC which functions independently of others under the consortium, these institutional RECs must apply for PHREB accreditation;
5. Cluster RECs (C-RECs). These RECs are formed by groups of institutions that cannot form individual RECs. The management and administration of a C-REC is determined by the memorandum of agreement among these institutions. A C-REC shall register and may apply for PHREB accreditation as one REC;
6. Research Site-based RECs (R-RECs). These RECs operate within and for research sites. An R-REC shall apply for PHREB accreditation as a whole unit regardless of the number of sites or facilities the research will engage.

## **GENERAL POLICIES**

The following policies shall be applicable:

1. All health-related research protocols or proposals involving human participants shall be reviewed by an REC. Health research is generation

of data that may contribute to new knowledge 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. The *World Health Organization (WHO) Standards and Operational Guidance for Ethics Review of Health-Related Research with Human Participants 2011 Preface*, states on its preface that Health-related research includes biomedical, behavioral, social science, and epidemiological research.

Research proposals involving indigenous cultural communities/indigenous peoples (ICCs/IPs) shall secure ethical clearance from a PHREB Level 2 or 3 Accredited REC and approval from the National Commission for Indigenous Peoples (NCIP). Ethical review of the protocol shall follow the guidelines stipulated in the *National Ethical Guidelines for Health Research*.

Research protocols/proposals involving use of Animals are reviewed by an Institutional Animal Care and Use Committee (IACUC).

Protocols with biosafety issues or pose hazards to the environment including those involving animals and plants need review and approval by the National Committee on Biosafety of the Philippines (NCBP) as stipulated in the *National Ethical Guidelines for Health Research*.

In some institutions, the above functions (human and animal involvement and biosafety) may be performed by a single committee, provided the appropriate expertise exists in the said committee;

2. All RECs shall undergo accreditation by PHREB according to a set of criteria (Section IV: Accreditation Criteria).

The REC shall apply for the appropriate level of accreditation based on the requirements described in Section VI: Procedures and Requirements for PHREB Accreditation;

3. Members of the Accreditation Team shall be identified following a process of selection and compliance with training requirements under the supervision of the PHREB Committee on Standards and

Accreditation (PHREB CSA); and

4. Accreditation fees shall be determined and approved by PHREB. Other expenses associated with an Accreditation Visit shall be shouldered by the applicant REC.

## **ACCREDITATION CRITERIA**

The PHREB CSA shall evaluate the REC according to seven (7) criteria using specific characteristics/elements as indicators, as follows:

1. Functionality of structure and composition
  - 1.1. Independence,
  - 1.2. Multidisciplinarity,
  - 1.3. Gender representation,
  - 1.4. Age representation,
  - 1.5. Ethics training,
  - 1.6. Expertise, and
  - 1.7. Management of Conflict of Interest
  
2. Adherence to international, national guidelines and policies
  - 2.1. Membership structure,
  - 2.2. Policy on review of research involving human participants,
  - 2.3. Regularity of meetings,
  - 2.4. Quorum,
  - 2.5. SOPs, and
  - 2.6. Institutional support
  
3. Adequacy of SOPs and consistency of implementation
  - 3.1. The SOP Manual should have an OVERVIEW that presents the environment where the REC operates, the Vision-Mission of the Institution, an organizational chart showing the location of the REC and how it relates with the other units, institutional policies related to human research protection, research ethics review, history and mandate of the REC and the international and

national ethics research guidelines and regulations guiding the REC.

3.2. SOP Chapters:

- 3.2.1. REC Structure and Composition;
- 3.2.2. Management of Initial Submissions (including Re-submissions);
- 3.2.3. Management of Post Approval Submissions;
- 3.2.4. Review Procedures (Expedited and Full Review);
- 3.2.5. Meeting Procedures;
- 3.2.6. Documentation of REC Actions;
- 3.2.7. Management and Archiving of Files;
- 3.2.8. Site Visits;
- 3.2.9. Management of Queries/Complaints; and
- 3.2.10. Writing and Revising SOPs

3.3. SOP Manual includes REC forms such as appointment letters of REC members, forms, templates of REC communications, and others deemed necessary by REC.

3.4. Consistency of implementation:

- 3.4.1. Timeliness
- 3.4.2. Decision making process

4. Completeness of review process

- 4.1. Adequate assessment forms,
- 4.2. Consistent and meaningful use of assessment forms,
- 4.3. Comprehensive discussion of technical and ethical issues, and
- 4.4. Assignment of appropriate reviewers

5. Adequacy of after review process

- 5.1. REC requirement for submission of reports,
- 5.2. Inclusion of reports in the meeting agenda, and
- 5.3. Assessment of the reports



6. Adequacy of administrative support
  - 6.1. Availability of a regular support staff,
  - 6.2. Provision of an office and equipment (e.g., provision of security of files), and
  - 6.3. Support for REC operations
  
7. Efficiency of the recording and archiving system
  - 7.1. Availability of updated logbooks,
  - 7.2. Availability of updated database, and
  - 7.3. Systematic filing of administrative and protocol-related documents (e.g., active files and archives)

## **ACCREDITATION LEVELS**

The level of accreditation is indicative of both the type of research and the degree of risk involved in the protocols/proposals reviewed by the REC.

PHREB shall grant any of the following levels of accreditation to an REC after an evaluation process:

### **1. Level 1 Accreditation**

Level 1 accredited REC reviews research with minimal risk to participants.

A risk is minimal when 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 (*National Ethical Guidelines for Health Research 2011*).

Level 1 accreditation is applicable to newly constituted RECs (i.e., less than one year of operations)

## 2. Level 2 Accreditation

Level 2 accredited REC reviews all types of research except clinical trials required for FDA registration of new drugs. These may entail more than minimal risk to participants. Post-marketing studies may be reviewed by Level 2 RECs.

## 3. Level 3 Accreditation

Level 3 Accredited REC reviews all types of research including studies required for FDA registration of food, drugs, and devices. Level 3 RECs may be invited by the FDA to conduct regulatory reviews on behalf of the latter. Level 3 Accredited RECs shall comply with ICH-GCP standards.

## REQUIREMENTS AND PROCEDURES FOR ACCREDITATION

### 1. Level 1 Accreditation

The REC must demonstrate sufficient competency and efficiency in ethical review, adhere to a set of appropriate SOPs, and have **adequate** administrative support as shown by an assigned office with standard equipment, a budget that supports honoraria for and training of REC members.

- 1.1. REC applicants for Level 1 accreditation shall submit the following documents:
  - 1.1.1. Cover Letter;
  - 1.1.2. Copy of the institutional issuance on the constitution and terms of reference (TOR) of REC;
  - 1.1.3. Manual of SOPs for REC activities (refer to Section IV. Item No. 3);
  - 1.1.4. Accomplished PHREB Form No. 1.1: Application for Accreditation;
  - 1.1.5. Accomplished PHREB Form No. 1.3: Protocol Summary, in the past year (if available); and
  - 1.1.6. Accomplished PHREB Form No. 1.4: Self-Assessment for Level 1.

- 1.2. A provisional certificate of Level 1 accreditation for one year shall be issued by PHREB after evaluation of the submitted documents. The formal awarding of the certificate shall be held either in March or in August of the year.
- 1.3. The REC shall be included in the list of accredited RECs in the PHREB website.
- 1.4. After the first year, the REC may apply for either one of the following:
  - 1.4.1. An extension of Level 1 accreditation for another two (2) years, approval of which will be based on an evaluation of the following submissions:
    - 1.4.1.1. PHREB Form No. 1.2: Annual Report;
    - 1.4.1.2. PHREB Form No. 1.3: Protocol Summary; and
    - 1.4.1.3. Copy of the minutes of the three (3) most recent REC meetings.
  - 1.4.2. Level 2 or Level 3 Accreditation, with the submission of appropriate requirements (see Requirements And Procedures For Accreditation: Item No. 2 or 3, respectively)

## **2. Level 2 Accreditation**

The REC must demonstrate sufficient competency and efficiency in ethical review, adhere to a set of appropriate SOPs, have systematic filing, have adequate administrative support as shown by an assigned office with standard equipment, at least a part time dedicated support staff, a budget that supports honoraria for and training of the REC members, and a functional database.

- 2.1. REC applicants for Level 2 accreditation shall submit the following documents:
  - 2.1.1. Cover Letter;

- 2.1.2. Copy of the institutional issuance on the constitution and terms of reference (TOR) of REC;
- 2.1.3. Manual of SOPs (refer to Accreditation Criteria: Item No. 3);
- 2.1.4. Accomplished PHREB Form No. 1.1: Application for Accreditation;
- 2.1.5. Accomplished PHREB Form No. 1.3: Protocol Summary, for the past two years, including the current year ;
- 2.1.6. Accomplished PHREB Form No. 1.5: Self-Assessment for Level 2;
- 2.1.7. Files of three (3) research protocols that have been reviewed and approved by the REC. The protocol file should include:
  - 2.1.7.1. Copy of the initial and revised protocols, initial and revised informed consent forms, accomplished assessment forms (technical/scientific and informed consent review);
  - 2.1.7.2. Minutes of the meeting when the research protocol was discussed (initial and subsequent continuing reviews);
  - 2.1.7.3. Letters or communications with the researchers (decision and approval letters); and
  - 2.1.7.4. Progress or final reports and corresponding assessments.
- 2.1.8. Copies of the agenda and minutes of the most recent three (3) REC meetings; and
- 2.1.9. Photograph of the office showing the equipment and storage system.
- 2.2. The REC applicant shall comply with the following:
  - 2.2.1. Inclusion of a member who is a health or allied health practitioner and a social scientist, familiar with the types of research protocols being reviewed by the REC;
  - 2.2.2. Review of at least ten (10) protocols, five (5) of which

- should have undergone full review, within the past year; and
- 2.2.3. A dedicated office space, with basic equipment (computer with internet connection and printer, telephone, filing cabinets with locks), contents of the active and inactive cabinets or filing system, poster of the general flow chart of REC procedures, and a designated staff secretary.
- 2.3. Issuance of a certificate of Level 2 accreditation shall be based on the evaluation of compliance with the requirements:
    - 2.3.1. If compliance is satisfactory, the REC shall be given a Certificate of PHREB Level 2 Accreditation for three (3) years;
    - 2.3.2. If there are deficiencies, the REC shall be issued a one (1) year provisional Certificate of PHREB Level 2 Accreditation, within which, the REC shall comply with the recommendations to address the deficiencies. Extension of its accreditation for another two (2) years will be based on satisfactory REC compliance;
    - 2.3.3. The formal awarding of the certificate shall be held either in March or in August of the year; and
    - 2.3.4. The REC shall be included in the list of accredited RECs in the PHREB website.
  - 2.4. A Level 2 accredited REC may apply for Level 3 Accreditation, with the submission of appropriate requirements (see Requirements and Procedures for Accreditation, Item No. 3) including inclusion of a medical member who is an experienced clinical trialist and another medical member who has been or is currently a member of a Level 3 accredited REC.

A provisional Level 3 accreditation for one year may be issued that shall allow the REC to accept review of sponsored clinical trials.

### 3. Level 3 Accreditation

The REC must demonstrate sufficient competency and efficiency in ethical review, adhere to a set of appropriate SOPs, have systematic filing, have adequate administrative support as shown by, but not limited to, an assigned office with standard equipment, a full time dedicated support staff, a budget that supports honoraria for and training of the REC members, and a functional database.

3.1. REC applicants for Level 3 accreditation shall submit the following documents:

- 3.1.1. Cover letter;
- 3.1.2. Accomplished PHREB Form No. 1.1: Application for Accreditation;
- 3.1.3. Accomplished PHREB Form No.1.3: Protocol Summary, in the last two years, including the current year;
- 3.1.4. Accomplished PHREB Form No. 1.6: Self-Assessment for Level 3; and
- 3.1.5. REC Manual of SOPs (refer to Accreditation Criteria: Item No. 3)

3.2. The REC applicant shall comply with the following:

- 3.2.1. All members should have basic research ethics training;
- 3.2.2. Majority of the members, including the Chair, should have GCP training within the past three (3) years;
- 3.2.3. At least one (1) member should have training in SOP writing;
- 3.2.4. All members should provide evidence of training in the use of the REC SOPs; and
- 3.2.5. A dedicated office space, basic office equipment (computer with internet connection and printer, telephone, filing cabinets with locks, poster of the general flow chart of REC procedures and a full-time staff secretary).

- 3.3. The REC shall undergo an Accreditation Visit that will involve the following:
  - 3.3.1. Preliminary coordination between PHREB and host REC regarding schedule of visit and logistics;
  - 3.3.2. The accreditation visit shall include: opening and closing meetings, interview of REC members and staff, inspection of the REC office, including the archives, an observation of an REC meeting and review of documents (e.g., SOPs, membership files, selected protocol files, SAE files, file of agenda and minutes of meetings, communications file, log book and databases).
- 3.4. Issuance of Accreditation Certificate will be processed as follows:
  - 3.4.1. CSA will send the report to the REC within forty-five (45) calendar days after the visit;
  - 3.4.2. REC shall submit an action plan to CSA within forty-five (45) calendar days after receipt of the CSA Report;
  - 3.4.3. A follow-up visit may be scheduled by the CSA to determine compliance with the action plan;
  - 3.4.4. CSA shall recommend the appropriate accreditation of the REC;
  - 3.4.5. PHREB shall award a certificate of accreditation with a specified period of validity of three (3) years. The formal awarding of the certificate shall be held either in March or in August of the year; and
  - 3.4.6. The REC shall be included in the list of accredited RECs in the PHREB website.

## **RESPONSIBILITIES OF AN ACCREDITED REC**

### **1. Posting of PHREB Accreditation Certificate**

The REC shall post or display its duly-secured certificate of PHREB accreditation in a conspicuous area within its office.

2. Submission of Annual Report within the first quarter of the following year using the PHREB Form No. 1.2: Annual Report which will reflect the following:
  - 2.1. Changes in committee chair and membership;
  - 2.2. Trainings attended by current members;
  - 2.3. Number and type of protocols reviewed, approved, revised, and disapproved;
  - 2.4. Summary of recognitions received by the REC or significant events that have affected the performance of its duties; and
  - 2.5. Challenges and issues encountered.
3. Reporting of any controversial or important ethical issues in the course of its work
4. Willingness to be monitored by PHREB

Annual report and other reports should be sent to the PHREB Secretariat, through:

Philippine Health Research Ethics Board  
c/o PCHRD, 3<sup>rd</sup> Floor, Room 306  
DOST Main Building, General Santos Avenue,  
Bicutan, 1631 Taguig City  
Telephone: (02) 837 75 37/Telefax: (02) 837 29 24  
Email address: [ethics.secretariat@gmail.com](mailto:ethics.secretariat@gmail.com)

## **RENEWAL OF ACCREDITATION CERTIFICATE**

Within two (2) months before the expiry of its accreditation, an REC shall apply for renewal by complying with the requirements/responsibilities of accredited RECs (Section VI: Procedures and Requirements for PHREB Accreditation).



## **BASES FOR WITHDRAWAL OF ACCREDITATION**

The accreditation of an REC may be withdrawn due to the following:

1. Non-compliance with PHREB reportorial and other Requirements

An REC that fails to submit an annual report for two (2) consecutive years shall have its certification withdrawn and its name delisted from the PHREB accredited RECs.

2. Unjustified issuance of ethical clearance (e.g., violation of national laws and guidelines, lack of due diligence, etc.) that resulted in harm to participants.

## **FEES**

PHREB shall charge application and accreditation processing fees based on the level of accreditation applied for.

The mechanism of payment is facilitated by the Philippine Council for Health Research and Development (PCHRD) which will issue periodic advisory on the matter in PHREB website (<http://ethics.healthresearch.ph/>).

Other expenses which may be incurred during Accreditation Visits (for Level 3) may vary depending on site specific logistical requirements (e.g., travel and accommodation).

## **ACCREDITATION OF SPECIALTY CLINICS**

### *Introduction*

The level of accreditation of specialty clinics needs special attention because of concerns in providing appropriate care to research participants who may need medical care that is not covered by the specialty offered in the facility, and in the management of conflict of interest when the pool of consultants where both researchers or investigators and REC members are derived, is small. The following policies have been formulated to address the aforementioned issues.

## *Scope*

These policies cover specialty clinics defined as stand-alone health care facilities that offer specific medical specialty services only (e.g., dermatology, ophthalmology, hematology, dialysis, etc.). These policies do not cover health care facilities that offer stem cell therapy/research.

## *Policies*

1. Application for all levels shall require accomplishment of the attached Application Form 1.1a that is specific for Specialty Clinics. The application form shall provide information on:
  - 1.1. Type of specialty services;
  - 1.2. Involvement in the production of health products including food preparations or supplements;
  - 1.3. Number of active consultant staff (full time or part-time) with reference to practice privileges;
  - 1.4. Nature of studies conducted;
  - 1.5. Description of the REC (number of members with at least one non-affiliated medical member in the same specialty, officers, specialty, affiliation, scientist or non-scientist, gender, age representation, and record of research ethics training); and
  - 1.6. Affiliation with or geographic access to a health facility with general medical services.
2. Application for Level 1 shall be processed according to the 2016 PHREB ACCREDITATION POLICIES AND REQUIREMENTS.
3. Processing and approval of an application for Levels 2 and 3 Accreditation shall take into consideration among others: an acceptable ratio (at least 10:1) of active consultant members of the REC to potential researchers and the accessibility of a health facility that offers general medical services to research participants, if needed.

## **APPENDIX F: STANDARD OPERATING PROCEDURES OF RESEARCH ETHICS COMMITTEES**

The work of RECs can be greatly helped by its SOPs which are detailed, written instructions, in a certain format, describing all activities and action undertaken by the REC 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 REC.

The objectives of REC SOPs include:

1. Defining the process for formulating, writing, implementing, and amending procedures within the REC;
2. Serving as an operating manual;
3. Providing clear instructions in the ethical review process;
4. Improving ethical review through consistent written procedures; and
5. Providing basis for continuous quality improvement of the research review process.

The SOPs explain the processes for constituting the REC, 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 REC as well as lessen possible areas of conflict.

SOPs shall be publicly available to all, both electronically and in hard copy. The REC shall use the most recent approved version of its SOP manual while retaining all previous versions in its files. The SOP manual of an REC must be made available to relevant bodies and individuals.

All kinds of forms to be used by REC – 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 researchers electronically. Flow charts may be included in the SOP to make visible, at a glance, the sequence of processes/tasks to be done.

SOPs may be organized into ten major activities. Some activities may have several related SOPs. This system of organizing SOPs need not be used by all RECs. For example, in RECs with limited activities, a straightforward listing of SOPs may suffice and be simpler to use.

### **SOP 1: REC Structure and Composition**

- 1.1. Selection and Appointment of Members
- 1.2. Designation of Officers
- 1.3. Appointment of Independent Consultants

### **SOP 2: Management of Initial Submissions and Resubmissions**

### **SOP 3: Management of Post Approval Submissions**

- 3.1. Review of Progress, Final, and Early Termination Reports, and Protocol Amendments
- 3.2. Review of SAE and SUSAR Reports
- 3.3. Review of Protocol Deviations and Violations
- 3.4. Review of Applications for Continuing Review

### **SOP 4: Review Procedures**

- 4.1. Expedited Review
- 4.2. Full Review

### **SOP 5: Meeting Procedures**

- 5.1. Preparing for a Meeting
- 5.2. Preparing the Meeting Agenda
- 5.3. Conduct of Regular and Special Meetings

### **SOP 6: Documentation of REC Actions**

- 6.1. Managing the Meeting Minutes
- 6.2. Communicating REC Decisions

### **SOP 7: Management and Archiving of Files**

- 7.1. Managing REC Incoming/Outgoing Communications
- 7.2. Managing Active Files (Administrative and Study Files)
- 7.3. Archiving of Terminated, Inactive, and Completed Files
- 7.4. Managing Access to Confidential Files

**SOP 8: Site Visits**

**SOP 9: Management of Queries/Complaints**

**SOP 10: Writing and Revising SOPs**

## APPENDIX G: THE PHREB STANDARD OPERATING PROCEDURE TEMPLATE

The recommended sections of each standard operating procedure (SOP) are as follows:

1. The **HEADER** consists of the name and logo of the Institution, title of the SOP (i.e., Activity), the SOP Number, Version Number, Date of Approval, and Effective Date. The header codifies the SOP through the SOP number and version number. The version number and pertinent dates are changed whenever the SOP is revised.

The suggested format for the **HEADER** is as follows:

|                                     |                         |                        |  |
|-------------------------------------|-------------------------|------------------------|--|
| <i>Name and Logo of Institution</i> | <i>REC Name</i>         | <i>SOP No:</i>         |  |
|                                     | <b>TITLE OF THE SOP</b> | <i>Version No:</i>     |  |
|                                     |                         | <i>Approval Date:</i>  |  |
|                                     |                         | <i>Effective Date:</i> |  |

2. The **POLICY STATEMENT** section consists of statement/s of institutional or committee policies upon which the activity and procedures are based. This section may also include specific provisions from international and national guidelines pertinent to the activity.
3. The **OBJECTIVE OF THE ACTIVITY** section is a statement that explains the purpose of the activity (e.g., for the SOP on Preparing for a Meeting, the objective may be stated as “The preparation for meetings aims to ensure that all meeting requirements are met such as logistics, documents, and agenda”).
4. The **SCOPE** section identifies the limits of applicability of the SOP. This section also indicates from which step the activity will begin to which step the activity will end.
5. The **RESPONSIBILITIES** section identifies the person/s and/or office/s in charge of implementing the SOP and their corresponding roles and

responsibilities. It is good to draft the workflow (see section 5) first before accomplishing this section in order to ensure that all the responsibilities are properly accounted for.

6. The **WORKFLOW** section is a diagram representing the different steps involved in the activity. It may also be illustrated as a flowchart using standard symbols like circles (denoting the start and end steps), rectangles (denoting the specific steps), and diamonds (for decision points). The person/s doing the action in each step is identified.
7. The section on **DETAILED DESCRIPTION OF PROCEDURES** describes the manner and timeline in each step. The person/s responsible and the forms to be used are also included. In filling out this section, it is important to be guided by the workflow. For example, if there are five steps in the workflow, then there should be five steps described in this section.
8. The **GLOSSARY** section includes terms that need to be defined, acronyms, and abbreviations that need to be explained. The list of terms in the different SOPs is not comprehensive, the REC may need to expand this as necessary. (Note: the glossaries of the different SOPs may be put together in one list and included as an annex or appendix of the whole SOP Manual).
9. The **FORMS** section lists the specific forms used in the activity (e.g., application form, checklist, review guide, communication templates).
10. The **HISTORY** section is a tabulation of the version dates and number, authors, and description of major changes that the SOP has undergone. For example, the versions of an SOP on Designation of Officers may be represented as follows:

| <b>Version No.</b> | <b>Date</b>         | <b>Authors</b> | <b>Main Change</b>                             |
|--------------------|---------------------|----------------|--|
| <i>01</i>          | <i>2010 July 15</i> | <i>ABC</i>     | <i>First draft</i>                             |
| <i>02</i>          | <i>2013 May 01</i>  | <i>DEF</i>     | <i>Added functions of the member-secretary</i> |

|           |                     |                    |   |
|-----------|---------------------|--------------------|---|
| <i>03</i> | <i>2015 June 03</i> | <i>ABC<br/>DEF</i> | <i>Included a co-chair<br/>and corresponding<br/>responsibilities</i> |
|-----------|---------------------|--------------------|---|

- 11.** The **REFERENCES** section is a list of guidelines, other institutional SOPs, and manuals used in the development of the SOP.



## APPENDIX H: SAMPLE APPLICATION FORM FOR ETHICS REVIEW OF RESEARCH PROPOSALS

**Instructions to the Researcher:** Please accomplish this form and ensure that you have included in your submission the documents that you checked below (*in Section 3. Checklist of Documents*).

| I. GENERAL INFORMATION  |  |  |   |
|---|--|--|---|
| TITLE OF STUDY  |  |  |   |
| REC CODE<br><i>(To be provided by REC)</i>                            |  | STUDY SITE   |   |
| NAME OF RESEARCHER  |  | CONTACT INFORMATION  | TEL NO:   |
|   |  |  | MOBILE NO:  |
| CO-RESEARCHER/S<br><i>(if any)</i>                                    |  |  | FAX NO:   |
|   |  |  | EMAIL:  |
| NAME OF INSTITUTION   |  |  |   |
| INSTITUTION ADDRESS   |  |  |   |
| TYPE OF STUDY   | <input type="checkbox"/> Clinical Trial ( <i>Sponsored</i> )<br><input type="checkbox"/> Clinical Trials ( <i>Researcher-Initiated</i> )<br><input type="checkbox"/> Health Operations Research ( <i>Health Programs and Policies</i> )<br><input type="checkbox"/> Social or Behavioral Research<br><input type="checkbox"/> Public Health or Epidemiologic |  | <input type="checkbox"/> Biomedical research ( <i>Retrospective, Prospective and Diagnostic Studies</i> )<br><input type="checkbox"/> Stem Cell Research<br><input type="checkbox"/> Genetic Research<br><input type="checkbox"/> Others: _____ |
|   | <input type="checkbox"/> Multicenter ( <i>International</i> )  | <input type="checkbox"/> Multicenter ( <i>National</i> )                       | <input type="checkbox"/> Single Site  |
| SOURCE OF FUNDING   | <input type="checkbox"/> Self-Funded<br><input type="checkbox"/> Government-Funded<br><input type="checkbox"/> Scholarship/Research Grant<br><input type="checkbox"/> Institution-Funded   |  | <input type="checkbox"/> Sponsored by Pharmaceutical Company<br>Specify: _____<br><input type="checkbox"/> Others: _____  |
| DURATION OF THE STUDY   | START DATE:  |  | NUMBER OF STUDY PARTICIPANTS  |
|   | END DATE:  |  |   |
| HAS THE RESEARCH UNDERGONE TECHNICAL REVIEW?                          |  | <input type="checkbox"/> YES ( <i>please attach technical review results</i> ) | <input type="checkbox"/> NO   |
| HAS THE RESEARCH BEEN SUBMITTED TO ANOTHER RESEARCH ETHICS COMMITTEE? |  | <input type="checkbox"/> YES   | <input type="checkbox"/> NO   |

|   |  |   |
|---|--|---|
| <b>II. BRIEF DESCRIPTION OF THE STUDY</b> <i>(use additional sheet if necessary)</i>  |  |   |
|   |  |   |
| <b>III. CHECKLIST OF DOCUMENTS FOR SUBMISSION</b>   |  |   |
| <p><b>BASIC REQUIREMENTS:</b></p> <p><input type="checkbox"/> Letter request for review</p> <p><input type="checkbox"/> Endorsement/Referral Letter</p> <p><input type="checkbox"/> Foreign Institutional Ethics Review Approval (if applicable)</p> <p><input type="checkbox"/> Full Proposal/Study Protocol</p> <p><input type="checkbox"/> Technical Review Approval</p> <p><input type="checkbox"/> Curriculum Vitae of Researcher</p> <p><input type="checkbox"/> Informed Consent Form</p> <p style="margin-left: 20px;"><input type="checkbox"/> English version</p> <p style="margin-left: 20px;"><input type="checkbox"/> Filipino version</p> <p style="margin-left: 20px;"><input type="checkbox"/> Others _____</p> <p><input type="checkbox"/> Assent Form <i>(if applicable)</i></p> <p style="margin-left: 20px;"><input type="checkbox"/> English version</p> <p style="margin-left: 20px;"><input type="checkbox"/> Filipino version</p> <p style="margin-left: 20px;"><input type="checkbox"/> Others _____</p> | <p><b>SUPPLEMENTARY DOCUMENTS</b> <i>(if applicable):</i></p> <p><input type="checkbox"/> Questionnaire</p> <p><input type="checkbox"/> Data Collection Forms</p> <p><input type="checkbox"/> Product Brochure</p> <p><input type="checkbox"/> Philippine FDA Marketing Authorization or Import License</p> <p><input type="checkbox"/> Permit(s) for special populations</p> <p style="margin-left: 20px;">_____</p> <p><input type="checkbox"/> Others</p> <p style="margin-left: 20px;">_____</p> |   |
| <p><b>ACCOMPLISHED BY:</b></p> <p style="text-align: center;">_____</p> <p style="text-align: center;"><i>(Signature over printed name)</i></p>   | <p><b>DATE SUBMITTED:</b></p>  |   |
| <b>----- TO BE FILLED OUT BY THE REC SECRETARIAT -----</b>  |  |   |
| <b>COMPLETENESS OF DOCUMENT</b>   | <input type="checkbox"/> Complete<br><input type="checkbox"/> Incomplete   | <div style="border: 1px solid black; width: 100%; height: 100%;"></div> <p>(place stamp here)</p> |
| <b>REMARKS</b>  |  |   |
| <b>DATE RECEIVED:</b>   |  |   |
| <b>RECEIVED BY:</b>   |  |   |

## APPENDIX I: RESEARCH PROPOSAL TEMPLATE

*(Adapted from the DOST-PCHRD)*

### **(1) COVER SHEET**

The cover sheet should contain the following information:

- Revision date and number
- Title of the research
- Signatures and dates:
  - Author(s)
  - Implementing agency
  - Cooperating agency
  - Approval of primary investigator
- Contact numbers of authors and cooperating agency

### **(2) TABLE OF CONTENTS**

This section contains a complete table of contents including a listing of all appendices

### **(3) INTRODUCTION**

This section contains a brief summary of the background information relevant to the research design and protocol methodology. Sufficient information includes description of disease/condition of interest and present knowledge of the subject matter of the research. This information is necessary in order to understand the rationale for the research.

### **(4) PROGRAM OR PROJECT TITLE**

The title is the distinctive name given to the research proposal (program or project), which describes the work scope in specific, clear, and concise terms.

A program is a group of inter-related research projects requiring an interdisciplinary or multidisciplinary approach to meet established goal(s) within a specific time frame. A project on the other hand is a basic unit in the investigation of a specific research problem with predetermined objectives to be accomplished within a specific time frame.

### **(5) PROGRAM OR PROJECT LEADER**

This indicates the name of the program and or project leader, his or her designation or title in his or her agency, field of specialization and his or her mailing address, telephone and fax numbers. Percentage time to be

devoted to his or her research should also be indicated.

A program leader is one who directly plans, organizes, supervises the over-all activities of a research, and is directly responsible for the conduct of one of the projects of said program.

A project leader is one who directly plans, organizes, and supervises, and conducts the implementation of a basic unit of investigation of a specific research problem.

**(6) IMPLEMENTING AGENCY**

This refers to the agency(ies) implementing the research proposal

**(7) COOPERATING AGENCY**

This refers to the agency(ies) which is/are expected to cooperate or contribute to the research work.

**(8) SIGNIFICANCE OF THE PROPOSAL**

This is the rationale of the research. It answers the question, “what is the research for?”

**(9) LITERATURE REVIEW**

This section should discuss literatures relevant and specific to the topic of the research proposal. It should be complete enough so the reader can be convinced that the research proposal being presented is built upon sound information base, addresses current country health priorities and will contribute something new to health and/or allied health sciences.

**(10) OBJECTIVES**

This section enumerates the goals that the program or project would attempt to achieve. If possible, delineate the general from the specific objectives. Research objectives should be: Specific, Measurable, Attainable, Relevant and Time-bound. If the proposal is a program, the program objectives as well as specific project objectives should be indicated.

**(11) EXPECTED OUTPUT(S)**

This refers to the end results (e.g., production technology or knowledge) expected upon completion of the research. The output(s) needs to be identified to highlight impact/importance of the research.

**(12) END-USERS OR TARGET BENEFICIARIES**

This refers to the probable end-users or beneficiaries of the research output and the number and locality of beneficiaries, if applicable.

**(13) DURATION OF PROGRAM OR PROJECT**

This refers to the planned start date, completion date, and duration in months.

**(14) METHODOLOGY**

**Research Design** – this section indicates how the research objectives will be achieved. It includes a description of the type of research design (e.g., cross sectional, case control, cohort, etc.)

**Research Population** – this is required for studies involving animals and humans. This section states the number of research participants required to enter and complete the research. A brief definition of the type of research participant required is also described.

**Inclusion Criteria** – this section describes the criteria each research participant must satisfy to enter the research. These criteria may include, but are not limited to the following: age, sex, race, diagnosis or condition, method of diagnosis, and diagnostic test.

**Exclusion Criteria** – this section details the criteria that would eliminate a participant from participation in the research.

**Sample Size Computation** – this section describes the type of sampling design and the assumptions used to compute the sample size.

**Research Site** – this section details the location, station, or unit where research will be conducted.

**Research Plan** – this section explains the plan of action, procedures and methods to be used during the research. Detailed methodology is described for laboratory, diagnostic, interviews, and manner of data collection. Special instrumentation may be described in a subsection (instrumentation or data collection tools, special equipment, etc.)

**Case Report Form** – the case report form (CRF) should be attached to the research proposal. If the CRF is in electronic format, a printed copy should be attached as an appendix.

**Variables to be Investigated** – dependent/outcome and independent variables

**(15) PLANS FOR DATA PROCESSING AND ANALYSIS**

- Computer facilities to be used, software packages
- Statistical tools or tests to be used
- Dummy tables

**(16) WORK PLAN SCHEDULE**

This is brief description in chronological order of each activity to be undertaken. The plan of work of a project should reflect the schedule of the study components. For the program, individual schedules of each of the projects should be supplied. A Gantt chart of activities should be given. This chart will indicate the relative time frame and schedule of the major activities of the proposal, including plans for research utilization.

**(17) ETHICAL AND BIOSAFETY CLEARANCE**

Ethical clearance from the agency’s Research Ethics Committee (REC) is required for research involving the use of human participants. In the absence of the REC, the implementing agency may submit their research proposal for ethical review to the National Ethics Committee (NEC). *An ethical clearance is required prior to review of the proposal.*

Likewise, biosafety clearance is needed to ensure that all studies dealing with genetic engineering and pathogenic organisms in the Philippines are conducted under reasonably safe conditions. If the implementing agency has no built-in Institutional Biosafety Committee, then the proposal could be submitted for review by the DOST’s National Committee on Biosafety of the Philippines (NCBP).

**(18) RESEARCH UTILIZATION**

This section should indicate the strategies to be used in disseminating and ensuring utilization of the expected research results. For product-based research, proposal should include the prospective technology user, as well as, plans for technology transfer.

### **(19) ESTIMATED BUDGETARY REQUIREMENTS**

Indicate the annual budget of the proposal according to source of funds. For the first year, specify the budget for major expense items. For succeeding years, only the total annual budget is required initially. The detailed breakdown of financial assistance requested should be in accordance with the New Government Accounting System (NGAS); the counterpart funding of the implementing agency as well as other agencies cooperating in the project should also be reflected. Details of the financial requirements per expense item and source of funds are illustrated at the end page.

Under the Personnel Services (PS), segregate the number and positions of those who will be receiving salaries from those who will be entitled to honoraria. Salaried personnel will consist of those who will work full time for the project.

Part-time staff to be hired for the research will be entitled to honoraria. Likewise, the Project Leader and the consultants will be recipients of honoraria. Indicate the recommended salaries/honoraria rates per position and the coverage of their service periods.

For Maintenance and Other Operating Expenses (MOOE), the traveling expenses of transportation of one's personal and essential baggage, per diems while in route or away from permanent station and items necessarily incidental thereto in connections with the research work. The item on supplies and materials will include expenses on consumable and semi-expendable field/laboratory/office supplies and materials needed in the course of the research. Budget for sundry will consist of expenses on communications, repairs and maintenance, estimated cost for research utilization (RU) component, computerization, and miscellaneous expenses. Details for each line item should be provided.

The Capital Outlay (CO) details the budgetary requirement of the research for equipment items needed for the project. Indicate the quantity, unit cost and total amount.

An administrative cost equivalent to 7.5% of total costs under PS and MOOE can be included as part of the budget. This item corresponds to the

overhead expenses (PS and MOOE) incurred by the implementing agency in managing, evaluating and monitoring the program/project.

**(20) CURRICULUM VITAE**

This portion provides relevant information regarding the proponent’s research capability

**(21) ENDORSEMENT FROM THE AGENCY HEAD**

This is indicative of the support of the implementing agency to the research project in terms of use of facilities and equipment, and assistance in undertaking the project.

**(22) BIBLIOGRAPHY**

An alphabetical, numerical list referencing or of source of relevant information or literature as used in referred medical journals or other international journals, should be followed.

**(23) LINE ITEM BUDGET**

*Example of the Line Item Budget Table is as follows:*

| PARTICULARS   | Sources of Funds and Amount (PHP) |                    |               |
|---|-----------------------------------|--------------------|---------------|
|   | PCHRD ASSISTANCE                  | AGENCY COUNTERPART | OTHER SOURCES |
| <b><i>I. Personal Services (PS)</i></b>                           |                                   |                    |               |
| <i>a. Salaries</i>  |                                   |                    |               |
| <i>b. Honoraria</i>   |                                   |                    |               |
| <b><i>PS SUB TOTAL</i></b>  |                                   |                    |               |
| <b><i>II. Maintenance and Other Operating Expenses (MOOE)</i></b> |                                   |                    |               |
| <i>a. Traveling expenses</i>                                      |                                   |                    |               |
| <i>b. Supplies and materials expenses</i>                         |                                   |                    |               |
| <b><i>MOOE SUBTOTAL</i></b>                                       |                                   |                    |               |
| <b><i>III. Capital Outlay</i></b>                                 |                                   |                    |               |
| <b><i>CAPTAL OUTLAY SUBTOTAL</i></b>                              |                                   |                    |               |
| <b><i>GRAND TOTAL</i></b>   |                                   |                    |               |



## APPENDIX J: SAMPLE WORKSHEET FOR PROTOCOL ASSESSMENT

(Adapted from the NEC)

|   |   |                              |                              |                             |
|---|---|------------------------------|------------------------------|-----------------------------|
| TITLE OF STUDY  |   |                              |                              |                             |
| REC CODE  |   | TYPE OF REVIEW               |                              |                             |
| PROPONENT   |   | INSTITUTION                  |                              |                             |
| REVIEWER  |   | PRIMARY REVIEWER?            | <input type="checkbox"/> YES | <input type="checkbox"/> NO |
| <b>-- GUIDE QUESTIONS FOR REVIEWING THE PROPOSAL OR PROTOCOL --</b>   |   |                              |                              |                             |
| 1. Is/Are the research question(s) reasonable?  | <input type="checkbox"/> UNABLE TO ASSESS | <input type="checkbox"/> YES | <input type="checkbox"/> NO  |                             |
| <i>If NO or UNABLE TO ASSESS, please explain.</i>   |   |                              |                              |                             |
| 2. Are the study objectives specific, measurable, attainable, and reasonable?   | <input type="checkbox"/> UNABLE TO ASSESS | <input type="checkbox"/> YES | <input type="checkbox"/> NO  |                             |
| <i>If NO or UNABLE TO ASSESS, please explain.</i>   |   |                              |                              |                             |
| 3. Does the research need to be carried out with human participants?  | <input type="checkbox"/> UNABLE TO ASSESS | <input type="checkbox"/> YES | <input type="checkbox"/> NO  |                             |
| <i>If NO or UNABLE TO ASSESS, please explain.</i>   |   |                              |                              |                             |
| 4. Does the protocol present sufficient background information or results of previous studies prior to human experimentation? | <input type="checkbox"/> UNABLE TO ASSESS | <input type="checkbox"/> YES | <input type="checkbox"/> NO  |                             |
| <i>If NO or UNABLE TO ASSESS, please explain.</i>   |   |                              |                              |                             |
| 5. Does the study involve individuals who are vulnerable?   | <input type="checkbox"/> UNABLE TO ASSESS | <input type="checkbox"/> YES | <input type="checkbox"/> NO  |                             |
| <i>If YES or UNABLE TO ASSESS, please explain.</i>  |   |                              |                              |                             |

|  |   |                              |                             |
|--|---|------------------------------|-----------------------------|
| 6. Are appropriate mechanisms in place to protect the vulnerable potential participants? | <input type="checkbox"/> UNABLE TO ASSESS | <input type="checkbox"/> YES | <input type="checkbox"/> NO |
| <i>If NO or UNABLE TO ASSESS, please explain.</i>  |   |                              |                             |
| 7. Are there probable risks to the human participants in the study?                      | <input type="checkbox"/> UNABLE TO ASSESS | <input type="checkbox"/> YES | <input type="checkbox"/> NO |
| 8. Does the protocol adequately address the risk/benefit balance?                        | <input type="checkbox"/> UNABLE TO ASSESS | <input type="checkbox"/> YES | <input type="checkbox"/> NO |
| <i>If NO or UNABLE TO ASSESS, please explain.</i>  |   |                              |                             |
| 9. Are toxicological and pharmacological data adequate?                                  | <input type="checkbox"/> NOT APPLICABLE   | <input type="checkbox"/> YES | <input type="checkbox"/> NO |
| <i>If NO, please explain.</i>  |   |                              |                             |
| 10. Is the informed consent procedure/form adequate and culturally appropriate?          | <input type="checkbox"/> NOT APPLICABLE   | <input type="checkbox"/> YES | <input type="checkbox"/> NO |
| <i>If NO, please explain.</i>  |   |                              |                             |
| 11. Are the proponents adequately trained and do they have sufficient experience?        | <input type="checkbox"/> UNABLE TO ASSESS | <input type="checkbox"/> YES | <input type="checkbox"/> NO |
| <i>If NO or UNABLE TO ASSESS, please explain.</i>  |   |                              |                             |
| 12. Is the research facility appropriate?  | <input type="checkbox"/> UNABLE TO ASSESS | <input type="checkbox"/> YES | <input type="checkbox"/> NO |
| <i>If NO or UNABLE TO ASSESS, please explain.</i>  |   |                              |                             |
| 13. Do you have any other concerns?  |   |                              |                             |

**Recommendation:**

- Exempt from Review
- Approved
- Minor Revisions Required

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- Major Revisions Required

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- Disapproved

*Reasons for disapproval:*

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Signature over Printed Name  
of Reviewer

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Review Date

## APPENDIX K: INFORMED CONSENT FORM TEMPLATE FOR CLINICAL STUDIES

*Adapted from the WHO Informed Consent Template*

*([http://www.who.int/rpc/research\\_ethics/informed\\_consent/en/](http://www.who.int/rpc/research_ethics/informed_consent/en/))*

*(This template is for either clinical trials or clinical research. Language used throughout form should be at the level of a Filipino local student in Grade 6 to 8)*

[INSTITUTIONAL LETTER HEAD]

**Informed Consent Form for [Name the group of individuals for whom this informed consent form is written. Because research for a single project is often carried out with a number of different groups of individuals - for example healthcare workers, patients, and parents of patients - it is important that the group for whom this particular consent is identified.]**

[Name of Principle Investigator]

[Name of Organization]

[Name of Sponsor]

[Name of Project and Version]

### **PART I: INFORMATION SHEET**

#### **INTRODUCTION**

Briefly state who you (researcher) are and explain that you are inviting them to participate in the research you are doing. Inform them that they may talk to anyone they feel comfortable talking with about the research and that they can take time to reflect on whether they want to participate or not. Assure the participant that if they do not understand some of the words or concepts, that you will take time to explain them as you go along and that they can ask questions now or later.

#### **PURPOSE OF THE RESEARCH**

Explain in lay terms why you are doing the research. The language used should clarify rather than confuse. Use local and simplified terms for a disease (e.g., local name of disease instead of malaria, mosquito instead of anopheles, “mosquitoes help in spreading the disease” rather than “mosquitoes are the vectors”). Avoid using terms like pathogenesis,

indicators, determinants, equitable etc. There are guides on the internet to help you find substitutes for words which are overly scientific or are professional jargon.

### **TYPE OF RESEARCH INTERVENTION**

Briefly state the type of intervention or procedure that will be undertaken. This will be expanded upon in the procedures section (below) but it may be helpful and less confusing to the participant if they know from the very beginning whether, for example, the research involves a vaccine, an interview, a biopsy or a series of finger pricks.

### **PARTICIPANT SELECTION**

State why this participant has been chosen for this research. People often wonder why they have been chosen to participate and may be fearful, confused or concerned.

### **VOLUNTARY PARTICIPATION**

Indicate clearly that they can choose to participate or not. State, what the alternative - in terms of the treatment offered by the clinic - will be, if they decide not to participate. State, only if it is applicable, that they will still receive all the services they usually do whether they choose to participate or not. This can be repeated and expanded upon later in the form as well, but it is important to state clearly at the beginning of the form that participation is voluntary so that the other information can be heard in this context.

*Include the following section only if the protocol is for a clinical trial:*

### **INFORMATION ON THE TRIAL DRUG [Name of Drug]**

1. Give the phase of the trial and explain what that means. Explain to the participant why you are comparing or testing the drugs.
2. Provide as much information as is appropriate and understandable about the drug such as its manufacturer or location of manufacture and the reason for its development.
3. Explain the known experience with this drug
4. Explain comprehensively all the known side-effects/toxicity of this drug, as well as the adverse effects of all the other medicines that are being used in the trial

## **PROCEDURES AND PROTOCOL**

Describe or explain the exact procedures that will be followed on a step-by-step basis, the tests that will be done, and any drugs that will be given. Explain from the outset what some of the more unfamiliar procedures involve (placebo, randomization, biopsy, etc.) Indicate which procedure is routine and which is experimental or research. Participants should know what to expect and what is expected of them. Use active, rather than conditional, language. Write "we will ask you to...." instead of "we would like to ask you to....".

In this template, this section has been divided into two: firstly, an explanation of unfamiliar procedures and, secondly, a description of process.

### **A. Unfamiliar Procedures**

This section should be included if there may be procedures which are not familiar to the participant.

*If the protocol is for a clinical trial:*

1. Involving randomization or blinding, the participants should be told what that means and what chance they have of getting which drug (i.e., one in four chances of getting the test drug).
2. Involving an inactive drug or placebo, it is important to ensure that the participants understand what is meant by a placebo or inactive drug.
3. Which may necessitate a rescue medicine, then provide information about the rescue medicine or treatment such as what it is and the criterion for its use. For example, in pain trials, if the test drug does not control pain, then intravenous morphine may be used as a rescue medicine.

*If the protocol is for clinical research:*

Firstly, explain that there are standards and guidelines that will be followed for the treatment of their condition. Secondly, if as part of the research a biopsy will be taken, then explain whether it will be under local anesthesia, sedation or general anesthesia, and what sort of symptoms and side effects the participant should expect under each category.

*For any clinical study (if relevant):*

If blood samples are to be taken explain how many times and how much in a language that the person understands. It may, for example, be inappropriate to tell a tribal villager that blood equal to a wine-glass full will be taken but it may be very appropriate to use pictures or other props to illustrate the procedure if it is unfamiliar.

If the samples are to be used only for this research, then explicitly mention here that the biological samples obtained during this research procedure will be used only for this research, and will be destroyed after \_\_\_\_ years, when the research is completed. If the tissues/blood samples or any other human biological material will be stored for a duration longer than the research purpose, or is likely to be used for a purpose other than mentioned in the research proposal, then provide information about this and obtain consent specifically for such storage and use in addition to consent for participation in the study - (see last section).

## **B. Description of the Process**

Describe to the participant what will happen on a step-by-step basis. It may be helpful to the participant if you use drawings or props to better illustrate the procedures. A small vial or container with a little water in it is one way of showing how much blood will be withdrawn.

## **DURATION**

Include a statement about the time commitments of the research for the participant including both the duration of the research and follow-up, if relevant.

## **SIDE EFFECTS**

Potential participants should be told if there are any known or anticipated side effects and what will happen in the event of a side effect or an unexpected event.

## **RISKS**

Explain and describe any possible or anticipated risks. Describe the level of care that will be available in the event that harm does occur, who will provide it, and who will pay for it. A risk can be thought of as being the possibility that harm may occur. Provide enough information about the risks

that the participant can make an informed decision.

### **BENEFITS**

Mention only those activities that will be actual benefits and not those to which they are entitled regardless of participation. Benefits may be divided into benefits to the individual, benefits to the community in which the individual resides, and benefits to society as a whole as a result of finding an answer to the research question.

### **REIMBURSEMENTS**

State clearly what you will provide the participants with as a result of their participation. WHO does not encourage incentives. However, it recommends that reimbursements for expenses incurred as a result of participation in the research be provided. These may include, for example, travel costs and money for wages lost due to visits to health facilities. The amount should be determined within the host country context.

### **CONFIDENTIALITY**

Explain how the research team will maintain the confidentiality of data, especially with respect to the information about the participant which would otherwise be known only to the physician but would now be available to the entire research team. Note that because something out of the ordinary is being done through research, any individual taking part in the research is likely to be more easily identified by members of the community and is therefore more likely to be stigmatized.

### **SHARING THE RESULTS**

Where it is relevant, your plan for sharing the information with the participants should be provided. If you have a plan and a timeline for the sharing of information, include the details. You should also inform the participant that the research findings will be shared more broadly, for example, through publications and conferences.

### **RIGHT TO REFUSE OR WITHDRAW**

This is a reconfirmation that participation is voluntary and includes the right to withdraw. Tailor this section to ensure that it fits for the group for whom you are seeking consent. The example used here is for a patient at a clinic.



## **ALTERNATIVES TO PARTICIPATING**

Include this section only if the study involves administration of investigational drugs or use of new therapeutic procedures. It is important to explain and describe the established standard treatment.

## **WHO TO CONTACT**

Provide the name and contact information of someone who is involved, informed, and accessible (a local person who can actually be contacted. State also that the proposal has been approved and how).

## **PART II: CERTIFICATE OF CONSENT**

This section should be written in the first person and have a statement similar to the one in bold below. If the participant is illiterate but gives oral consent, a witness must sign. A researcher or the person going over the informed consent must sign each consent. The certificate of consent should avoid statements that have "I understand...." phrases. The understanding should perhaps be better tested through targeted questions during the reading of the information sheet (some examples of questions are given above), or through the questions being asked at the end of the reading of the information sheet, if the potential participant is reading the information sheet himself or herself.

**I have read the foregoing information, or it has been read to me. I have had the opportunity to ask questions about it and any questions that I have asked have been answered to my satisfaction. I consent voluntarily to participate as a participant in this research.**

**Print Name of Participant:** \_\_\_\_\_

**Signature of Participant:** \_\_\_\_\_

**Date:** [MM/DD/YYYY]

### *If Illiterate*

A literate witness must sign (if possible, this person should be selected by the participant and should have no connection to the research team). Participants who are illiterate should include their thumb-print as well.

**I have witnessed the accurate reading of the consent form to the potential participant, and the individual has had the opportunity to ask questions. I confirm that the individual has given consent freely.**

**Print name of witness \_\_\_\_\_ Thumb print of participant:**  
**Signature of witness \_\_\_\_\_**  
**Date: [MM/DD/YYYY]**



**STATEMENT BY THE RESEARCHER OR PERSON TAKING CONSENT**

**I have accurately read out the information sheet to the potential participant, and to the best of my ability made sure that the participant understands that the following will be done:**

- 1.
- 2.
- 3.

**I confirm that the participant was given an opportunity to ask questions about the study, and all the questions asked by the participant have been answered correctly and to the best of my ability. I confirm that the individual has not been coerced into giving consent, and the consent has been given freely and voluntarily.**

**A copy of this Informed Consent Form has been provided to the participant.**

**Print Name of Researcher or person taking the consent**

\_\_\_\_\_  
**Signature of Researcher or person taking the consent**

\_\_\_\_\_  
**Date: [MM/DD/YYYY]**

## **APPENDIX L: INFORMED CONSENT FORM TEMPLATE FOR SURVEYS, INTERVIEWS, AND FOCUS GROUP DISCUSSIONS**

*Adapted from the WHO Informed Consent Template*

*([http://www.who.int/rpc/research\\_ethics/informed\\_consent/en/](http://www.who.int/rpc/research_ethics/informed_consent/en/))*

*(This template is for research interventions that use questionnaires, in-depth interviews or focus group discussions.)*

[INSTITUTIONAL LETTER HEAD]

**Informed Consent Form for [Identity of the particular group of individuals (e.g., clients, patients, community leaders, service providers) in the project for whom this consent is intended]**

[Name of Principle Investigator]

[Name of Organization]

[Name of Sponsor]

[Name of Project and Version]

### **PART I: INFORMATION SHEET**

#### **INTRODUCTION**

Briefly introduce the proponent and concerned organization, emphasize that this is an invitation to participate in a study/research and that he or she can take time to reflect on whether he or she want to participate or not. Assure the participant that he or she does not understand some of the words or concepts, that these will be explained and that he or she can ask questions at any time.

#### **PURPOSE OF THE RESEARCH**

Explain the research question in ordinary, non-technical terms. Use local and simplified words rather than scientific terms and professional jargon. Consider local beliefs and knowledge when deciding how best to provide the information.

#### **TYPE OF RESEARCH INTERVENTION**

Briefly state the type of intervention that will be undertaken. This will be expanded upon in the procedures section but it may be helpful and less

confusing to the participant if they know from the very beginning whether, for example, the research involves a vaccine, an interview, a questionnaire, or a series of finger pricks.

### **PARTICIPANT SELECTION**

Indicate why you have chosen this person to participate in this research. People wonder why they have been chosen and may be fearful, confused or concerned.

### **VOLUNTARY PARTICIPATION**

Indicate clearly that they can choose to participate or not. State, only if it is applicable, that they will still receive all the services they usually do if they choose not to participate. Explanation: It may be more applicable to assure them that their choosing to participate or not will not have any bearing on their job or job-related evaluations. This can be repeated and expanded upon later in the form as well. It is important to state clearly at the beginning of the form that participation is voluntary so that the other information can be heard in this context. Although, if the interview or group discussion has already taken place, the person cannot 'stop participation' but request that the information provided by them not be used in the research study.

### **PROCEDURES**

- A. Provide a brief introduction to the format of the research study and in which part of the study he or she will be involved.
- B. Explain the type of questions that the participants are likely to be asked in the focus group, the interviews, or the survey. If the research involves questions or discussions which may be sensitive or potentially cause embarrassment, inform the participant of this.

#### *In focus group discussions:*

Give the location of the FGD, describe the FGD process, inform the participant that there will be 7-8 other persons with similar experiences, that the discussion will be guided by a moderator who is trained to do so, whether the discussion will be recorded, how confidentiality will be kept and how long the records will be stored. Give the participant an idea on what topics will be taken up, that questions the participant has about the study

may also be raised and discussed and that he or she does not have to share any knowledge that he or she is not comfortable sharing. It is also important for the participant to know that he or she can still opt out of the study even after the FGD by requesting that his or her participation not be cited part of the data.

*For interviews:*

Inform the participant about the location of the interview (or a preferred location of the participant) and identity of the interviewer. Assure the participant that he or she does not wish to answer any of the questions during the interview, the interviewer will move on to the next question; that no one else but the interviewer will be present unless he or she would like someone else to be there. Describe how the interview will be recorded and kept confidential. Explain how long the study records will be kept and subsequently destroyed.

*For questionnaire surveys:*

Describe how the survey will be distributed and collected. Inform the participant that he or she may answer the questionnaire personally, or it can be read to him or her; answered aloud and written down by a member of the research team. Assure the participant that if he or she does not wish to answer any of the questions, this may be skipped and he or she can proceed to the next question. The information recorded is confidential, name is not included on the forms, only a number will identify him or her, and no one else except [name of person(s) with access to the information] will have access to the results of the survey.)

**DURATION**

Include a statement about the time commitments of the research for the participant including both the duration of the research and follow-up, if relevant.

**RISKS**

Explain and describe any risks that can be anticipated or that are possible. The risks depend upon the nature and type of qualitative intervention, and should be, as usual, tailored to the specific issue and situation.

If the discussion is on sensitive and personal issues (e.g., reproductive and

sexual health, personal habits, etc.) or confidential in nature, then there is a risk of embarrassment, discomfort or fear. Assure the participant that he or she does not have to answer any question or take part in the discussion, interview, or survey if he or she feels the question(s) are too personal or if talking about them makes him or her uncomfortable.

## **BENEFITS**

Benefits may be divided into benefits to the individual, benefits to the community in which the individual resides, and benefits to society as a whole as a result of finding an answer to the research question. Mention only those activities that will be actual benefits and not those to which they are entitled regardless of participation.

## **REIMBURSEMENTS**

State clearly that the participants will not receive payments beyond reimbursements for expenses incurred as a result of their participation.

## **CONFIDENTIALITY**

Explain how the research team will maintain the confidentiality of data with respect to both information about the participant and information that the participant shares. Outline any limits to confidentiality. Inform the participant that because something out of the ordinary is being done through research, any individual taking part in the research is likely to be more easily identified by members of the community and therefore more likely to be stigmatized. If the research is sensitive and/or involves participants who are highly vulnerable - research concerning violence against women for example - explain to the participant any extra precautions you will take to ensure safety and anonymity.

*(The following applies to focus groups)*

Focus groups provide a particular challenge to confidentiality because once something is said in the group it becomes common knowledge. Explain to the participant the group participants shall be encouraged to respect confidentiality, but that this cannot be guaranteed.

## **SHARING THE RESULTS**

If there is a plan and a timeline for the sharing of information, include the details. The participant may also be informed that the research findings will

be shared more broadly, for example, through publications and conferences.

**RIGHT TO REFUSE OR WITHDRAW**

Reiterate that participation is voluntary and includes the right to withdraw. Tailor this section to ensure that it fits for the group for whom one is seeking consent. Participants should have an opportunity to review their remarks in individual interviews and erase part or all of the recording or note.

**WHO TO CONTACT**

Provide the name and contact information of someone who is involved, informed and accessible - a local person who can actually be contacted. State also the name (and contact details) of the local REC that has approved the proposal.

**PART II: CERTIFICATE OF CONSENT**

This section must be written in the first person. It should include a few brief statements about the research and be followed by a statement similar to the one in bold below. If the participant is illiterate but gives oral consent, a witness must sign. A researcher or the person going over the informed consent must sign each consent.

*This section is mandatory*

**I have read the foregoing information, or it has been read to me. I have had the opportunity to ask questions about it and any questions I have been asked have been answered to my satisfaction. I consent voluntarily to be a participant in this study.**

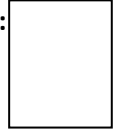
**Print Name of Participant:** \_\_\_\_\_  
**Signature of Participant:** \_\_\_\_\_  
**Date:** [MM/DD/YYYY]

*If Illiterate*

A literate witness must sign (if possible, this person should be selected by the participant and should have no connection to the research team). Participants who are illiterate should include their thumb print as well.

**I have witnessed the accurate reading of the consent form to the potential participant, and the individual has had the opportunity to ask questions. I confirm that the individual has given consent freely.**

**Print name of witness \_\_\_\_\_ Thumb print of participant:**  
**Signature of witness \_\_\_\_\_**  
**Date: [MM/DD/YYYY]**



**STATEMENT BY THE RESEARCHER OR PERSON TAKING CONSENT**

**I have accurately read out the information sheet to the potential participant, and to the best of my ability made sure that the participant understands that the following will be done:**

- 1.
- 2.
- 3.

**I confirm that the participant was given an opportunity to ask questions about the study, and all the questions asked by the participant have been answered correctly and to the best of my ability. I confirm that the individual has not been coerced into giving consent, and the consent has been given freely and voluntarily.**

**A copy of this Informed Consent Form has been provided to the participant.**

**Print Name of Researcher or person taking the consent**

\_\_\_\_\_  
**Signature of Researcher or person taking the consent**

\_\_\_\_\_  
**Date: <MM/DD/YYYY>**



## **APPENDIX M: INFORMED ASSENT FORM TEMPLATE FOR MINORS OR CHILDREN (12 TO UNDER 15 YEARS OLD)**

*Adapted from the WHO Assent Template*

*([http://www.who.int/rpc/research\\_ethics/informed\\_consent/en/](http://www.who.int/rpc/research_ethics/informed_consent/en/))*

*(Language should be at a level appropriate to the child's age and development. This template is written for a pre-adolescent or young adolescent.)*

**Informed Assent Form for [Description of Group of Children Involved]**

**[Name of Principle Investigator]**

**[Name of Organization]**

**[Name of Sponsor]**

**[Name of Project and Version]**

### **PART I: INFORMATION SHEET**

#### **INTRODUCTION**

Introduce the researcher and provide a brief description of the study. Clearly state that you are doing research. Inform the child that parental consent is also necessary. Let them know that they can speak to anyone they choose about the research before they make up their mind.

#### **PURPOSE**

Explain the purpose of the research in clear simple terms.

#### **CHOICE OF PARTICIPANTS**

Explain why they are being invited to be in the research. It is important to address any fears they may have about why they were chosen.

#### **PARTICIPATION IS VOLUNTARY: Do I have to do this?**

State clearly and in child-friendly language that the choice to participate is theirs. If there is a possibility that their decision not to participate might be over-ridden by parental consent, this should be stated clearly and simply.

#### **INFORMATION ON THE TRIAL DRUG [Name of Drug]:**

*Include the following section only if the protocol is for a clinical trial:*

**[Name of Drug]: What is this drug and what do you know about it?**

1. Give the phase of the trial and explain what that means. Explain to the participant why you are comparing or testing the drugs.
2. Provide as much information as is appropriate and understandable about the drug such as its manufacturer or location of manufacture and the reason for its development.
3. Explain the known experience with this drug.
4. Explain comprehensively all the known side-effects and toxicity of this drug, as well as the adverse effects of all the other medicines that are being used in the trial.

**PROCEDURES**

Explain the procedures and any medical terminology in simple language. Focus on what is expected of the child. Describe which part of the research is experimental.

**RISKS**

Explain any risks using simple, clear language. Describe what have been found as cause for worry previously and how the researchers will do their best to ensure that this will not happen and if it does, he or she will be attended to promptly. Include the importance of complying with the scheduled visits in order to address concerns and issues about the study.

**DISCOMFORTS**

If there will be any discomforts (e.g., hurt from injection, reddening and swelling) state these clearly and simply. Address what may be some of the child's worries, for example, missing school or extra expense to parents.

**BENEFITS**

Describe any benefits to the child (and to others).

**REIMBURSEMENTS**

Mention any reimbursements (e.g., travel expenses and reimbursement for time lost) or forms of appreciation that will be provided. Any gifts given to children should be small enough to not be an inducement or reason for participating.

## **CONFIDENTIALITY**

Explain what confidentiality means in simple terms (*for example: We will not tell other people that you are in this research and we will not share information about you to anyone who does not work in the research study. After the research is over, you and your parents will be told which of the two injections you received and the results.*) State any limits to confidentiality. Indicate what their parents will or will not be told.

## **COMPENSATION**

Describe how the research study group will take care of the child if he or she gets sick or hurt because of participation in the study. Describe the arrangement in accordance with the ability of the child to understand and explain that parents have been given more information.

## **SHARING THE FINDINGS**

Explain that the research findings will be shared in a timely fashion but that confidential information will remain confidential. If you have a plan and a timeline for the sharing of information, include the details. Also tell the child that the research will be shared more broadly (i.e., in a book, journal, conferences, etc.).

## **RIGHT TO REFUSE OR WITHDRAW**

Re-emphasize that participation is voluntary and describe any limits to this. He or she can think about it and decide later. It will also be ok to say “yes” now and change his or her mind later.

## **WHO TO CONTACT**

List and give contact information for those people who the child can contact easily (a local person who can actually be contacted). Tell the child that he or she and parents can also talk to anyone they want to about this (e.g., their own doctor, a family friend, a teacher).

## **PART 2: CERTIFICATE OF ASSENT**

This section can be written in the first person. It should include a few brief statements about the research and be followed by a statement similar to the one identified as 'suggested wording' below. If the child is illiterate but gives oral assent, a witness must sign instead. The researcher or the person going over the informed assent with the child must sign all assents.

*(Example: I understand the research is about testing a new vaccine for malaria and that I might get either the new vaccine which is being tested or the vaccine which is currently being used. I understand that I will get an injection and that I will come for regular monthly check-ups at the clinic where I will give a blood sample with a finger prick.)*

**I have read this information (or had the information read to me) I have had my questions answered and know that I can ask questions later if I have them.**

**I agree to take part in the research.**

**Print name of child:** \_\_\_\_\_

**Signature of child:** \_\_\_\_\_

**Date:** [DD/MM/YYYY]

*(If illiterate)*

A literate witness must sign (if possible, this person should be selected by the participant, not be a parent, and should have no connection to the research team). Participants who are illiterate should include their thumb print as well.

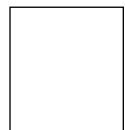
**I have witnessed the accurate reading of the assent form to the child, and the individual has had the opportunity to ask questions. I confirm that the individual has given consent freely.**

**Print name of witness (not a parent)** \_\_\_\_\_

**AND Thumb print of participant**

**Signature of witness** \_\_\_\_\_

**Date:** [DD/MM/YYYY]



**I have accurately read or witnessed the accurate reading of the assent form to the potential participant, and the individual has had the opportunity to ask questions. I confirm that the individual has given assent freely.**

**Print name of researcher: \_\_\_\_\_**

**Signature of researcher: \_\_\_\_\_**

**Date: [DD/MM/YYYY]**

**STATEMENT BY THE RESEARCHER/PERSON TAKING CONSENT**

**I have accurately read out the information sheet to the potential participant, and to the best of my ability made sure that the child understands that the following will be done:**

- 1.**
- 2.**
- 3.**

**I confirm that the child was given an opportunity to ask questions about the study, and all the questions asked by him or her have been answered correctly and to the best of my ability. I confirm that the individual has not been coerced into giving consent, and the consent has been given freely and voluntarily.**

**A copy of this assent form has been provided to the participant.**

**Print Name of Researcher/person taking the assent \_\_\_\_\_**

**Signature of Researcher /person taking the assent**

\_\_\_\_\_

**Date: [DD/MM/YYYY]**

**Copy provided to the participant \_\_\_\_\_ (initialled by researcher/assistant)**

**Parent/Guardian has signed an informed consent**

**\_\_\_ Yes \_\_\_ No \_\_\_\_\_ (initialled by researcher/assistant)**

## APPENDIX N: SAMPLE INFORMED CONSENT ASSESSMENT CHECKLIST

(Adapted from the NEC)

|   |  |                   |                              |                             |
|---|--|-------------------|------------------------------|-----------------------------|
| TITLE OF STUDY  |  |                   |                              |                             |
| REC CODE  |  | TYPE OF REVIEW    |                              |                             |
| PRINCIPAL INVESTIGATOR  |  | INSTITUTION       |                              |                             |
| REVIEWER  |  | PRIMARY REVIEWER? | <input type="checkbox"/> YES | <input type="checkbox"/> NO |
| -- GUIDE QUESTIONS FOR REVIEWING THE INFORMED CONSENT PROCESS AND FORM --   |  |                   |                              |                             |
| 1. IS IT NECESSARY TO SEEK THE INFORMED CONSENT OF THE PARTICIPANTS?  |  |                   |                              |                             |
| <input type="checkbox"/> UNABLE TO ASSESS <input type="checkbox"/> YES <input type="checkbox"/> NO  |  |                   |                              |                             |
| <b>IF NO</b> , please explain   |  |                   |                              |                             |
| If <b>YES</b> , are the participants provided with sufficient information about the following items?  |  |                   |                              |                             |
| <ul style="list-style-type: none"> <li>Purpose of the study?</li> </ul>   |  |                   | <input type="checkbox"/> YES | <input type="checkbox"/> NO |
| <ul style="list-style-type: none"> <li>Expected duration of participation?</li> </ul>   |  |                   | <input type="checkbox"/> YES | <input type="checkbox"/> NO |
| <ul style="list-style-type: none"> <li>Procedures to be carried out?</li> </ul>   |  |                   | <input type="checkbox"/> YES | <input type="checkbox"/> NO |
| <ul style="list-style-type: none"> <li>Discomforts and inconveniences?</li> </ul>   |  |                   | <input type="checkbox"/> YES | <input type="checkbox"/> NO |
| <ul style="list-style-type: none"> <li>Risks (including possible discrimination)?</li> </ul>  |  |                   | <input type="checkbox"/> YES | <input type="checkbox"/> NO |
| <ul style="list-style-type: none"> <li>Random assignment to the trial treatments? (if applicable)</li> </ul>  |  |                   | <input type="checkbox"/> YES | <input type="checkbox"/> NO |
| <ul style="list-style-type: none"> <li>Benefits to the participants?</li> </ul>   |  |                   | <input type="checkbox"/> YES | <input type="checkbox"/> NO |
| <ul style="list-style-type: none"> <li>Alternative treatments/procedures? (if applicable)</li> </ul>  |  |                   | <input type="checkbox"/> YES | <input type="checkbox"/> NO |
| <ul style="list-style-type: none"> <li>Compensation and/or medical treatments in case of injury?</li> </ul>   |  |                   | <input type="checkbox"/> YES | <input type="checkbox"/> NO |
| <ul style="list-style-type: none"> <li>Who to contact for pertinent questions and/or for assistance in a research-related injury?</li> </ul>                                      |  |                   | <input type="checkbox"/> YES | <input type="checkbox"/> NO |
| <ul style="list-style-type: none"> <li>Refusal to participate or discontinuance at any time will involve penalty or loss of benefits to which the subject is entitled?</li> </ul> |  |                   | <input type="checkbox"/> YES | <input type="checkbox"/> NO |
| <ul style="list-style-type: none"> <li>Extent of confidentiality?</li> </ul>  |  |                   | <input type="checkbox"/> YES | <input type="checkbox"/> NO |

|   |                              |                             |
|---|------------------------------|-----------------------------|
| 2. IS THE INFORMED CONSENT WRITTEN OR PRESENTED IN NON-TECHNICAL LANGUAGE THAT PARTICIPANTS CAN UNDERSTAND? | <input type="checkbox"/> YES | <input type="checkbox"/> NO |
| 3. DOES THE PROTOCOL INCLUDE AN ADEQUATE PROCESS FOR ENSURING THAT CONSENT IS VOLUNTARY?                    | <input type="checkbox"/> YES | <input type="checkbox"/> NO |
| 4. DO YOU HAVE ANY OTHER CONCERNS?  |                              |                             |

**Recommendation:**

- Exempt from Review
- Approved
- Minor Revisions Required

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- Major Revisions Required

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- Disapproved

*Reasons for disapproval:*

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Signature over Printed Name  
of Reviewer

---

Review Date

## **APPENDIX O: COMPOSITION OF THE PHILIPPINE HEALTH RESEARCH ETHICS BOARD**

*(as of August 2017)*

**LEONARDO D. DE CASTRO, PhD**

Philosophy

*Chair*

**MARIA SALOME N. VIOS, MD**

Medicine

*Chair, Committee on Standards and Accreditation*

**RICARDO M. MANALASTAS, JR., MD**

Health Research

*Chair, Committee on Information Dissemination, Training, and Advocacy*

**CARMEN V. AUSTE, MA**

Community

*Chair, Committee on Patient, Family, and Community Engagement*

**CLEMEN C. AQUINO, DPhil**

Social Science

**GEMMA N. BALEIN, DDM**

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**ALBERTO T. MUYOT, LLB**

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*Ex officio Member*

**JAIME C. MONTOYA, MD, MSc, PhD, CESO III**

Philippine Council for Health Research and Development

*Ex officio Member*



## **APPENDIX P: COMPOSITION OF THE NATIONAL ETHICS COMMITTEE**

*(as of August 2017)*

**FILIPINAS F. NATIVIDAD, PhD**

Molecular Biology

*Chair*

**RICARDO M. MANALASTAS, JR., MD**

Clinical Research

*Co-Chair*

**MARILYN R. CANTA, PhD**

Non-scientist

**LEONARDO D. DE CASTRO, PhD**

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**MARITA V. T. REYES, MD**

Health Research

**FELICIDAD H. ROMUALDEZ**

Community Representative

**MA. CARMEN C. TOLABING, MD, MPH**

Epidemiology and Biostatistics

## APPENDIX Q: THE AD HOC COMMITTEE FOR UPDATING THE NATIONAL ETHICAL GUIDELINES

**THE AD HOC COMMITTEE FOR UPDATING THE NATIONAL ETHICAL GUIDELINES** patiently and carefully reviewed and revised the old guidelines, and formulated new ones in order to provide researchers and RECs 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:

|  |  |
|--|--|
| <b>MARITA V. T. REYES, MD</b><br><i>(Chair)</i>        | Member, National Ethics Committee  |
| <b>LEONARDO D. DE CASTRO, PhD</b><br><i>(Co-Chair)</i> | Chair, PHREB   |
| <b>RICARDO M. MANALASTAS, JR., MD</b>                  | Chair, PHREB Committee on Information Dissemination, Training, and Advocacy (CIDTA)    |
| <b>EDLYN B. JIMENEZ, MIRB</b>                          | Coordinator,<br>UP Manila Research Ethics Board (UPM REB)                              |
| <b>ROSARIO ANGELES T. ALORA, MD</b>                    | Member, PHREB CIDTA<br>Head, Bioethics Committee<br>University of Santo Tomas Hospital |
| <b>CECILIA V. TOMAS, MD</b>                            | Member, PHREB Committee on Standards and Accreditation (CSA)                           |
| <b>EVANGELINE O. SANTOS, MD</b>                        | Clinical Associate Professor<br>College of Medicine, UPM<br>Member, PHREB CSA          |

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*Technical Contributor*

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Ms. Michelle Larin

Philippine Health Research Ethics Network  
Philippine Social Science Council  
Philippine Clinical Research Professionals  
International Rice Research Institute  
National Economic and Development Authority - Region II  
National Economic and Development Authority - Region IV-A  
National Economic and Development Authority - Region VIII  
National Economic and Development Authority - Social Development Staff  
Department of Health - Health Policy Development and Planning Bureau  
United Laboratories, Inc., Medical Affairs Division

## GLOSSARY

**Active Principle or Ingredients** – substances in a medicinal preparation that bring about the clinical effects expected; the constituents in a medicinal preparation that exert an effect pharmacologically as distinct from the fillers, wetting agents, and other excipients included in the preparation.

**Adverse Drug Reaction** – all noxious and unintended responses to a medicinal product related to any dose (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). 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; a response to a marketed medicinal product 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-GCP). *See also Adverse Events, Serious Adverse Event, and Suspected Unexpected Serious Adverse Reaction*

**Adverse Events** – any untoward or undesirable medical occurrence in a research participant or patient in clinical investigation after use or administration of an investigational product (ICH-GCP). *See also Adverse Drug Reaction, Serious Adverse Event, and Suspected Unexpected Serious Adverse Reaction*

**AIDS** – or Acquired Immunodeficiency Syndrome; the clinical manifestation 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; may include reflexology, acupuncture, chiropractic, nutritional therapy, and other similar methods (Traditional and Alternative Medicine Act, 1997). *See also Complementary and Alternative Medicine*

**Anonymization** – process of removing the link between the research participant and their personally identifiable data, in such a way that the research participant cannot be traced and determined. *See also De-identified*

**Anonymized Sample or Data** – biospecimen 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 action or decision issued by a regulatory body (e.g., RECs); for REC approval please see The Research Ethics Review Process (page 36).

**Archival Research** – study 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; a requirement for research, in

addition to consent given by a parent or LAR; agreement by an individual not competent to give legally valid informed consent, like a child, to participate in research.

**Assisted Reproductive Technology** – treatment or procedures that include in-vitro handling of human oocytes and human sperm or embryos for the purpose of establishing a pregnancy (e.g., in-vitro fertilization and transcervical embryo transfer, gamete intrafallopian transfer, zygote intrafallopian transfer, tubal embryo transfer, gamete and embryo cryopreservation, oocyte and embryo donation, and gestational surrogacy).

**Autonomy** – the right or power or ability or capacity to govern oneself or make an informed or uncoerced decision.

**Behavioral Genetics** – 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 bio-behavioral mechanisms and social processes that are relevant to public health or disease prevention and promotion, etiology, diagnosis, treatment, and rehabilitation.

**Belmont Report** – statement of basic ethical principles governing research involving human participants published by the National Commission for the Protection of Human Subjects in 1979 on the conduct of biomedical and behavioral research involving human subjects, including guidelines to ensure that research is conducted in accordance with the three identified principles: respect for persons, beneficence, and justice.

**Beneficence** – the ethical principle of protecting persons from harm by maximizing anticipated benefits and minimizing possible risks of harm. *See also Ethical Principles and Benefits*

**Benefits** – any direct or indirect good effect, or something of positive value, from the research study, to the health or welfare to the participants. *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 study to make the estimate of a treatment effect deviate from its true value (ICH-GCP).

**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.

**Biosimilars** – biopharmaceutical product that is similar to a licensed biologic product in terms of quality, safety and efficacy.

**Blinding** – also known as masking, is a procedure in which one or more parties of the study are kept unaware of the treatment assignment(s). Single blinding usually refers to the subjects being unaware which treatment he or she is receiving, while double-blinding usually refers to the subjects, researcher(s), monitor(s), and, in some cases, data analyst(s) being unaware of the treatment assignment(s) (ICH-GCP). *See also Double Blinding*

**Clinical Equipoise** – a state or condition, based on available data, of genuine uncertainty on the part of the researcher(s) and/or a community of medical experts exists regarding the comparative therapeutic merits of each arm in a study.

**Clinical Research Organization** – *See Contract Research Organization*

**Clinical Trial** – a systematic study on pharmaceutical products in human subjects (including research participants 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). *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 Research Ethics Committee** – an REC shared by (common to) several institutions where the volume of research and resources do not make it feasible to have an REC in each institution.

**Comparator (product)** – an investigational or marketed product (i.e., active control), or placebo, used as reference in a clinical trial (ICH-GCP); a pharmaceutical or other product (which may be a placebo) used as a reference in a clinical trials (WHO).

**Compassionate Use** – permission given by the national regulatory authority in particular the FDA, to make investigational new drugs and devices that are not yet approved for marketing, for use of very or terminally ill research participants having no other treatment alternatives.

**Compensation** – payment and/or medical care received or provided to research participants which may include reimbursement for lost earnings, travel costs, and other expenses incurred as a study participant and recompense for injury, inconvenience, and time spent; does not refer to remuneration in exchange for participating in the study. *See Remuneration*

**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.

**Confidentiality** – refers to the protection of personal information and communication related to research participants, by keeping other parties from accessing the information without their consent.

**Conflict of Interest** – circumstance that creates a risk that professional judgments or actions concerning a primary interest (e.g., obtaining scientifically valid results, promoting and protecting the integrity of research, safety and well-being of research participants, etc.) will be unduly influenced by a secondary interest (e.g., personal or financial gain, career advancement, etc.) (adapted from Lo & Fields, 2009).

**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 research participants, collection, and analysis of data, and preparation of application documents to a national regulatory agency; person or organization (commercial, academic, or other) contracted by the sponsor to perform one or more of a sponsor’s trial-related duties and functions (ICH-GCP).

**Control** – standard by which experimental observation are evaluated; group of clinical trial participants who do not receive the drug or treatment being investigated as part of the trial.

**Controlled Trials** – 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 research participants or within research participants.

**Conventional 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 research participant, 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; may be offered prior to sensitive testing (pre-test counseling) and/or after testing (post-test counseling) for comprehensive care.

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

**Debriefing** – process of giving previously undisclosed information about the research project to the participants following completion of their participation in research.

**Deception** – 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** – statement of ethical principles, developed by the World Medical Association (WMA), for medical research involving human subjects, including research on identifiable human material and data.



**De-identification** – removal of elements (e.g., name, birth date, social security number, home address, telephone number, e-mail address, medical record numbers, health plan beneficiary numbers, full-face photographic images, etc.) connected with data which might aid in associating those data with an individual. *See also Anonymization*

**Deoxyribonucleic Acid (DNA)** – fundamental substance of which genes are composed; 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.

**Diagnosis** – procedure or technique used in the identification of a disease or determination of the health status of an individual.

**Direct Benefits** – Gain, advantage, or good effect derived by a research participant immediately or closely arising from the use of an experimental substance or device. *See also Benefits*

**Disapproval** – unfavorable or negative action on a request; for REC disapproval please see The Research Ethics Review Process (page 36).

**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** – termination of participation of a research participant before the completion of all protocol procedures, initiated either by the participant (dropout) or by the researcher for safety or other reasons (withdrawal).

**Domestic Violence** – or domestic abuse; brutality or cruelty committed by one family or household member against another; violent conflict between household members resulting in physical harm, sexual assault, fear, and other vicious action.

**Double Blinding** – experimental method in which neither the participant nor any of the researcher or sponsor staff who are involved in the treatment or clinical evaluation of the participants are aware of the treatment received (ICH-GCP). *See Blinding*

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

**Effectiveness** – degree to which a diagnostic test or treatment produces a desired result in research participants.

**Efficacy** – 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; ability of a treatment modality to produce an effect to alleviate a disease.

**Eligibility Criteria** – list of criteria or conditions that describes both inclusionary and exclusionary factors to guide enrollment of participants into a study. *See Inclusion Criteria and Exclusion Criteria*

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

**Equipoise** – state in which a researcher is uncertain about which arm of a clinical trial would be therapeutically superior for a research participant. *See also Clinical Equipoise*

**Ethical Clearance** – also called ethical approval; a certification that a research proposal has complied with ethical requirements; action of an REC on a research protocol that signifies approval and permission to proceed with the research. *See also Approval*

**Ethics Review** – evaluation of a research protocol by an REC to promote the safety and protection of the dignity of human participants; systematic process by which an REC evaluates a research protocol to determine if it follows ethical and scientific standards for carrying out research on human participants, and assesses protocol compliance with the guidelines to ensure that the dignity, rights, safety and well-being of research participants are promoted.

**Exclusion Criteria** – factors utilized to determine whether an individual is ineligible to participate in a clinical trial or research. *See also Eligibility Criteria*

**Experimental Design** – the study plan that addresses the conceptual framework and enables the researchers to test their hypothesis by reaching valid conclusions about relationships between independent and dependent variables (Key, 1997).

**Family Studies (in genetic research)** – mapping of disease genes through the establishment of genetic linkage within a family.

**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 or unstructured group discussion of 6-12 persons facilitated by a trained professional.

**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.

**Gender** – socially defined feminine or masculine roles, attitudes, and values.

**Gene** – the functional and physical unit of heredity passed from parent to offspring.

**Genetic 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 Counseling** – 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 of developing or transmitting it, and the ways in which it may be prevented or ameliorated.

**Good Clinical Practice (GCP) Guidelines** – an international ethical and scientific quality standard 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 (ICH-GCP).

**Good Laboratory Practices (GLP) Guidelines** – standards and procedures whereby a laboratory achieves a defined consistent, and reliable standard in performing laboratory tests and activities.

**Good Manufacturing Practice (GMP) Guidelines** – 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.

**Guardian** – one who is legally responsible for the care and management of the person or property of an incompetent person or a minor; someone who can make important personal decisions in behalf of another person. *See also Legally Authorized Representative*

**Health Equity** – the absence of systematic disparities in health (or in major social determinants of health) among groups with different levels of underlying advantage or disadvantages (e.g., wealth, power, and prestige).

**Health Research** – research that seeks to understand the impact of health policies, programs, processes, actions, or events originating any sector; to assist in developing interventions that will help prevent or mitigate the impact; and to contribute to the achievement of health equity, and better health for all. *See also Clinical Research*

**Herbal Medicines** – finished, labeled medicinal products that contain, as active ingredient(s), serial or underground part(s) of plant or other materials (e.g., juices, gums, fatty oils, essential oils, and other substances of this nature) or combination thereof, whether in the crude state or as plant preparations (TAMA 1997); medicines containing plant material(s) combined with chemically defined active substances, including chemically defined isolated constituents of plants, are not considered herbal medicines.

**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 Test** – immunology-based laboratory test that establishes the presence of HIV infection in an individual.

**Homeopathy** – 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.

**Human Subjects** – *See Research Participants*

**Human Zygote** – *See Zygote*

**Hypothesis** – tentative explanation for an observation, phenomenon, or scientific problem that can be tested by further investigation.

**Incapacity** – a person's mental status and means that signifies the 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.

**Inclusion Criteria** – factors used to judge a participant's eligibility to participate in a research. *See also Eligibility Criteria*

**Identifiable Personal Information** – information on a particular person who expects that such information shall be held in privacy (e.g., culture, age, religion and social status, as well as their life experience and educational, medical, family, relationship, or employment histories).

**Indigenous Cultural Communities (ICCs)** – *See Indigenous Peoples*

**Indigenous Knowledge (IK)** – the information base for a society, which facilitates communication and decision-making (Flavier et al., 1995); the local knowledge – knowledge that is unique to a given culture or society.

**Indigenous Herbal Medicines** – herbal preparations used in a local community or region and is very well known through long usage by the local population in terms of its composition, treatment, and dosage.

**Indigenous Peoples (IP)** – group of people or homogenous societies identified by self-ascorption and ascription by others, who have continuously lived as organized community on communally bounded and defined territory, and who have, under claims of ownership since time immemorial, occupied, possessed and utilized such territories, sharing common bonds of language, customs, traditions and other distinctive cultural traits, or who have, through resistance to political, social and cultural inroads of colonization, nonindigenous religions and cultures, became historically differentiated from the majority of Filipinos (IPRA 1997).

**Indirect Benefits** – positive effects that may not immediately be derived from the participation of a research participant in a study (e.g., contributing to knowledge, sharing

ones experiences to benefit others, feelings of altruism and usefulness). *See also Benefits and Direct Benefits*

**Information in the Public Domain** – data or information available and open to public observation (e.g., list of names in the telephone directory, or events in streets and public transportation).

**Informed Consent** – a decision to participate in research, made 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 (adapted from CIOMS, 2009).

**Informed Consent Process** - manner of obtaining agreement from a potential research participant to take part in an investigative study, or from a patient to undergo a medical intervention, including written and/or verbal means, as approved by an REC.

**Informed Consent Form** – written documentation of an informed consent that contains the essential information (see page 11) regarding a study or medical intervention and is signed by the research participant, patient, or LAR whichever is applicable.

**International Collaborative Research** – joint or shared conduct of research by at least two countries or governments (e.g., Philippines and one other foreign government or country). See Ethical Guidelines for International Collaborative Research (page 170).

**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** – research that includes measures or technology to improve health or condition of an individual or a group of individuals or purposely change the course of the disease.

**Invasive Procedure** – sampling using a method involving intrusion into the human body (e.g., obtaining a blood sample by using a needle and syringe) (UNESCO, 2004).

**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 a 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-GCP).

**Investigator** – a person responsible for the conduct of the clinical trial at a trial site (ICH-GCP). *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; principle that refers primarily to

distributive justice, which requires the equitable distribution of both the burdens and the benefits of participation in research requiring fairness in distribution of burdens and benefits. *See also Ethical Principles*

**Legally Authorized Representative** – an individual who can, in accordance with the law, provide consent on behalf of the research participant who is incapable of giving or who has diminished capacity to give informed consent. *See also Guardian*

**Legitimate Purpose** – a principle which states that the processing of information shall be compatible with a declared and specified purpose which must not be contrary to law, morals, or public policy (Data Privacy Act of 2012 IRR).

**Medical Device** – instrument, apparatus, implement, machine, invention, implant, in vitro reagent, or other article, intended to affect the structure or function of the body, for diagnosis, treatment, or prevention of disease, but does not function through chemical action within or on the body. *See also Medical Device*

**Medical Member** – an REC member who has education and training related to the medical sciences (e.g., physicians, dentists, therapists, etc.). *See also Scientist Member*

**Minimal Risk** – a classification of risk in research 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.

**Minors** – persons who have not yet reached the age of majority which is 18 years old in the Philippines (Act Lowering the Age of Majority from 21 to 18 or RA 6809).

**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 GCP for Trials of Pharmaceutical Products).

**Monitoring** – the act of overseeing the progress of a clinical trial, and of ensuring that it is conducted, recorded, and reported in accordance with the protocol, SOPs, GCP, and the applicable regulatory requirement(s) (ICH-GCP).

**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** – clinical trial conducted according to a single protocol but at more than one site, and therefore, carried out by more than one investigator (ICH-GCP).

**Mutagenicity** – capacity of a chemical or physical agent to cause genetic alterations.

**Nanomedicine** – 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 (a nanometer is one-billionth of a meter), where unique phenomena enable novel applications.

**National Healthcare Delivery System** – the country’s total structures both private and public organizations, agencies, and individuals, including policies and mechanisms, which provide healthcare to individuals and communities.

**National Unified Health Research Agenda (NUHRA)** – an evolving document, based from continuous regional and national consultations with stakeholders, which serves as the template for health research and development efforts in the Philippines.

**Non-disclosure of Data** – the withholding of or restriction of access to 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** – the principle that proscribes the deliberate infliction of harm on persons.

**North-South Research Collaboration** – the relationship or interaction between the developed and developing countries or rich and poor countries.

**Nuremberg Code** – a code of ethics in research containing 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.

**Participatory Research** – research that involves the participation of the researcher 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.

**Peer Review** – examination of the research design and methodology of a research by expert(s) in the same field or similar level of expertise.

**Pharmacodynamics** – refers to the relationship between drug concentration at the site of action and the resulting effect, including the time course and intensity of therapeutic and adverse effects.

**Pharmacogenetics** – field of biochemical genetics concerned with drug responses due to genetically controlled variations.

**Pharmacokinetics** – study of the time course of drug absorption, distribution, metabolism, and excretion.

**Phase I Clinical Trial** – 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 research participants for safety and, in some cases, early evidence of effectiveness.

Phase I studies can involve one or a combination of the following (Guidelines on General Considerations for Clinical Trials (ICH-E8). Published in the Federal Register on December 17, 1997 (62 FR 66113)). US Department of Health and Human Services, Food and Drug Administration):

- a) Estimation of Initial and Safety Tolerability
- b) Pharmacokinetics – assessing the drug’s absorption, distribution, metabolism and excretion either a separate study or part of an efficacy, safety and tolerability
- c) Pharmacodynamics – to provide an estimate of the activity and potential efficacy and may guide the drug’s dosage and dose regimen
- d) Early measurement of drug’s activity

**Phase II Clinical Trial** – consists of controlled clinical trials designed to demonstrate efficacy and relative safety of the investigative new drug. Normally, these are performed on a limited number of closely monitored 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).

Some innovative pharmaceutical companies have added an additional layer called Phase Ib/Ila before proceeding to Phase II. The former 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 establish the pharmacokinetics of multiple doses of the drug and monitor any effects on biological markers of disease activity.

**Phase III Clinical Trial** – trial(s) in larger (and possibly varied) research participant 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. This is performed after a reasonable probability of a drug’s effectiveness has been established. These trials should preferably be of a randomized double-blind design, but other designs may be acceptable (e.g., long-term safety studies).



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). Generally, the conditions under which these trials are carried out should be as close as possible to normal conditions of use (WHO).

**Phase IV Clinical Study** – research conducted after the national drug registration authority (i.e., FDA) has approved a drug for distribution or marketing. This phase is carried out on the basis of the product characteristics on which the marketing authorization was granted and is normally in the form of 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 normally considered as trials for new pharmaceutical products (WHO).

**Philippine Health Research Ethics Board** – the national policymaking body on health research ethics, created under DOST Special Order No. 091, which is mandated to ensure that all phases of health research shall adhere to the universal ethical principles that value the protection and promotion of the dignity of health research participants.

**Philippine National Health Research System** – framework anchored on the principles of Essential National Health Research on inclusiveness, participation, quality, equity, efficiency and effectiveness, which connect to, and converge with, the wider health, economic, political, educational, and science and technology systems of the Philippines (PNHRS Act).

**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 may be an inactive pill, liquid, or powder that has no treatment value.

**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.

**Principal Investigator** – the chief or person primarily responsible for the implementation of a research project or clinical trial. *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, claim, state, ability, or condition of an individual, group, or institution to conceal, seclude, hide themselves or information about themselves and thus reveal or expose

themselves selectively; a conceptual space defining the individual's boundary as a person, intrusion of which is limited by human rights and by law.

**Product Adulteration** – presence of foreign substances or impurities in the drug preparation that results in dilution or loss of its efficacy.

**Proportionality** – principle which states that the processing of information shall be adequate, relevant, suitable, necessary, and not excessive in relation to a declared and specified purpose (Data Privacy Act of 2012).

**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** – document that describes the objective(s), design, methodology, statistical considerations, and organization of a research (ICH-GCP); the definitive document of the research or study that provides guidance for those who will conduct the research, reference for evaluators and reviewers, template for validation, substantiation for intellectual property claims, and legacy of the proponent.

**Protocol Amendment** – 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 begun.

**Psychosocial Needs** – the needs of an individual pertaining to her social and psychological well-being.

**Quality of Life** – state or condition wherein an individual is able to live as how one normal person wants to live his or her life.

**Quasi-experimental Design** – a research design, like an experimental design, but does not make use of random assignment to groups,

**Randomization, Random Assignment** – process of assigning research participants to treatment or control groups using an element of chance to determine the assignments in order to reduce bias (ICH-GCP).

**Remuneration** – payment for participation in research. *See also Compensation*

**Reportable Negative Events (RNEs)** – experiences of researchers that involve personal safety issues (related to both research and research participant) in the conduct of research, such as sexual harassment, physical threats, stalking, and other hostile reactions.

**Reportability (of test results)** – the inclusion of an event (e.g., a diagnosis, evidence of violence against persons, etc.) in a list of items that are mandated by law to be reported to

the DOH 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** – an activity that aims to develop or contribute to knowledge that can be generalized (including theories, principles, relationships), or any accumulation of information using scientific methods, observation, inference, and analysis.

**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** – the primary subjects of a study; individuals who participate in a clinical trial, either as recipients of the investigational product(s) or intervention, or as control (ICH-GCP).

**Respect for Persons** – ethical principle which emphasizes the protection of the autonomy of all people and treating them with courtesy and respect and allowing for informed consent.

**Respondent** – person or group of persons answering or replying to research questions or providing the data that are collected during the research. *See also Research Participants.*

**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. *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*

**Scientist Member** – an REC member who has education, training, or extensive experience in the sciences.

**Serious Adverse Event (SAE)** – 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 in research participant or prolongation of hospitalization, causes significant disability, incapacity, and congenital anomaly or another episode which is considered a significant hazard to the participant.

**Side Effect** – undesired effect of a treatment which is either immediate or long-term.

**Sponsor** – an individual, company, institution, or organization which takes responsibility for the initiation, management, and/or financing of a clinical trial.

**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.

**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.

**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)** – serious adverse reaction in research participants who were given a drug, which 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. *See also Adverse Drug Reaction and Adverse Events*

**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 researcher(s).

**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.

**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.

**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 disorders (TAMA 1997).

**Traditional Healer** – the relatively old, highly placed, respected person in the community, with a profound knowledge of traditional remedies (TAMA 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 (TAMA 1997).

**Traditional Medicine Expert** – healthcare provider employing traditional medicine modalities to cure disease.

**Transparency** – principle which states that the data subject must be aware of the nature, purpose, and extent of the processing of his or her personal data, including the risks and safeguards involved, the identity of personal information controller, his or her rights as a data subject, and how these can be exercised; and that any information and communication relating to the processing of personal data should be easy to access and understand, using clear and plain language (Data Privacy Act 2012).

**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.

**United Nations Declaration of Rights of Indigenous Peoples (UNDRIP)** – a statement adopted by the UN General Assembly which affirms 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.

**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).

**Vulnerability** – the state of being relatively or absolutely incapable of deciding for oneself whether or not to participate in a study, for reasons such as physical and mental disabilities, poverty, asymmetric power relations, and marginalization, among others.

**Vulnerable Persons or Groups** – individuals or groups which require special protection because of certain characteristics or situations that render them relatively or absolutely incapable of deciding for themselves whether or not to participate in a study.

**Western medicine** – or biomedicine, allopathy, regular medicine, conventional medicine, mainstream medicine, orthodox medicine or cosmopolitan medicine. *See Conventional Medicine*

**Zygote** – the product of the biological union of the human sperm and egg (process of fertilization).

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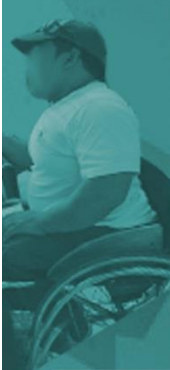
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