NATIONAL ETHICAL GUIDELINES

FOR RESEARCH INVOLVING HUMAN PARTICIPANTS

2022

PHREB PNHRS

NATIONAL ETHICAL GUIDELINES
FOR RESEARCH INVOLVING HUMAN PARTICIPANTS
2022

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

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PHREB Resolution No. 001
Series of 2022

R E S O L U T I O N

APPROVAL OF THE "2022 NATIONAL ETHICAL GUIDELINES FOR RESEARCH INVOLVING HUMAN PARTICIPANTS"
***AD REFERENDUM* DATED MARCH 1, 2022**

Following 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.

COGNIZANT that the National Ethical Guidelines for Health and Health Related Research needs to be updated regularly to adapt to scientific, technological, and social advancements, and changes in international guidelines as well as comparable national documents;

MINDFUL of the need to provide more specific guidance in the areas of social research, internet research, research on disaster, calamities, epidemic or complex emergencies and health policy and systems research;

CONSIDERING the continuing rapid developments in health and health-related science, technology, innovation, and the social sciences; and

PROMOTING respect for the rights and welfare of all individuals and communities involved as participants in health and health-related social science research;

The Philippine Health Research Ethics Board hereby:

APPROVES and PROMULGATES these guidelines, *Ad Referendum*, which shall be known as the **2022 NATIONAL ETHICAL GUIDELINES FOR RESEARCH INVOLVING HUMAN PARTICIPANTS;**

DIRECTS the PHREB Secretariat to cause the publication of the NEGRIHP 2022 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 March 1, 2022.

PHILIPPINE HEALTH RESEARCH ETHICS BOARD

SONIA E. BONGALA, MD

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LEONARDO D. DE CASTRO, PhD

PHREB Resolution No. 002
Series of 2022

R E S O L U T I O N

RECOGNIZING 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 for Health and Health Related Research 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 04 January 2021, with Dr. Ma. Salome N. Vios as the Chair, Dr. Ricardo M. Manalastas, Jr. as Vice-Chair, and the following as members: Dr. Carl Abelardo Antonio, Dr. Roland Panaligan. Dr. Ruben Mendoza, and Prof. Edlyn Jimenez;

WHEREAS, the Ad Hoc Committee has completed its draft and the Philippine Health Research Ethics Board (PHREB) has examined, deliberated over, amended and approved the 2022 National Ethical Guidelines for Research Involving Human Participants (NEGRIHP);

WHEREAS, the PHREB recognizes the dedication, thoroughness, and perseverance of the Ad Hoc Committee in putting the 2022 NEGRIHP together, engaging in extensive consultations, and completing the document for final approval;

The Philippine Health Research Ethics Board hereby:

CONVEYS its sincere gratitude and appreciation to the Ad Hoc Committee for completing the draft revision of the National Ethical Guidelines and successfully concluding its task.

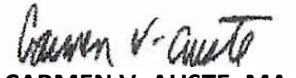
APPROVED, on March 1, 2022.

PHILIPPINE HEALTH RESEARCH ETHICS BOARD

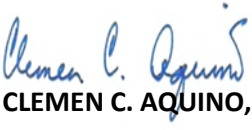
SONIA E. BONGALA, MD

GEMMA N. BALEIN, DDM

ALBERTO T. MUYOT, LLM



CARMEN V. AUSTE, MA



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JAIME C. MONTOYA, MD, MSc, PhD, CESO II

LEONARDO D. DE CASTRO, PhD

FOREWORD

The term "Human Research Participant" in this document reflects the multiple human dimensions that are highlighted in the definition of health by the World Health Organization (WHO) as "a state of complete physical, mental and social well-being and not merely the absence of disease or infirmity." Being true to the WHO definition of health, the 2022 National Ethical Guidelines for Research Involving Human Participants (NEGRIHP) does not shy away from providing ethical guidance for social research and other studies that relate to the broad understanding of human health. This revision makes abundantly clear the recognition that much of social research has to do with the human participant's physical, mental, and social well-being.

Human participants obviously need protection in studies other than those that fall under the limited scope of biomedical research. The risks involved in social research can be great and research protocols should be subjected to ethical scrutiny just as in other forms of human research. In the NEGRIHP, the Philippine Health Research Ethics Board (PHREB) reaffirms its commitment to the protection of vulnerable human participants by complying with the legal mandate contained in the Philippine National Health Research System Law (PNHRS Law): "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." The NEGRIHP also takes note of the Implementing Rules and Regulations of the PNHRS Law, which defines health as the "optimal state of physical, mental and social well-being and the ability to function at the individual level."

Today's human research participant is exposed to increasingly exploitative circumstances. Driven by powerful consumer-oriented market forces, technological advances pose double-edged challenges. The benefits beckon with disarming irresistibility while risks lurk in the background, hardly palpable to the ordinary person. For example, online and social media research often appear friendly and innocent while subtly being dismissive of the most basic of human right – privacy, confidentiality, and the right to choose. In the context of the COVID-19 pandemic, online and social media have been used extensively for recruitment, consent taking, alternative

documentation, polls, surveys, data gathering, and other research procedures. Some have deliberately used the pandemic as an excuse for sidestepping basic human rights, albeit unjustifiably. As a consequence, vulnerabilities in human research participants have been magnified.

The 2022 NEGRIHP should be understood as a document that seeks to protect the most vulnerable of human research participants in all areas of research that relate to their health, and in the context of existing and emergent challenges that face all research stakeholders. Leading up to the completion of this document, the Ad Hoc Committee conducted the broadest consultation possible within the time that it was given. In the process, it engaged the assistance of experts in various fields of medicine, social and behavioral sciences, law, information and communications technology, bioethics, religion, and philosophy while also listening to lay persons, community representatives, indigenous populations and other ethnic groups, representatives of government agencies, and everybody who wanted to contribute. As in similar undertakings, some recommendations could not fully be accommodated because of differences with positions that exhibit greater coherence with the concerns addressed in the entirety of the Guidelines, because a higher priority has had to be given to a competing position, or because the recommendations could not fully be aligned with the imperative to protect the human research participant in studies covered by the broad WHO definition of health and the PNHRS iteration. In any case, the comments, suggestions, and recommendations all deserve everyone's gratitude as each contributed significantly to the process of putting ideas in proper perspective and arriving at the finished product a guidance document that is dedicated to the most vulnerable of human research participants. Human research participants should ultimately be regarded as human research partners and we hope the 2022 National Ethical Guidelines for Research Involving Human Participants puts us well on the way to making that a reality.

PROF. LEONARDO D. DE CASTRO, PhD
Chair, PHREB

MESSAGE

The Department of Science Technology - Philippine Council for Health Research and Development (DOST-PCHRD) expresses its gratitude to the Philippine Health Research Ethics Board (PHREB) for being a reliable partner in ensuring the ethical conduct of health and health-related research in the country.

For the scientific community, the recent years have been outlined by fast-changing demands, extraordinary challenges, and remarkable progress. The emergence of COVID-19 in 2020 brought about the urgent need for health solutions and prompt decision-making from health leaders across the globe. While we, health researchers, must immediately respond to these calls, it is also part of our duty to ensure that the actions we take always adhere to universal principles of the protection of human participants in research.

As the national policy-making body in health research ethics in the country, the PHREB is mandated to guide the Philippine health research community towards the ethical conduct of research, especially amid the global health crisis. The PHREB ensures this by regularly updating the National Ethical Guidelines for Health and Health-related Research. This year, the Board is launching the 2022 National Ethical Guidelines for Research Involving Human Participants, with additional and updated sections to serve as necessary guidance to researchers in conducting research in the new normal. The Council is certain that these updated guidelines will enable streamlined health research processes and contribute to higher quality health research in the country.

Mabuhay ang PHREB!

JAIME C. MONTOYA, MD, MSc, PhD, CESO II
Executive Director, DOST-PCHRD

MESSAGE

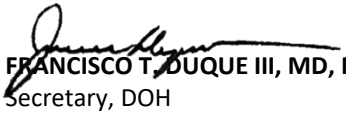
It is with great gratitude that I congratulate the Philippine Health Research Ethics Board for the publishing of the National Ethical Guidelines for Research Involving Human Participants!

Health has been a vital factor of a country's advancement since time immemorial. As we navigate through the reverberations caused by the COVID-19 pandemic, innovation in all aspects of public health is of utmost importance. This elevation trickles down to the research, evidence, and data on which certain implementations are based upon — even more reason why our focus is navigated through scientific basis and experience. With the various developments in the international and local health fields, it is essential to recognize that these changes are always for the benefit of the Filipino people, especially those who immensely participate in the process of research and development.

The Philippine Health Research Ethics Board upholds the perseverance that the entire organization puts to place for the guidelines to which research and technological advancements are rooted from. By providing ethical change to the community, the organization improves the quality of the Filipino life-giving assurance that the research caters to the needs of both the Filipino people and the public health sector. The Department of Health (DOH) recognizes the leadership it holds when it comes to spearheading the country to a people-centered health system through Universal Health Care. Given this, a vital component of the mission is to collaborate with stakeholders that envision a similar perception. Further, the utilization of both national and international networks to provide the most benefit to the research innovations of the country continuously supply sustainability to the entire health system. Further, through our combined accomplishments, a unified Philippine health system will be achieved.

On this note, the DOH will ceaselessly continue to support the organization in all its future endeavors. Once again, on behalf of the Department, I would like to congratulate the Philippine Health Research Ethics Board for yet another milestone that is conducive to the betterment of the public health system. May your perseverance, passion, and purpose reach milestones in the coming years.

Maraming salamat at mabuhay tayong lahat!



FRANCISCO T. DUQUE III, MD, MSc
Secretary, DOH

MESSAGE

My warmest felicitations to the Philippine Health Research Ethics Board (PHREB) as it publishes a new version of the National Ethical Guidelines for Health and Health-Related Research (NEGHHR).

Research plays an important role in society because it generates new knowledge. In particular, health research can provide important information about disease trends and risk factors, outcomes of treatment or public health interventions, functional abilities, patterns of care, healthcare costs and use, and a lot more. It is important to help improve health care services, which contributes to improving the health of the people.

I am therefore confident that this publication will respond to changes in the health research landscape since the last revision of the Guidelines in 2017.

I encourage administrators, faculty, researchers and educators to 1.) proactively continue to be keener in pursuit for innovative, required, and somewhat disruptive processes to improve it and to be at par with those globally competitive institutions and; 2.) to reflect on how they will tailor their programs or projects in order to focus on our society's particular problems and obtain the results they seek. May this publication provide wide-ranging discussions and information where ideas and trends on various fields co-create a sustainable future for all of us.

Together, let us work to develop quality and innovative research that can improve the lives of millions of Filipinos.

Congratulations and Mabuhay!

J. PROSPERO E. DE VERA III, DPA
Chairman
Commission on Higher Education

MESSAGE

As the Philippines' leading health research university, UP Manila conducts integrative and collaborative basic, applied, and clinical research and development on the health sciences that contribute to generating knowledge and technologies and shaping national policies and programs. Integral to the fulfillment of this task is its mandate to engage in research in an ethical, trustworthy, and responsible manner.

We commend the Philippine Health Research Ethics Board (PHREB) for its vigilant and sustained efforts to come up with relevant, updated, and harmonized guidelines for the conduct of health researches in the country.

As one of the implementing institutions of the Philippine National Health Research System, UP Manila is in solidarity with the PHREB in its efforts to strengthen strategies and initiatives in research ethics review. This is being done through the UP-Manila Research Ethics Board (UPMREB) that integrated research ethics units in the university and the restructured Research Grants and Administration Office (RGAO) that mandates and facilitates applicable ethics approval for all health research conducted by UP Manila personnel.

I thank the PHREB for leading anew the revision and publication of this manual retitled "National Ethical Guidelines for Health and Health-related Research that was retitled "National Ethical Guidelines for Research Involving Human Participants" for the 2022 edition. With the country still battling the COVID 19 pandemic, the revised guidelines adhere and align well with national and international standards and guidelines for the conduct of research amid the crisis. The revised guidelines will facilitate greatly UP Manila's continuing 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 NEGRIHP 2022

The 2022 NEGRIHP has 28 sections. The NEGRIHP is divided into two major chapters: (1) General Guidelines on ethical review of research protocols and (2) Special Guidelines arranged as specific research areas, populations, and methodology.

Twenty appendices (A to W) are provided in these Guidelines. Appendices A and B are excerpts from the Philippine National Health Research System (PNHRS) 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 memoranda related to ethics review of research involving human participants. Appendix E is the workflow for REC-NCIP review of protocols involving IPs. Appendices F, G, and H provide the guidelines and policies for accreditation of RECs as well as the recommended content and format of their SOPs. Appendices I, J, and K are sample templates for the application of ethics review and writing of research proposals respectively. Appendices L, M, N, O, P, Q, and R are sample templates of documents relevant to the review of research (i.e., Worksheet for Protocol Assessment, worksheet for social research, and ICF Checklist Assessment), and informed consent and assent forms. Lastly, Appendices S, T, U, V, W show the composition of PHREB, NEC, Ad Hoc Committee, List of Contributors, and Acknowledgements.

The readers need to familiarize themselves with the General Guidelines (pages 13-82), 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, internet research), are fully described in the Special Guidelines respectively. The Special Guidelines complement those in the General Guidelines and should not be considered 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, “A dissemination plan for the study results shall be included in the protocol. Dissemination is essential to achieving

social value" In the Elements of Research Ethics can be cited as (NEGRIHP 2022, Elements of Research Ethics, Guideline 4)

- The provision, "The Rules and Regulations Governing Accreditation of Facilities Engaging in Human Stem Cell Research and Cell-based Therapies (DOH 2013-12) categorize aborted human fetal cells and their derivatives for human treatment and research is prohibited" in Research on Stem Cell and Cell-based Therapy can be cited as (NEGRIHP 2022, Research on Stem Cell and Cell-based Therapy, Guideline 11).

The technical terms defined in the Glossary must be understood and used in the context of the specific provisions in the 2022 NEGRIHP. 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.

For questions, please contact:

The PHREB Secretariat
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INTRODUCTION

Every five years or so, the Philippine Health Research Ethics Board (PHREB) updates the National Ethical Guidelines for Research as part of its mandate based on the PNHRS Act (RA 10532). 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 (NEGHHR 2017)." Thus, an Ad Hoc Committee was once again convened in December 2020 to draft the 2022 edition. The core members of this committee are Dr. Carl Antonio, Prof. Edlyn Jimenez, Dr. Roland Panaligan, Dr. Ricardo Manalastas, Dr. Ruben Mendoza, and Dr. Salome Vios with Dr. Rosario Angeles T. Alora, Dr. Leonardo D. de Castro, Dr. Marita V. T. Reyes, and Dr. Cecilia V. Tomas as technical advisers. Topic experts (*see List of Contributors*) were invited to prepare the working drafts. Dr. Rowena Genuino served as a copy editor. The draft of the 2022 NEGRIHP underwent several reviews by stakeholders including a general public consultation (November 4 to December 2, 2021) before it was finalized. It must be mentioned that the PHREB Secretariat, composed of Angeline Abad, Daphne Joyce Maza, and Pamela Miranda, did wonderful work in putting together all the drafts. I take this opportunity to thank all those who lent their time and expertise in making the 2022 edition meaningful to the research stakeholders.

The definition of research, health, and research involving human participants, was revisited. The Ad Hoc Committee reiterated the definition of research and health as defined in the PNHRS Act (*see section on Elements of Research Ethics*). The Introduction to the 2017 edition, summarizes 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." Health, on the other hand, as defined in the PNHRS is a state of optimal physical, mental, and social well-being and the ability to function at the individual level. This aligns with the WHO definition of health, which is the "state of state of complete physical, mental, and social well-being and not merely the absence of disease or infirmity." Likewise, research involving human participants, as defined by the Declaration of Helsinki (2013), include any social science, biomedical, behavioral, or epidemiologic activity that does not only involve direct interaction of the researcher with

an individual or groups of individuals but also includes research using identifiable human materials and data. With the broad definitions of these terms, the 2022 national guidelines make it more encompassing in scope.

The most noticeable change in the 2022 edition of the National Ethical Guidelines is in the title: from ***National Ethical Guidelines for Health and Health-Related Research (NEGHHR)*** to ***National Ethical Guidelines for Research Involving Human Participants (NEGRIHP)***. The new title makes the guidelines more inclusive of all types of research involving human participants and resolves the issue often raised on whether "non-health" research needs to undergo ethics review as long as it involves human participants.

In one of the meetings of the Ad Hoc Committee, the members reflected on how social realities impact not only health research but research in general, and the role played by social science research in promoting social change and the well-being of individuals. When outcomes of research are applied to the real world without considering its social context, the potential beneficiaries may deem the research outcomes irrelevant and will not appreciate the extent of research work that was done. The importance of social research in health is well recognized. However, health is just one of the disciplines, which include economics, environmental science, genetics, psychology, anthropology, and education, where social research plays a major role in advancing the disciplines. There are obvious gaps identified in the guidance for ethics review of social research. Thus, the Ad Hoc Committee widened the scope of the section on Health-related Social Research to Ethical Guidelines for Social Research.

The updating of the 2022 NEGRIHP took place amid the raging COVID-19 pandemic that exposed the vulnerabilities of health care and research systems of countries and exacerbated the inequities throughout the world. The pandemic gave rise to new ethical challenges in research in the country. The demand for a timely, rapid, and quality review of protocols for new vaccines and therapies, the application of online platforms during the review process by RECs, the use of placebo versus EUA (Emergency Use Authorization) vaccines as the control group in vaccine trials, and the inclusion of pregnant women and children early on in vaccine trials were just some of the ethical challenges posed by the pandemic. The section on Research Involving Populations in Disaster Situations has been extensively

revised to address the ethical challenges in research during calamities and other types of emergencies.

The Ad Hoc Committee members were also mindful of ethical issues in the use of emerging technologies in biomedical, health, and social sciences research; in particular, the use of the internet and digital tools. Maintaining privacy and confidentiality in the movement of data from the participant to the internet server to the researcher and sometimes to third parties has become a source of great concern for researchers and RECs. The sections on the Elements of Research Ethics and Internet Research have been revised to guide research stakeholders to adequately meet the requirements of the Data Privacy Act of 2012. In addition, the section on Research on Emerging Technologies has been updated with the addition of a part on artificial intelligence and virtual reality to address ethical issues in the use of artificial intelligence and virtual reality as a research tool or as a research topic in themselves.

The DOST reported that the Philippines' 1990–2015 Millennium Development Goals (MDG) "only made some progress" (https://www.dost.gov.ph/knowledge-resources/news/59-infographics/infographics-2015/1393-millennium-development-goals.html). The country adopted anew a set of goals known as the 2015–2030 Sustainable Development Goals (SDGs), which the UN and its member states have endorsed. The goals that SDGs set are those that the country must attain to ensure the well-being of its citizenry by 2030. The conveners recognize that "ending poverty and other deprivations must go hand-in-hand with strategies that improve health and education, reduce inequality, and spur economic growth – all while tackling climate change" (https://sdgs.un.org/goals). Furthermore, for countries to meet the SDGs, it is proposed that global partnership is a key to its success. Institutions, whether government or non-government, therefore, need to craft policies and institute programs that are evidence-based, sustainable, and collaborative. The updates that are contained in the 2022 NEGRIHP are indeed timely in providing ethical guidance in the conduct of various types of research to address the gaps in the various domains of the SDGs whether it be research on infectious diseases, non-communicable diseases, environmental research, social research, or health economics. The sections on Guidelines for Health Policy and Systems Research and Research on

Health Economics and Outcomes Research are new sections in the National Ethical Guidelines that will assist policy makers and program developers in their research protocol development and provide RECs guidance to evaluate proposals in these areas. Guidelines for international research, women's concerns in clinical trials, gender issues, and ethical issues in community engagement including research on indigenous peoples have been substantially updated.

In recent years more and more research and academic institutions around the country, whether they conduct research that are health-related or not, have seen the value of ethics review as part of quality assurance in their research work. PHREB hopes that the 2022 NEGRIHP will be a useful tool for researchers, RECs, and other research stakeholders in their research endeavors to ensure protection of human participants and integrity of data.

Ma. Salome N. Vios

MARIA SALOME N. VIOS, MD
Chair
Ad hoc Committee for Updating of the National Ethical Guidelines for Health and Health-Related Research

LIST OF ACRONYMS

ACCSQ-MDPWG	ASEAN Consultative Committee on Standards and Quality — Medical Device Product Working Group
ACC	ASEAN Cosmetic Committee
ACM	Association for Computing Machinery
ADAP	Alzheimer's Disease Association of the Philippines
AI	artificial intelligence
AIDS	acquired immune deficiency syndrome
AFP	Armed Forces of the Philippines
AO	Administrative Order
ART	assisted reproductive technology
ARV	antiretroviral
ASA	Association of Social Anthropologists of the UK and the Commonwealth
CARE	CAse REports Checklist
CDRRHR	Center for Device Regulation, Radiation Health and Research
CHED	Commission on Higher Education
CIOMS	Council for International Organizations of Medical Sciences
CBD	Convention on Biological Diversity
COP	Compliance Officer for Privacy
COPE	Committee on Publication Ethics
COI	conflict of interest
CRO	Clinical Research Organization or Contract Research Organization

CV	curriculum vitae
DA	Department of Agriculture
DPA	Data Privacy Act
DPO	Data Protection Officer
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
ELBW	extremely low birth weight
EO	Executive Order
ESOMAR	European Society for Opinion and Market Research
FDA	Food and Drug 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
HEOR	health economics and outcomes research
HPSR	health policy and systems research
HIV	human immunodeficiency virus
HPTN	HIV Prevention Trials Network
HTA	health technology assessment

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
IHBSS	Integrated HIV Behavioral and Serologic Surveillance
IKSPs	Indigenous Knowledge System and Practices
IPs/ICCs	indigenous peoples/indigenous cultural communities
IPOPHL	Intellectual Property Office of the Philippines
IPRA	Indigenous Peoples' Rights Act
IRR	implementing rules and regulations
ISPOR	Professional Society for Health Economics and Outcomes Research (formerly, the International Society for Pharmacoeconomics and Outcomes Research)
IUI	intrauterine insemination
IVD	in vitro diagnostic
KFPE	Commission for Research Partnerships with Developing Countries
LAR	legally authorized representative
LBW	low birth weight

LUA	limited use agreement
MARP	most-at-risk-population
MMSE	mini-mental state examination
MOA	memorandum of agreement
MOU	memorandum of understanding
MSM	men who have sex with men
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
NOAEL	no observed adverse effect level
NPC	National Privacy Commission
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
PPTCT	prevention-of-parent to child transmission
PSREI	Philippine Society of Reproductive Endocrinology and Infertility
PWD	persons with disabilities
PWIDs	persons who inject drugs
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
SJREB	Single Joint Research Ethics Board
SOP	standard operating procedure
SUSAR	suspected unexpected serious adverse reactions
TAMA	Traditional and Alternative Medicine Act
TGW	Transgender women
THAC	traditional and alternative health care
TM	traditional medicine

TWG	technical working group
UHC	universal health coverage
UNDRIP	United Nations Declaration on the Rights of Indigenous Peoples
UNESCO	United Nations Educational, Scientific and Cultural Organization
UPM	University of the Philippines Manila
UPM REB	University of the Philippines Manila Research Ethics Board
V-AR	virtual and augmented reality
VLBW	Very low birth weight
WHO	World Health Organization

GENERAL GUIDELINES

ELEMENTS OF RESEARCH ETHICS

The Philippine Health Research and Ethics Board, consistent with the PNHRS Act 10532 and for the purpose of this guideline, defines health as a state of optimal physical, mental, and social well-being and the ability to function at the individual level. Furthermore, research in relation to health shall refer to the development of knowledge to understand health challenges and mount an improved response to them. This covers the full spectrum of research in five generic areas of activity:

(1) measuring the problem
(2) understanding its cause(s)
(3) elaborating solutions
(4) translating the solutions or evidence into policy, practice, and products
(5) evaluating the effectiveness of solutions

From the above definition of health research, the 2017 edition of the National Ethical Guidelines for Research defined health research based on its objectives that seek 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. Health-related research, on the other hand, are those 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. Furthermore, health as defined by the PNHRS is consistent with the WHO definition of health which is a state of complete physical, mental, and social well-being and not merely the absence of disease or infirmity. This broad definition of health makes the 2022 edition more inclusive to all types of research involving human beings.

An ethical assessment of health and social research requires a framework consisting of principles, values, and key procedures. This framework should be well-defined and clearly stated in a research proposal. 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 contribution 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 the 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. Overall, the methodology, including the study design, environment and participants, instruments/tools, data gathering/collection procedures, and analysis, should be able to generate information or knowledge 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. An informed consent, to comply with these ethical guidelines, is a competent participant's decision to take part in research after receiving and understanding complete and relevant information about the study as well as their rights, without having been subjected to coercion, undue influence, inducement, or intimidation.

7. Obtaining informed consent is a process that begins when initial contact is made with a potential participant and continues

throughout the study. By informing the potential participants of the purpose/s of the research project, repetition and explanation, answering their questions as they arise, ensuring that they understand each procedure, and obtaining agreement from them, researchers elicit their informed consent, and in doing so, manifest respect for their dignity and autonomy.

8. For most 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 their assent and the consent of a legally authorized representative (LAR), according to applicable laws.

9. In obtaining informed consent, sponsors, and researchers have the duty to avoid coercion, undue influence, inducement, or intimidation.

10. Informing the potential participant shall not be simply a ritualistic recitation of the contents of a written document. Rather, the researcher shall convey the information, whether orally, in writing, in other modes of communication, in a language and manner that suit the individual's capacity and level of understanding.

Essential Information for Participants

11. The researcher shall ensure that the prospective participant has adequately understood the information mentioned in the succeeding paragraphs. The researcher shall give each participant the full opportunity to ask questions, and should answer them honestly, promptly, and completely. The potential participant should be allowed to think over, reflect, and discuss with relevant stakeholders.

12. The researcher shall provide the following information to the potential research participant, whether orally, in writing, or both, in a language that suits the participant's level of understanding:

12.1. The individual is invited to participate in the research, which is being undertaken by the researcher (name of the researcher) from the institution (name of institution), and participation is voluntary;

12.2. The reasons for considering the individual suitable for the study;

12.3. The individual is free to refuse to participate in the research without penalty or loss of benefits to which they are entitled. The purpose/s 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, or social intervention;

12.4. The expected duration of the individual's participation (including the 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;

12.5. 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. Risks to other contacts aside from the spouse should be disclosed.

12.6. The direct benefits, if any, expected to accrue to individuals for participating in the research;

12.7. 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;

12.8. The expected contribution of the study to scientific knowledge and the expected benefits to the community or society at large;

12.9. 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;

12.10. The provisions to ensure respect for the privacy of research participants and the confidentiality of records in which they are identified, including documentation through the taking of pictures and recording of the interview and that these might be displayed in publications and conferences or fora;

12.10.1. Where collected research data or research results include personal information, the research participant must give consent not just to the collection of personal information but also to the dissemination and sharing of that information, including such information contained in recorded interviews and pictures.

12.10.2. Regarding sharing, the participant must also know to whom their personal information will be shared.

12.10.3. Research participants must be made aware of the potential risks posed by the dissemination, disclosure, or sharing of their information.

12.10.4. Even if research participants have granted consent to the dissemination, disclosure, or sharing of such information, researchers have an ethical duty to see to it that such dissemination, disclosure, or sharing will not subject participants to risk of serious harm. It would be prudent for researchers to consult experts or the REC regarding ethical dilemmas presented by the participant's expressed wish for him to be identified or to have their statements attributed to them and on the

other hand, reputational, legal, and other risks to decide on whether such information should be disseminated, disclosed, or shared.

12.11. Legal or other limits to the researcher's ability to safeguard confidentiality, and the possible consequences of breaches of confidentiality;

12.12. The sponsors or funders of the research, the institutional affiliation of the researchers, and the nature and sources of funding for the research;

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 they are entitled;

12.14. Informed consent includes asking whether a participant consents to future processing of their personal data, identifiable biological specimens, and medical records including storage, use for subsequent research, sharing of specimens and data, and final disposition of collected data, information, and identifiable biological specimens.

12.15. If the personal data, medical records, and specimens collected will not be destroyed after research, where, how, and for how long they are going to be stored and for what purposes;

12.16. That the research participants have the right to decide about future uses, sharing, or destruction of collected personal data, identifiable specimens, and medical records;

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

12.18. The extent of the researcher's responsibility to ensure needed services to the research participant;

12.19. 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 the funding of such treatment;

12.20. That under the Data Privacy Act (DPA), the participant has the right to information, access, correction, deletion, data portability, to complain before the National Privacy Commission (NPC) and receive damages for the violation of their data privacy rights where applicable. Such rights may be exercised by the data participant's heirs in the event of the former's incapacity or death. In applicable cases, the protocol must explain why data participant rights need to be limited to protect research integrity as allowed by the DPA.

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. Data privacy queries or concerns of the participants;

12.22.4. Related concerns and grievances; and

12.22.5. Management of research-related injuries.

Documentation of Consent

13. As a rule, documentation of informed consent includes an actual signature or thumb mark of the prospective participant on the informed consent form. To further ensure participant voluntariness and understanding of the execution of the informed consent, and to protect both participant and researcher particularly for highly sensitive and controversial studies/research, notarization of the informed consent may be considered as an option.

    13.1. Advances in technology for documentation of informed consent (e.g., electronic signature, electronic informed consent form, consent statements in online forms, recordings) may be utilized subject to the approval by the REC.

14. When the use of an informed consent form is not feasible or is unacceptable to the prospective participant, a description of the process, attested by a witness who is acceptable to the participant, may be substituted, subject to the approval of the REC. Other ways of obtaining or documenting informed consent may be explored, subject to the approval of the REC.

Waiver of Informed Consent

15. Waiver of individual informed consent is to be regarded as exceptional and must be approved by a 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 if all the 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 the elements in the informed consent may be waived or amended (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 amendment 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.

17.4. The participants will be provided with additional pertinent information after their participation (whenever appropriate).

Renewing Consent

18. Informed consent, as a requirement for data collection, should be time-bound, and may be withdrawn earlier or rescinded by the participant. The informed consent of each research participant shall be renewed under any of the following conditions:

18.1. If there are any significant changes in the circumstances or procedures of the research;

18.2. If new information becomes available that could affect the willingness of research participants to continue to participate;

18.3. In long-term studies at predetermined intervals even if there are no changes in the design or objectives of the research; or

18.4. In long-term studies where minors become adolescents or adolescents become adults (*see section on Research Involving Minors or Children*).

Vulnerability of Research Participants

19. Vulnerable participants shall require special protection, as they have certain characteristics or are in special situations that tend to magnify their vulnerabilities or expose them to risks they may otherwise be unwilling to take. 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, 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 (*see section on Clinical Research*).

22. Competent advice and assistance shall be provided to participants who, due to social, economic, political, or medical disadvantages, are more likely 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.

Benefits, Risks, and Safety

23. Research can only be justified if there is a reasonable likelihood that the participants or the population to which they belong stand to derive benefits from it.

24. All research involving human participants shall be preceded by careful assessment of predictable risks, burdens, and foreseeable benefits to the research participant or others.

25. Every precaution shall be taken to minimize the negative impact of the study on the research participant's well-being. All efforts should be done to maximize the potential benefits.

26. Research shall be conducted only if there is an acceptable positive benefit-risk ratio and the participants who are going to be affected give their consent to assume research-related risks (e.g., adverse events, data sharing).

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 must respect participants' right to privacy. Unless required by law, the confidentiality of information shall always be observed. Records that link individuals to specific personal information shall not be released. This requirement shall be included in the informed consent form.

30. Researchers shall refrain from identifying individuals or groups when the release of information about them can expose them to possible harm or social stigma.

    30.1. Release of information should be included among the items in the informed consent form; the participant must be specifically asked if he/she consents to release information collected in the study and informed of the potential risks and consequences, if any, of such release.

31. 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:

    31.1. 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 relevant legal authorities to forestall imminent harm to self or others;

        31.1.1. Prepare a concrete and realistic protocol for reporting and referral if imminent harm or a criminal act is disclosed or discovered in the process of data collection

32. Researchers shall recognize that collecting data using group methods (e.g., FGDs) has implications for the privacy and confidentiality of individual participants and possibly third parties. Therefore, adequate safeguards must be provided.

33. The researcher shall describe their data management and 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. (See the section below on Adherence to the Applicable Provisions of the Data Privacy Act of 2012). For example, the researcher shall provide adequate and clear privacy instructions to research assistants, transcribers of audio recordings, translators of transcriptions, database managers, and programmers.

Justice

34. In research involving human participants, the principle of justice refers primarily to the equitable distribution of both the burdens and the benefits of participation in research. It is unjust for one group in society to bear the costs of research while another group reaps its benefits. Research should not worsen existing health and social inequities.

34.1. There shall be fair selection in the choice of population, sampling, and assignments.

34.2. Appropriate care shall be provided to research participants regardless of their economic status, gender, race, or creed.

34.3. There shall be just compensation for harms brought about by participation in the research.

34.4. 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 the inconvenience. The

payments shall not be so large as to induce prospective participants to participate in the research against their better judgment (undue inducement). Payments or reimbursements should be given on the day of the follow-up or the procedure and not at the end of the study. The participants should be protected from all possible forms of exploitation.

35. Individuals and communities shall have access to benefits related to participation in the study.

Transparency

36. Ethical research shall be characterized by transparency. All parties must be transparent about matters relating to their involvement and this includes any actual or potential conflict of interests. Transparency is not opposed to privacy. On the contrary, transparency – especially in research purposes, policies, procedures, governance, accountability, funding, oversight – is an element of ethical research that promotes confidence in the research enterprise, even when privacy and anonymity need to be preserved in matters of personal data. The need for transparency also entails disclosure of research results to research participants and other stakeholders.

37. 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.

38. Disclosure of research results to research participants shall occur only when all the following apply:

    38.1. The findings are scientifically valid and confirmed.

    38.2. The findings have significant implications for the participant's well-being.

38.3. The course of action to ameliorate these concerns is readily available when research results are disclosed to its participants.

39. Transparency imposes responsibilities on researchers to disclose information about their affiliations, loyalties, financial or other competing interests that may affect their objectivity and the integrity of their research output.

40. Transparency also requires research participants to be truthful in declaring their health conditions and candid in expressing their concerns about their involvement in research.

Adherence to the Applicable Provisions of the Data Privacy Act of 2012

41. The following are reminders for researchers regarding the Data Privacy Act of 2012.

42. Researchers may invoke the exemption for processing of personal information for research purposes, under Section 4d of the DPA provided that:

42.1. The processing of personal information for research purposes is intended for a public benefit.

42.2. Reasonable and appropriate physical, organizational and technical security measures are used to protect the personal data of participants.

42.3. Such flexibility for research purposes, including the waiver of consent requirements and the limitation of the rights of data subjects, is consistent with legal and ethical standards. One way of demonstrating compliance with ethical standards is by obtaining ethics clearance from a PHREB accredited IRB/REB/REC. (See NPC Advisory Opinion 2018-54 https://www.privacy.gov.ph/wp-content/files/attachments/advopn/2018/AONo_2018-054.pdf).

43. The determination of the appropriate level of security measures must consider the nature of the personal data to be protected, the risks represented by the processing, size of the organization and complexity of its operations, current data privacy best practices, and the cost of security implementation (See Section 20 of the DPA).

44. The proper personal information controller (individual researcher or group of researchers or research and development institution as defined under RA 10055 or the Technology Transfer Act of 2009) and the former's DPO must be registered with the National Privacy Commission (NPC) under NPC MC 2017-01 (NPC, 2017a).

44.1. For research done by a juridical person (e.g., a research and development institute, association with a separate juridical personality), the juridical person's DPO may oversee compliance with the DPA. On the other hand, such a juridical person may consider appointing and registering a DPO or Compliance Officer for Privacy (COP) for each research project to see to it that the requirements of the DPA are complied with.

44.2. For research done by independent individuals or groups of individuals not under a juridical person, the individual researcher will automatically be a DPO. In the case of a group of researchers, the lead researcher shall appoint a DPO from among the members of the research team.

45. Researchers should have ready mechanisms in place in the event of a personal data breach. Their duly authorized representative shall promptly notify the Commission and affected data subjects when sensitive personal information or other information that may, under the circumstances, be used to enable identity fraud are reasonably believed to have been acquired by an unauthorized person, and the researchers or the Commission believes that such unauthorized acquisition is likely to give rise to a real risk of serious harm to any affected data subject. The notification shall at least describe the nature of the breach, the sensitive personal

information possibly involved, and the measures taken by the researchers to address the breach. Notification may be delayed only to the extent necessary to determine the scope of the breach, to prevent further disclosures, or to restore reasonable integrity to the information and communications system. As a rule, notice shall be given to participants and the National Privacy Commission within 72 hours from knowledge of such data breach. Researchers must carefully study and comply with all the applicable requirements of NPC MC 2016-03 (NPC, 2016) which includes conducting a privacy impact assessment to craft a research protocol that incorporates privacy by design.

46. The Institutional DPO shall provide the detailed policy/guidelines in how the protocol and conduct of research can comply with the DPA.

ENSURING QUALITY RESEARCH

Scientific and Ethical Considerations in Research

The quality of research derives from both scientific and ethical considerations. Such considerations include appropriate delineation of the roles and responsibilities of various stakeholders (e.g., researchers, sponsors, research ethics committees), and acceptable instruments commonly used in research. This section represents the minimum considerations based on best practices, guidelines, and policies related to the conduct of research involving humans.

The Research Protocol

The protocol is the definitive document of the research or study. It guides those who will conduct the research, reference for evaluators and reviewers, template for validation, substantiation for intellectual property claims, and the legacy of the proponent. Therefore, 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. Whether invasive, intrusive, or not, all procedures 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.

6. Based on the type of study, the protocol should be written in an inclusive language (*see Glossary*).

Qualifications of Researchers

The researcher is the individual who is ultimately responsible and accountable for the research. The ethical issues in the use of human participants in research are addressed, in part, by the assurance that the researcher is qualified. Such qualifications need to be provided by the researcher and vetted by the researcher, the research ethics committee (REC), the sponsors, and when applicable, other authorized bodies.

7. Persons engaged in research involving human participants shall have integrity, scientific competence, social awareness, cultural sensitivity, intellectual humility, vigilance, and preparedness for safety issues.
8. The researcher shall have the education, training, ability, and resources to conduct the proposed study.
9. The researcher shall be knowledgeable on updated or recent literature on the research topic.

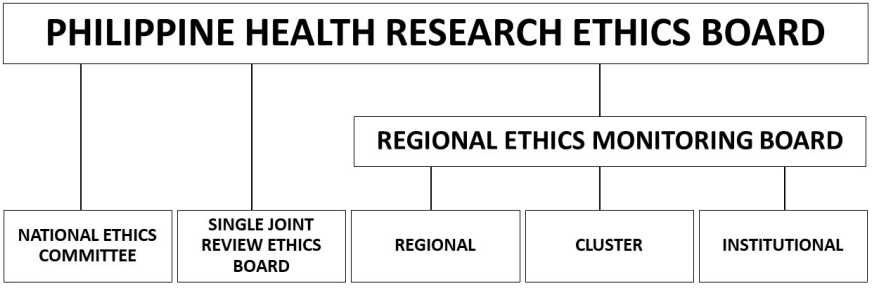
The Research Ethics Review

National Governance in Research Ethics Review

The body responsible for research ethics in the Philippines is the Philippine Health Research Ethics Board (PHREB). PHREB was established in 2006 through the authority of the Department of Science and Technology (DOST) (DOST Special Order No. 091 s 2006). It was eventually created as the national policy-making body in health research ethics when the Philippine National Health Research System (PNHRS) was legislated through the PNHRS Act of 2013 (RA 10532) on 07 May 2013.

Under the national commitment to protect human participants and promote integrity in research, the PHREB collaborates with the PNHRS implementing agencies (DOST, Department of Health [DOH], Commission on Higher Education [CHED]). It also coordinates with local and national agencies (e.g., National Commission on Indigenous Peoples [NCIP], Food and Drug Administration [FDA], National Privacy Commission [NPC]) that can guarantee compliance of all relevant research stakeholders with the national ethical guidelines. Compliance with the national guidelines must be pursued through these agencies' respective regulatory mandates.

10. Under the PNHRS, research ethics review in the Philippines is implemented through oversight of the PHREB:



Philippine Health Research Ethics Board (PHREB)

11. The 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 Department of Health (DOH), and the Commission on Higher Education (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 include representatives from people's organizations and the youth sector. Both the chair and co-chair have two-year terms.

    PHREB is a national policy-making body specifically to:

    11.1. Formulate and update guidelines for the ethical conduct of human health research;

    11.2. Develop guidelines for the establishment and management of RECs and standardization of research ethics review;

    11.3. Monitor and evaluate the performance of institutional RECs in accordance with procedures outlined in a prior agreement;

    11.4. Promote the establishment of functional and effective RECs;

    11.5. Provide advice and make recommendations to the PNHRS Governing Council and other appropriate entities (including the Food and Drugs Administration [FDA]) regarding programs, policies, and regulations as they relate to ethical issues in human health research;

11.6. Initiate and contribute to discourse and discussions of ethical issues in human health research; and

11.7. Network with relevant local, national, and international organizations.

Regional Ethics Monitoring Board (REMB)

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

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

14. The REMBs, following the mandate of PHREB (Rule 23, PNHRS IRR), and 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.

15. REMBs shall be located within existing regional DOST, DOH, CHED offices, or designated institutions. Currently established REMBs are listed on the PHREB website (http://ethics.healthresearch.ph). REMBs shall be established to assist PHREB with the following functions:

    15.1. Information dissemination, training, and advocacy
    15.2. Monitoring performance of RECs in their respective regional areas
    15.3. Submission of annual reports to PHREB
    15.4. Development of quality assurance in the review of RECs in the region
    15.5. Implementation of policies and directions for health research ethics set by PHREB
    15.6. Other functions or tasks as deemed necessary

Research Ethics Committee

16. Research Ethics Committees (RECs) include the National Ethics Committee (NEC), Single Joint Research Ethics Board (SJREB), regional RECs, cluster RECs, and institutional RECs. The REC, regardless of type, should consider both the scientific and ethical aspects of the proposed research even when the REC is distinct from the technical review committee.

    16.1. National Ethics Committee

    The National Ethics Committee (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 the PHREB took over its policy-making role. In 2010, the NEC was temporarily phased out (DOST Special Order No. 383), only to be reactivated on 09 December 2013 because of the pressing need for a national body to review research that is of national importance, with the following functions:

    16.1.1. Ethics review of research proposals: 1) referred by other agencies especially government-funded research projects that are to be conducted in institutions that do not yet have their own Research Ethics Committees (REC); 2) directed to NEC by the Philippine Health Research Ethics Portal (PHREP); and 3) the NEC may deem appropriate to review.

    16.1.2. Assist institutional RECs in the resolution of difficult ethical issues;

    16.1.3. Provide input to the Philippine Council for Health Research and Development (PCHRD) and other government agencies, including the Philippine Food and Drug Administration (FDA), regarding ethical issues in relevant studies;

16.1.4. Provide applicable information to PHREB in the formulation of policies and guidelines in health research; and

16.1.5. Network with other national ethics bodies (i.e., National Bioethics Advisory Committee [NBAC], National Transplant Ethics Committee [NTEC], Philippine Genomics Center Ethical Legal Social Issues Program [PGC-ELSI]) in contributing to the development of an ethical research environment.

16.2. Single Joint Research Ethics Board

The Department of Health (DOH) established the Single Joint Research Ethics Board (SJREB) through Administrative Order 2017-0021 and Administrative Order 2019-0049. These mandate the standardization of multi-site review through a single joint review conducted for the approval of multi-site research participated in by identified sites where the protocol will be implemented. An SJREB review is mandatory for all DOH hospital RECs, although non-DOH RECs may participate during the review.

16.3. 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 community-based research without a specific responsible institution.

16.4. Cluster Research Ethics Committees

Several institutions may jointly form a common REC if it is not feasible to create 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.

16.5. Institutional Research Ethics Committees

Philippine institutions that engage in biomedical, behavioral, and social research shall establish an institutional REC, which shall

provide an 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, the REC must be independent of political, institutional, professional, and market influences in its composition, procedures, and decision-making.

17. As the list of accredited RECs is updated frequently, refer to the PHREB accredited RECs list in the PHREB website http://ethics.healthresearch.ph.

Guidelines for Research Ethics Committees

18. 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 reviews and monitoring of all research involving human participants.

19. RECs shall have standard operating procedures (SOPs) to make REC operations transparent, accountable, competent, timely, and consistent (WHO, 2011).

Composition

20. The REC shall be constituted by the institutional authority according to its policies on research and international and national standards. The institution's organizational chart shall include the location of the REC in relation to the other institutional units. This is 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.

21. Membership shall be multidisciplinary and multi-sectoral, with adequate age and gender representation.

22. Members shall have relevant scientific expertise, such as medical (in case of RECs reviewing clinical trials), social, or behavioral science,

or qualifications pertinent to the areas of research the REC is most likely to review. In addition, members with expertise in ethics, law, environment, and public health shall also be considered to reflect social and cultural diversity in research.

23. The REC shall include an individual (non-medical, non-scientist) who will represent the interests and concerns of the community, and serve as the voice of research participants, their families, and their communities.

24. At least one member shall be independent of the institution or research site (non-affiliated member) to ensure the independence of the REC.

25. The number of REC members shall be adequate to ensure that the review can be done efficiently and effectively following international and national standards.

Appointment of Members

26. When appointing members, the institution shall consider the following:

    26.1. The primary role of the non-medical, non-scientist member shall be to share their insights about the communities from which participants will be drawn and about the informed consent process and form.

    26.2. In RECs that review clinical studies (particularly clinical trials), it is recommended that the community representative be drawn from either a patient or family support organization or a patient advocacy organization.

    26.3. The officers and members of the REC shall be officially appointed by the administrative head of the institution.

26.4. The appointing official shall indicate the officers' and members' functions, terms of office, the scope of work, conditions of appointment, and compensation, if any.

26.5. The appointment document shall mention the responsibilities of members with special roles (e.g., officers, non-medical/non-scientist members, non-affiliated member).

26.6. Procedures for initial appointment and renewal of appointment, resignation, replacement; grounds for disqualification; and procedures on managing financial and other conflicts of interest (COI), shall be included in the standard operating procedures (SOP) manual.

26.7. Before serving as a regular member, each member of the REC shall sign both a confidentiality agreement and a disclosure agreement. The latter that states that they have no COI (e.g., financial interests in a sponsor company, affiliation with the funding agency, or even familial relationships with these parties) as a reviewer.

26.8. 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).

26.9. 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 the director of the institution or their agent) shall not serve as members of the REC or as its Chair (WHO, 2011).

Appointment of Independent Consultants

27. 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 participate in REC decision-making (no voting privilege).

28. Deliberations on research involving special participant groups or concerns (e.g., HIV, AIDS, the physically challenged) shall include the participation of advocates.

29. 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.

REC Support

30. 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 carry out its responsibilities.

Functions and Responsibilities

31. The REC shall act in the full interest of potential research participants and affected communities, considering the interests and needs of the researchers, and having due regard for the requirements of relevant regulatory agencies and applicable laws (WHO, 2000 and 2011). The REC should be updated regarding Philippine laws and policies of regulatory agencies about possible areas or groups for research.

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

    32.1. Review the scientific merit and ethical acceptability of the research involving human participants;

32.2. 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;

32.3. Ensure that the proposed research is responsive to the priorities and health needs of the country and that it meets the required ethical standards;

32.4. Issue the ethical approval required for the implementation of any research it has reviewed and approved;

32.5. Promote research integrity by identifying and resolving conflicts of interest;

32.6. Establish appropriate mechanisms in all stages of the research to:

32.6.1. Ensure the safety, protect the rights, and promote the welfare and well-being of research participants;

32.6.2. Guide research participants, including proponents and researcher;

32.6.3. Ensure prompt reporting of changes in the protocol and unanticipated problems;

32.6.4. Ensure the proper documentation of and adherence to the confidentiality rule and policy on informed consent; and

32.6.5. Monitor the progress of ongoing research until its completion.

32.7. 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;

32.8. Keep a systematic and organized record of all proposals reviewed, including actions taken and other pertinent information;

32.9. Submit an annual report to the PHREB (within the first quarter of the year ending on March 31), which shall contain the following:

32.9.1. The composition of the REC, including a short curriculum vitae (name of the person, educational attainment, most recent ethics training/seminars attended), and term of office of each member;

32.9.2. Members of the REC secretariat, office and email addresses, and contact numbers;

32.9.3. Number of meetings (regular and special) held during the year, including the date and venue;

32.9.4. 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

33. The REC shall regularly meet as a committee on a schedule 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.

34. For RECs with five to nine members, a quorum requires at least five members; otherwise, a quorum shall follow the 50% + 1 rule. A quorum also requires the presence of at least one non-medical or non-scientist and one non-affiliated member to make decisions about the proposed research (WHO, 2011). For interventional studies involving children, a quorum shall include the presence of a pediatrician or a child development expert, as needed by the protocol. In the absence of these required members, there is no quorum.

35. Deliberations of the REC shall be characterized by transparency and collegiality. A member involved in whatever capacity in the study or project under consideration shall inform the committee of this potential COI. Their further participation in the deliberations shall be determined accordingly. Those with COI shall not be present during the deliberations and decision-making. A principal investigator or researcher member may remain during the REC meeting to answer questions for clarification regarding their research but shall leave the room during the REC deliberation and decision-making.

36. 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) or the non-affiliated member. Strong objections shall be addressed and reasonably resolved.

Training

37. Members of the REC shall undergo initial and continuing training on the ethics and science of biomedical, socio-behavioral, and other research, and applicable laws such as the Philippine National Health Research System (PNHRS) Act, Indigenous Peoples Rights Act (IPRA), and Data Privacy Act of 2012 (DPA), pertinent to the types of protocols reviewed by the REC.

    37.1. Initial training shall be required of new members. If there is no basic ethics training available when 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.

37.2. Members shall be encouraged and supported to attend regular continuing education 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

38. 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

39. 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, Appendix G)

The Research Ethics Review Process

40. A REC conducts the ethical review of research proposals involving human participants 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.

41. Since the quality of the ethical review is a significant concern, the REC shall have a manual of SOPs that 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.

42. The ethical review of protocols involving several sites may be done as a joint review of a group of PHREB accredited RECs, such as the DOH Single Joint Research Ethics Board (SJREB), provided that the review is conducted according to SOPs approved by PHREB.

Required Documents for REC Review of an Initial Protocol Submission

43. The researcher shall be required to submit to the REC the following documents before the REC reviews their research proposal:

    43.1. 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;

    43.2. Clearance from technical or ethical review(s) from other committees (if any);

    43.3. The research protocol 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 a reference in the study and include ethical issues such as 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 unanticipated problems; and how informed consent will be obtained.

    43.4. Informed consent and assent documents (*see Informed Consent on page 15, Research Involving*

Minors or Children; and Template of Informed Consent and Assent). The informed consent and assent documents must be written both in English and in a local language appropriate to the level of understanding of the research participant (*see General Guidelines*). A sample template of statements to be written in an ICF is found on pages 353 to 370;

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

43.6. Study drug or medical device information like researcher brochures, published literature, and medical device manufacturer's design, if relevant;

43.7. 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);

43.8. Statement of on presence or absence of COI of the researcher;

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

43.10. Research agreements (e.g., Memorandum of Agreement [MOA] if the study is collaborative; Material Transfer Agreement [MTA], Intellectual Property Agreement, Investigational Device Exemption [IDE], Data Sharing Agreement [DTA]) when relevant;

43.11. Study or protocol budget;

43.12. The researcher shall submit to the REC the required number of copies or electronic files of the protocol package the REC requires for its review.

Initial Review Procedure

44. After receiving 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 logbook or an electronic database noting the submission date, protocol title, researcher or principal investigator, funding agency or sponsors, and other relevant fields.

45. The REC Chair, or their representative, shall determine the proposal's exemption from review or the kind of review required, whether full or expedited review.

46. Exempt from Review is the term used to denote that a protocol does not need to undergo 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.

47. 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.

48. Provided that protocols do not involve more than minimal risks or harms, the following may be considered by the REC for exemption from review:

    48.1. Protocols for institutional quality assurance purposes, evaluation of public service programs, public health surveillance, educational evaluation activities, and consumer acceptability tests;

    48.2. 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:

        48.2.1. 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

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

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

49. The REC may delegate the decision to exempt a protocol from review to an office or group of individuals for efficiency and in the interest of time. However, there must be assurance 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. A checklist or assessment form shall be used to determine exemption.

50. The REC, in its annual report submitted to the PHREB, shall include a list of all proposals or protocols that were exempted from review.

51. 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.

52. A full review shall be required for protocols that entail more than minimal risk to participants or involve vulnerability issues.

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

54. An expedited review can be done by the REC, at the level of the primary reviewers or the Chair, for proposals that do not need a full review, such as the following:

    54.1. Chart review

    54.2. Survey of non-sensitive nature

    54.3. Use of anonymous or anonymized laboratory/pathology samples or stored tissues or data

Protocol Review

55. Research protocols are evaluated relative to the elements of research ethics (*see Elements of Research Ethics*) and other considerations as follows:

    55.1. Social value: scientific validity, relevance to the community and national needs, suitability of the dissemination plan and beneficiaries;

    55.2. Informed consent: competence (of legal age and sound mind), mandated information to be disclosed based on the national guidelines (*see page 16*), comprehensibility of information (use of local and non-technical language), voluntariness (absence of coercion and undue influence), and articulation of consent (whether written or verbal);

    55.3. Risks, benefits, and safety: assessment of risks, favorable risk-benefit ratio, and access to favorable research outcomes;

    55.4. Privacy and confidentiality of information: respect for the right to privacy and mechanisms to protect confidentiality;

55.5. Justice: fairness of selection process, appropriate care, compensation and reimbursement, and access to benefits;

55.6. Transparency: management of COI, sharing of relevant information to participants, honesty in participation, and disclosure of research results;

55.7. Qualification of researcher: appropriate education, training, and experience that are specific and relevant to the research topic and population;

55.8. Adequacy of facilities: supportive of protocol procedures and well-being of participants;

55.9. Community involvement: respect for local traditions and culture, community empowerment, acknowledgment of participation; and

55.10. Legal responsibility for injuries in the conduct of the research, including insurance coverage, if any.

Action on Submissions

56. REC action shall standardize actions on submissions

56.1. **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. The approval document shall require the submission of the following continuing review submissions:

56.1.1. Progress report, at least once a year or as requested by the REC;

56.1.2. Final report;

56.1.3. Amendments;

56.1.4. SAEs and SUSARs;

56.1.5. Termination of the research before its anticipated completion date and the reason for it

56.1.6. Protocol deviations and violations; and

56.1.7. Reportable negative events or unanticipated problems (including social harm, other negative events).

56.2. **Modifications** (Minor or Major) Required, in which case, the REC shall communicate to the researcher, in writing, a clear description of required modifications to the protocol and protocol-related documents

56.3. **Disapproval,** in which case, the REC shall clearly state the reason(s) for disapproval

56.4. **Deferred or Pending,** if the REC action is postponed or withheld, or a decision of the REC cannot be made while awaiting further information, respectively

57. 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. Renewal applications must be received by the REC no earlier than 30 days before the expiry of the current approval.

Appeal for Reconsideration

58. It is the responsibility of the REC to create procedures and venues for resolving conflicts emanating from any REC action or decision pertinent to its primary mandate of protection of human participants in research. In case of an unfavorable decision, the researcher may make an oral or a written representation to the REC for reconsideration. On the other hand, the institution must

establish mechanisms to address other potential institutional conflicts, including but not limited to authorship, data sharing, and the like.

Withdrawal of Prior Approval

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

    Noncompliance with reporting requirements

    59.1. An undue or significant number of SUSARs directly or indirectly attributed to the research

    59.2. Protocol violations

    59.3. Valid serious complaints from participants

    59.4. Proven research misconduct

60. Procedures for withdrawal should be detailed in the SOP of the REC. Due process must be described in the post-approval SOPs of the REC, including appropriate application of criteria, notification of relevant parties, and communication with the researcher.

Monitoring Protocol Implementation

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

    61.1. An **amendment** is a written description of a proposed change(s) to REC-approved documents (i.e., protocol, informed consent documents, and other protocol-related documents) that is yet to be implemented. REC approval is required before its implementation.

61.2. **Deviation** from the approved research plan or protocol is a form of noncompliance with the conditions of REC approval and may cause approval to be revisited. The deviation is only justifiable where necessary to remove a research subject or participant from immediate danger or harm or when such changes are administrative or logistical (e.g., change of telephone numbers). The REC shall require the researcher to submit a report of deviation to the REC; or, as applicable, the REC shall inform the researcher of any violation that has come to the attention of the REC. The REC shall likewise require the researcher to address the deviation with both a corrective and preventive action and review the current approval of the study given the noncompliance.

61.3. Ethical approval is typically granted for a period of one year or less, depending on the risk assessment of the study protocol, which is determined during the initial review. A **progress report** must be submitted to the REC for review of renewal or extension of approval.

61.4. Any event related to a REC-approved protocol that may have ethical significance must be submitted by the researcher for the continuing review by the REC of the risk-benefit assessment. These events may come in the form of **reportable negative events** or **unanticipated problems** posing risks to participants or others because of or related to participation in research (*see Reportable Negative Events in Glossary page 412*).

Site Monitoring Visit

62. The REC or designated representative may also do an onsite visit of studies that it has approved. This may be done where there is a significant number of serious adverse events, new study sites, non-

compliance or suspicious conduct, failure to submit required reports, among others.

62.1. REC shall inform the researchers of the visit at a date agreeable to both.

62.2. 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.

62.3. After the site visit, a report is given to the principal researcher and the REC.

62.4. The REC may recommend corrective and preventive actions for observations made.

Review of SAE and SUSAR Reports

63. The REC shall have SAE/SUSAR report forms available that may be used for reporting by researchers required to monitor safety reports. The form should include the determination of the expectedness and relatedness of the SAE/SUSAR and its 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, including appropriate medical management of the participant.

64. SAE reports shall be evaluated by the REC with special attention to the SAEs from the site with approval from the REC.

Early Termination or Suspension of the Study

65. If a study is prematurely ended, the research must arrange for the appropriate management of participants who have already been recruited, including notifications. In the case of a clinical trial that is prematurely terminated or suspended for any reason, the principal investigator shall promptly inform the REC how this shall be managed and ensure appropriate therapy and follow-up of

participants. The researcher shall submit a written, detailed explanation of the termination or suspension in all cases.

Completion of the Research

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

Documentation and Archiving

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

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

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

70. Completed study files include all the above and the final report, which should be archived for a minimum of three years after the approval of the final report.

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

72. The REC shall maintain a file of research ethics review documents including, but not limited to:

    72.1. REC SOPs;

    72.2. International, national, and local guidelines;

72.3. Annual REC reports;

72.4. Curriculum vitae of REC members, including initial and continuing training in ethics review, GCP, among others, which shall be updated, signed, and dated;

72.5. Logbooks and electronic database to facilitate checking and follow-up of approved protocols;

72.6. Logbook or electronic tracking systems for inquiries and complaints (dated), especially from study participants with their contact numbers;

72.7. Logbook or electronic tracking system for SAEs from local study site; files of reports of SAEs from international sites are kept in another file;

72.8. Flow charts of REC procedures that shall be clearly visible to guests; and

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

Responsibility of the Research Adviser

73. 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.

74. The senior research or faculty adviser shall:

74.1. Guide the student or trainee in the development of a scientifically and ethically sound research protocol;

74.2. Assist the student or trainee in addressing ethical and scientific concerns raised by reviewing bodies;

74.3. 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;

74.4. Supervise the student or trainee in the proper collection and recording of data including the duty to maintain the confidentiality of the information and the privacy of human participants for all the phases of the research processes, including the disposal or archival of data;

74.5. Review interim and final reports for accuracy and consistency;

74.6. Share responsibility and accountability with the student/trainee for the ethical conduct of the research; and

74.7. Ensure that the research to be undertaken by undergraduate students involves only minimal risk (See Roles and Responsibilities of the Investigator or Researcher)

75. The institution must operationalize these responsibilities by creating policies related to accountability.

Responsibilities of the Research Institution

76. All institutions that are mandated to conduct research or those that allow or require their faculty, staff, students, or trainees to do research are considered in this guideline as "research institutions."

77. The research institutions shall:

77.1. Ensure the ethical conduct and monitoring of research being undertaken in the institution given the institution's available resources by taking reasonable steps to comply with existing research ethics regulations issued by various agencies. In the absence

of an institutional REC, the institution shall refer its researchers to other research ethics committees accredited by PHREB that can perform the review based on a REC reliance agreement with the institution.

77.2. 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.

78. Maintain an efficient recording system of research studies being done and their status and researchers involved in the study;

79. Establish SOPs regarding the review of research studies to be done in the institution, including fees to be charged;

80. Establish safety monitoring and management systems (for researchers and participants);

81. Put in place systems, subject to the available resources of the institution, to enable researchers to maintain the privacy and confidentiality of information on human participants, including secure processes for the sharing of data by the research community, as well as the disposal and archiving of data;

82. Provide opportunities for dissemination of results in collaboration with other stakeholders;

83. 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

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

85. Formulate appropriate policies based on the *doctrine of diligence of a good parent* (Philippine Civil Code Article 2180) to ensure the safety of research participants and the integrity of data, incorporating the following provisions but not limited to:

    85.1. requirement of ethical review of research protocol by a PHREB-accredited REC before its implementation;

    85.2. monitoring of the ethical implementation of the approved protocol by a PHREB-accredited REC;

    85.3. provision for administrative support by the institution for the day-to-day operations of the REC;

    85.4. appropriate respective legal responsibility of the institution, funding agency/sponsor, and faculty, staff, students, and trainees conducting research for any injuries that may result from the conduct of the research, including the insurance coverage, if there is any; and

    85.5. mechanisms to ensure the integrity of the scientific undertaking (e.g., the establishment of a Research Integrity Office).

Roles and Responsibilities of the Investigator or Researcher

86. For this set of guidelines, the term "researcher" refers to an individual or group of individuals who conceptualizes, initiates, and conducts a study.

87. In the subset of researchers that conduct clinical trials, the researcher is the "investigator," which refers to an individual or group of individuals responsible for conducting clinical trials involving investigational new drugs or devices, usually commissioned and sponsored by pharmaceutical companies or manufacturers.

87.1. The “Principal Investigator” is the lead implementer of the clinical trial protocol. “Co-Investigators” (Co-Is) are a subset of key personnel with special clinical trial responsibilities.

87.2. "Sub-investigators" are study team members who make critical clinical trial-related procedures and decisions. Generally, they are also study Co-Is but may also include study team members with vital and important trial-related roles.

87.3. All investigators have the same responsibilities pertinent to protecting human participants and ensuring the credibility of data, but they perform their tasks based on a clear delegation of responsibility emanating from the principal investigator.

88. 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. Researchers-in-training, such as undergraduate students and trainees, must be supervised by a senior researcher as a designated research adviser (*see section on Responsibility of the Research Adviser*)

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

89.1. Preparing the research protocol and ensuring its ethical acceptability by submission to the REC for review;

89.2. Obtaining ethical approval of the protocol and cooperating with the REC in the conduct of the clinical trial;

89.3. Bearing ultimate accountabilities for all activities associated with the protocol, including compliance with adopted international guidelines, national and local laws, institutional policies, and ethical principles;

89.4. Consulting or collaborating with colleagues in the scientific or academic community to which they belong 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;

89.5. Performing or delegating to qualified co-investigators or research staff all the necessary tasks to carry out their studies, while remaining ultimately responsible for the proper conduct of the study and fulfillment of all associated obligations;

89.6. Providing members of the research team with sufficient oversight, training, and information to facilitate appropriate safety procedures and protocol adherence;

89.7. Ensuring that adequate resources (facilities, equipment, supplies, and personnel) exist to:

89.7.1. Conduct the research (e.g., through internal or external funding for staff, facilities, and equipment);

89.7.2. Protect subjects; and

89.7.3. Ensure the integrity of the research.

89.8. Evaluating the resources available at each site where the research will be conducted in multicenter/site studies;

89.9. 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;

89.10. Providing evidence of Good Clinical Practice (GCP) training for clinical trials, Good Research Practice or Responsible Conduct of Research or equivalent, for all other types of studies, valid for three years. Training topics must include basic research ethics and Philippine regulations and guidelines.

89.11. 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 21);

89.12. Having adequate time to enlist the necessary number of participants for the research;

89.13. 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);

89.14. Informing the REC if a researcher or investigator can no longer fulfill their duties for any reason including, but not limited to, traveling for a prolonged period;

89.15. Cooperating always 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;

89.16. Bearing accountability for the content of all submissions (e.g., initial review, continuing review, adverse event reporting, reportable negative events or unanticipated problems, progress reports) to the REC and other review units and for ensuring that those documents are submitted promptly, as required by the REC and other review units (e.g., audit teams);

89.17. Conducting the research as specified in the REC-approved protocol and complying with all REC decisions pertinent to the REC-approved protocol;

89.18. 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;

89.19. Reporting promptly to the REC any additional risks that are identified during the research project;

89.20. 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 the REC approval for a study lapses for any reason, even if the researcher or investigator has submitted an application for continuing review on time 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);

89.21. Reporting promptly any event of ethical significance to the REC including, but not limited to:

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

89.21.2. Non-compliance with applicable laws, regulations, or REC requirements, whether by the researcher or investigator, research staff, or others, even if the non-compliance was unintentional or was discovered during quality assurance or quality improvement activities; and

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

89.22. Cooperating with:

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

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

89.22.3. 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.

89.23. Disclosing all financial and non-financial COI;

89.24. 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; and

89.25. Complying with the ICH-GCP guidelines in fulfilling all other duties in clinical trials that require FDA regulation

Responsibilities of Foreign Researchers

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

Requirements

91. Foreign researchers conducting human research in the Philippines, including the collection and storage of information and biospecimens, are required to:

    91.1. Demonstrate familiarity with the relevant provisions of the 2022 National Ethical Guidelines and the national governance structure for human protection in research;

    91.2. Comply with all Philippine regulations applicable to the study, including regulatory issuances by the PHREB; and

    91.3. Obtain approval from a PHREB-accredited REC.

92. Foreign researchers shall submit required documents to the concerned REC, which, in general, include the following:

    92.1. Letter requesting for ethics review
    92.2. Accomplished application for ethical review
    92.3. Latest version of the research protocol
    92.4. Informed consent form
    92.5. Data collection forms

92.6. Letter of endorsement from the foreign institution where the researcher is affiliated (if applicable)
92.7. Technical review approval
92.8. Ethical review clearance from the concerned foreign institutional REC
92.9. Curriculum vitae of the researcher

93. Ethical approval of the protocol shall be based on:

93.1. Relevance of the study to Philippine research priorities;
93.2. Acceptability of justification for choosing the Philippines as a research site;
93.3. Identification of a qualified and appropriate local researcher or adviser;
93.4. Scientific soundness;
93.5. Ethical soundness;
93.6. Familiarity of the researcher with the culture of the community research site;
93.7. Appropriate expertise of the researcher; and
93.8. Appropriate reporting and dissemination plan.

94. 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.

95. Ensuring compliance with international, foreign, and local laws and regulations shall be the responsibility of the entire research team. Both foreign researchers and local research collaborators shall be accountable to local authorities in cases of violations of local laws and regulations.

96. 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.

97. Safeguards shall be in place to protect sensitive and personal information that will be transmitted outside the country.

98. Compliance with local regulations shall be ensured by the foreign researcher.

Responsibilities of the Funding Agency and Sponsor

99. A sponsor is defined as an individual, company, institution, or organization responsible for initiating, managing, and financing 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 mainly responsible for financing or funding the research. The latter is what this guideline refers to as the "Funding Agency."

100. The funding agency shall:

    100.1. Ensure competent technical and ethical review of all research projects receiving its support;

    100.2. Ensure regular and timely release of funds to support research;

    100.3. Monitor the proper implementation of the protocol;

    100.4. Promote research integrity;

    100.5. Provide remedial support in case of incident problems;

    100.6. Ensure satisfactory completion of the project within a reasonable time; and

    100.7. Provide opportunities for dissemination of results.

101. The sponsor is expected to fulfill responsibilities specifically provided in the ICH-GCP Guidelines.

Guidance for Research Participants

102. Research participants are the primary subjects of a study. The research may involve recording and analyzing 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.

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

104. This section operationalizes research-related recruitment and participation, and a Filipino translation of the section is provided in the next section to enable wider access, especially by research participants.

105. Research is conducted according to the Protocol document (*see definition in page 411*). It is the principal reference for the implementation of the research. The protocol defines the information to be given to potential participants for their consideration when they are recruited for the research.

Informed Consent

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

107. This document is called the Informed Consent Form. Informed consent is a process by which a participant confirms their willingness to participate in a study after being informed of all aspects of the study relevant to the participant's decision to join. Informed consent is documented using a written, signed, and dated informed consent form.

108. The informed consent process requires communicating relevant information about the study to the participant before they decide to participate.

109. Willingness to participate is emphasized, such that joining a particular study shall not be obligatory; hence, prospective participants:

109.1. May consult family members or friends if they have issues about participation;

109.2. Should not be ashamed to turn down participation; and

109.3. 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.

110. The essential elements of the informed consent form are regulated by several international guidelines, adapted in the 2022 NEGRIHP to incorporate Philippine regulations (*see Elements of Research Ethics*), for information of researchers, research ethics committees, funding agencies, and other stakeholders. Since this current section is intended to assist research participants in understanding the informed consent form, that list is streamlined and simplified (in flexible order as needed by the study) as follows:

110.1. Who sponsors or funds the study?

110.2. Is there prior research about the subject of the study? In which countries was the study conducted, or will be conducted?

110.3. Who are the researchers, and what are their responsibilities?

110.4. What are the responsibilities of the participants?

110.5. What are the rights of participants, including the right to withdraw? (See Bill of Rights in Health Research, Studies, and Clinical Trials, Appendix Y)

110.6. What procedures will participants undertake?

110.7. Will there be a probability of random assignment of participants into groups that will undergo different procedures?

110.8. What are the reasonably foreseeable risks or inconveniences to the participants?

110.9. How long will the participation take?

110.10. Are there anticipated expenses to the participant for participating in the study?

110.11. Will there be payment or any form of compensation to the participant for participating in the study?

110.12. Who will be accountable in case participants are harmed?

110.13. How will the personal information of participants be protected?

110.14. Will there be post-study benefits? For example, treatment, membership in support groups, information regarding the results of the study

110.15. Will the participants' information (or, in some cases, bio-specimen) be used again for other research after the current project is complete? How will the information (or bio-specimen) be stored and re-used?

110.16. Was the study approved by a PHREB-accredited REC?

111. Research participants must have the capacity to understand information regarding study participation.

111.1. In what language was the informed consent document written?

111.2. Can participants easily understand the information about the study?

112. The participants themselves can give informed consent if they are:

112.1. Of legal age (18 years or above)
112.2. Of sound mind
112.3. Capable of understanding the nature of their participation

113. If the participant does not have the capacity to consent, representatives of the participant can consent on the participant's behalf, including:

113.1. Parent (if minor)
113.2. Spouse
113.3. Legally authorized representative

114. Participants may request additional information from the responsible parties in charge of the study if there are issues regarding the contents of the informed consent form. Responsible parties may be the:

114.1. Doctor (if the study is a clinical trial)
114.2. Researcher or investigator
114.3. Data Protection Officer or Compliance Officer for Privacy
114.4. The REC who gave ethical clearance for the study (the contact number of the REC shall be written in the informed consent form)

Gabay para sa mga Kalahok sa isang Pananaliksik [Filipino version of the above section]

115. Kalahok ang tawag sa mga taong sumasali sa isang pananaliksik kung saan sila mismo o ang kanilang personal na datos 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.

116. *Kadalasan ang mga kalahok ay nagkakaroon ng kaalaman tungkol sa layunin at mga pamamaraang gagamitin sa pag-aaral sa pamamagitan ng proseso ng maalam na pag sang-ayon* [informed consent].

117. 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, na siyang tumutukoy ng lahat ng impormasyon tungkol sa pag-aaral na kinakailangan upang makapagpasya ang mga maaaring maging kalahok kung sila ay sasali o hindi.

Pahintulot

118. 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, "Maalam na Pag Sang-Ayon." Ang "Maalam na Pag Sang-Ayon" 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.

119. Kasama sa prosesong ito ang pagbibigay-alam sa kalahok ng kaukulang impormasyon tungkol sa pananaliksik bago magpasyang sumali.

120. Ang pagsali sa isang pananaliksik ay hindi dapat sapilitan (boluntaryong pagsali), kung kaya ang mga kalahok ay:

120.1. Maaaring kumonsulta ng ka-pamilya o kaibigan kung may agam-agam;

120.2. Huwag mahiyang tumanggi sa mananaliksik; at

120.3. Maaaring tumiwalag anumang oras habang isinasagawa ang pananaliksik nang walang mawawalang dati nang tinatanggap na pribelehiyo.

121. Ang mahahalagang bahagi ng dokumento ng pahintulot ay nababatay sa ilang alituntuning ginagamit na ng buong mundo, na syang inangkop naman ng National Ethical Guidelines for Research Involving Human Participants upang isama ang mga panuntunang ginagamit natin dito sa Pilipinas (tingnan ang Elements of Research Ethics sa pahina 14), na binuo para sa impormasyon ng mga mananaliksik, ethics committee, sponsor o taga-pondo, at iba pang mga grupo. Dahil ang kasalukuyang seksyong ito ay nilayon na tulungan ang mga kalahok sa pananaliksik para maunawaan ang nilalaman ng dokumento ng pahintulot, ang listahang iyon ay ginawang simple at madaling maintindihan (maaring ibahin ang pagkakasunod-sunod) sa sumumusunod na listahan:

121.1. Sino ang nagpopondo o sponsor ng pag-aaral?

121.2. Ano na ang kaalaman o karanasan tungkol sa pinag-aaralan? Saang mga bansa ginawa o ginagawa ang pag-aaral na ito?

121.3. Sinu-sino ang at anu-ano ang responsibilidad ng mga mananaliksik? Kung sakaling nagkaroon ng 'injury' habaang kasali sa pananaliksik, sino ang mananagot?

121.4. Anu-ano ang mga responsibilidad ng mga kalahok?

121.5. *Anu-ano ang mga Karapatan ng mga Kalahok, tulad ng karapatang tumanggi?* (tingnan ang Bill of Rights in Health Research, Studies, and Clinical Trials, Appendix Y)

121.6. Anu-ano ang mga hakbang na pagdadaanan ng mga kalahok?

121.7. Ilalagay ba ang mga kalahok sa iba't ibang grupo o pamamaraan ng pag-aaral kung saan ang pagtatakda ay random o ala swerte?

121.8. Ano ang mga panganib na maaring idulot ng mga pamamaraan sa pag-aaral?

121.9. Gaano katagal ang pakikilahok?

121.10. Mayroon bang gastos ang pagsali?

121.11. Mayroon bang matatanggap na kabayaran ang mga kalahok?

121.12. Sino ang mananagot kung sakaling ang kalahok ay mapahamak o magkaroon ng pinsala?

121.13. Paano pangangalagaan ang mga personal na impormasyon na makukuha sa mga kalahok?

121.14. Mayroon bang ibibigay ang mananaliksik na mga benepisyo pagkatapos ng pag-aaral? Halimbawa ay gamutan, pagsama sa mga support groups at impormasyon tungkol sa resulta ng pagaaral

121.15. May plano bang gamitin muli sa ibang proyekto ang mga impormasyon (o kaya bio-specimen) galing sa mga kalahok pagkatapos makumpleto ang kasalukuyang proyekto? Paano itatabi o itatago ang mga impormasyon? Paano ang Sistema ng pagkuha

sa nakatagong impomasyon (o bio-specimen) upang ito ay gamitin muli?

121.16. Ang pag-aaral ba ay aprubado ng isang research ethics committee (REC) na awtorisado ng Philippine Health Research Ethics Board (PHREB)?

122. Ang mga kalahok ay dapat na may kakayahang maunawaan ang mga impormasyon tungkol sa pagsali.

122.1. Anong wika ang ginamit sa maalam na pahintulot?

122.2. Madali ba itong maunawaan ng mga kasali?

123. Maaaring magbigay ng maalam na pahintulot ang mga sumusunod:

123.1. Ang mga kasali mismo, kung sila ay:
123.2. Nasa hustong edad na (18 pataas);
123.3. May malinaw at tamang pag-iisip;
123.4. May kakayahang intindihin ang pagsali sa pag-aaral; at
123.5. Ang mga kinatawan ng kasali, kung walang kakayanan ang mga kasali na magbigay ng maalam na pahintulot, tulad ng:

123.5.1. Magulang (kung bata)
123.5.2. Asawa
123.5.3. Kinatawan ayon sa batas

124. Ang mga kasali o ang kanila kinatawan ay maaaring humingi ng karagdagang impormasyon mula sa mga sumusunod kung sila ay may agam-agam o katanungan ukol sa nilalaman ng pahintulot mula sa mga namamahala ng pag-aaaral. Ang mga namamahala ay maaaring ang:

124.1. Doktor (kung ang pananaliksik ay clinical trial)

124.2. Mananaliksik (kung hindi naman clinical trial)

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

Community Participation

125. Community participation is not only an ethical consideration but also has practical value. It aims to involve the communities themselves in the various aspects of the research and development process. Such a participatory process with the community is a continuum that includes community consultation in protocol development, appropriate information disclosure, informed consent, protection of confidentiality, right of dissent, community involvement in the actual conduct of research, and the sharing of benefits (Weijer & Emanuel, 2000). Community participation provides a proactive character in the research and establishes a symbiotic relationship in knowledge production.

126. Researchers shall consider actively engaging 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).

127. Community consultation shall be seriously taken into consideration when:

127.1. The study involves established community practices;

127.2. The results of the study may impact the health and welfare of the community constituents; or

127.3. The study outcome may bring economic benefit to the community.

128. Involvement of a community representative in the study team may be required when:

128.1. There is a risk that the study procedures may be disrespectful of community traditions and practices; or

128.2. The community itself requests representation in the ownership and outputs of the study.

129. The REC may invite a representative from the community during deliberations.

Guidance on Community Engagement and Gender Inclusivity in Research

Community participation in research is a broad description of all types of activities and all forms of contributions (e.g., source of information, collection of data, use of facilities, validation of results) of the community. It occurs in the conduct of a study that seeks to better understand and develop solutions to a health or social problem in the community. Community engagement in research refers to the deeper and meaningful involvement of community leaders and members in identifying the problem, validation of results, formulation of solutions, action implementation, and establishment of a monitoring system. Community engagement in research is a process of inclusive and equitable participation and makes special reference to gender inclusivity as equitable participation of different gender identities in the community.

This Guidance on Community Engagement and Gender Inclusivity is a component of Project ID P21-003, which received financial support from TDR, Special Programme for Research and Training in Tropical Diseases, co-sponsored by UNICEF, UNDP, the World Bank, and WHO.

130. Trust and respect between the community and the researcher shall be the foundation of community engagement and participation. To show respect when engaging with communities requires an acceptance that customs and cultures may be different and that researchers should behave in a way that does not offend.

131. In identifying the research topic or question, the researcher shall ensure its relevance to the well-being of the community and

the health and social challenges of the community. The researcher's agenda shall not be the primary driver. The needs of the local community shall be given priority. The health and social issues shall be determined by consultation with knowledgeable community members or based on public records. Equitable participation of different gender identities in the community in these consultations should be ensured.

132. The degree of Involvement of the community shall be described in the research design based on the SMART research objectives. Community preferences for engagement strategies shall be considered before ascertaining the degree of involvement.

133. The conceptual framework, research design, criteria for selection of participants, data collection methods, and needed community resources (both human and physical) shall be explained, fully reviewed, and discussed (rather than just presented) to the community officials/elders and concerned citizens. This will facilitate understanding and support.

134. Potential benefits and possible risks to the participants, their families, the community, and the environment shall be clearly and fully discussed with community representatives. These then shall be addressed for maximization and mitigation, respectively.

135. Researchers shall pay attention to community dynamics when seeking informed consent. Informed consent shall be obtained from everyone, but there may be another level of consent at the community level, which needs to be considered. For example, some communities require the approval of elder family members or clan heads before individual consent is given.

136. Community volunteers, if necessary, shall be identified through a transparent and unbiased process, and such volunteers shall be properly remunerated for services rendered. Equitable representation of gender identities in the community shall be observed.

137. It is strongly recommended that a barangay official/barangay committee representative be designated to provide oversight for the project. Selection of the barangay official of barangay committee representative should be made in consultation with community elders/officials and concerned citizens.

138. There should be communication and feedback mechanisms to ensure openness and 2-way communication throughout the study and beyond, including establishing a user-friendly complaints procedure

139. All processes shall be properly documented for authenticity and transparency.

140. The REC may invite a representative from the community during deliberations.

141. Ownership of data shall be agreed upon, and possible co-authorship of community members shall be discussed accordingly.

142. Research results will be validated at the end of the study through public presentation and discussion. The presentation shall be conducted in a language that is understandable and meaningful. Representation of gender identities in the community shall be observed.

143. Appropriate recommendations shall be shared with the community for adoption by and support of concerned barangay officials, community leaders, and constituents.

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. Research shall be aligned with the Harmonized National R&D Agenda (HNRDA) to ensure that the results of science and technology endeavors are geared towards and are utilized in areas of maximum economic and social benefit for the people.

3. Health research shall adhere to the National Unified Health Research Agenda (NUHRA), and the Regional Unified Health Research Agenda (RUHRA) must be firmly grounded through priority-setting.

4. Government funding agencies shall seriously consider the proposal's conformity with their respective research priorities.

Externally-Funded Collaborative Research

5. 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

6. The conduct of biomedical or behavioral research shall be in a manner that minimizes potential harm to the environment.

7. Research involving biological and hazardous materials, including those that involve genetic modification and manipulation of microorganisms and animal and plant tissue cells, must be reviewed and approved by a biosafety committee, the National

Committee of Biosafety of the Philippines (NCBP), before implementation.

Welfare of Animals

8. The use of animals for research shall comply with the Animal Welfare Act of 1998 (RA 8485), amendments to its certain sections (RA 10631), 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, 2nd edition, 2002 developed by the Philippine Association for Laboratory Animal Science (PALAS).

SPECIAL GUIDELINES

ETHICAL GUIDELINES FOR SOCIAL RESEARCH

Social research covers a wide range of academic disciplines with a host of interrelated and various theoretical and methodological approaches, even within a particular field of study. The human aspect of social science research makes it a complex endeavor and may lead to differences and divergences in ethical considerations and requirements. It typically takes place in the research participants' communities, homes, and workspaces. It involves in-person interactions that reveal internal or intimate aspects of the person, such as attitudes and behaviors about social relationships, family and work life, and lifestyle. Given this more immersive aspect of social research, ethics demands that social scientists conduct their research in ways that privilege and protect the safety and well-being of participants and acknowledge the participants' and their communities' indispensable contributions to scholarship. It is the responsibility of researchers to be aware of the ethical issues involved in their work, anticipate possible ethical concerns, craft protection strategies, and make the necessary referrals to RECs, others with relevant expertise, the appropriate organizations, and agencies if the need arises.

All social research must adhere to the General Guidelines, based on international ethical guidelines for research. These guidelines aim to encourage researchers to think through the ethical issues that may arise during the entire research process. They should 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 reflect on the above principles further critically, the guidelines contain references to ethics codes and legal norms relied upon as their basis.

Some theoretical perspectives and research methods use inductive logic to produce or develop theories and hypotheses during the fieldwork. It will not be immediately possible for researchers using such methods to provide RECs with specifically formulated research questions and instruments and to identify all possible participants whom the researcher may encounter during fieldwork. RECs shall recognize such perspectives and methods by

formulating procedures and mechanisms that allow for flexibilities in research design and modifications of topic focus as the research is carried out. For instance, protocol amendments, periodic monitoring, and continuing review are mechanisms that permit researchers and RECs to pursue ethical standards beyond the initial approval. Researchers using said perspectives and methods must deal with ethical issues during the protocol's continuing review and respond to different circumstances that may arise during the study.

General Issues

While most ethical concerns in social research are similar 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. Hence, it is critical that researchers seriously consider the various life situations of participants to address their concerns and issues adequately and more realistically.

The traditional relationship between the researchers and the people they study may at times involve an imbalance in power in favor of the researcher. The researcher may have greater access to resources than the people they study, especially if the sample population is a marginalized group. Researchers may unknowingly take advantage of this imbalance when seeking to enter communities, households, and the personal and social lives of participants.

Therefore, the burden is on the researcher to be reflexive in acknowledging and correcting imbalances in relating with respondents that are biased in favor of their objectives or that undermine the freedom and contributions of the participants. Research participants can be viewed rather as co-producers of knowledge, and researchers should undertake measures to clarify and balance the roles of all stakeholders involved in the study. An example of these measures would be to increase the level of participation

of the communities and persons being studied in designing the study or validating the study results. 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.

Respect for Persons in Social Research

In a study involving human subjects, a researcher enters a relationship with participants who are to be treated with respect, care, and empathy. This approach is fundamental in social research and incorporates at least two ethical convictions: first, that individuals have inviolable dignity and rights and hence, should each be recognized and treated as unique and autonomous, and second, that persons lacking or bereft of autonomy deserve preference and protection. This is why in all cases and situations, the well-being of every person takes precedence over scholarly advancement. Nothing can justify using a person merely as an instrument to develop, broaden, or contribute to knowledge.

As relational beings, researchers and participants live in a community, the good of which they ought to foster and promote. Researchers are to always relate to their research participants as *kapwa-tao*, a fellow human being with whom they have a common dignity, rights, and duties and with whom they are to practice reciprocity and solidarity with each other.

An essential way in which this respect for persons is expressed by researchers is through the informed consent process.

Informed Consent Process

1. A prospective participant is given a voluntary choice to participate in a study after being fully informed about its nature, purpose, procedures, and its potential risks and benefits. In some cases, their choice is hampered by their life situation or by other persons. For example, when potential respondents are under the authority of other persons who may want to provide consent on their behalf (e.g., prisons, schools, workplaces) and where their participation is important, researchers ought to provide measures that will empower them to be part of the study. Researchers need to ensure that individual consent is made

possible and that there are no negative consequences to refusing to participate in research.

2. The researcher shall dialogue with potential research participants about the research. They shall discuss all the important elements of the protocol with them, including 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. In addition, a researcher is to disclose their assumptions about the research to the research participants to allow for informed participation and collaboration and to address possible conflicts of interest.

3. Researchers shall take the necessary steps to ensure that participants truly understand their research involvement and what it demands of them. They shall explain the research protocol to participants and, if applicable, their community in a language and manner that enables their exercise of autonomy. This involves delineating sufficient space and time for the informed consent process prior to data collection and may involve community orientations, home visits, consultations, and the like. The researchers must spend sufficient time with their participants and engage them in dialogue. They are to make them understand that they will not be taken advantage of and that a healthy researcher-participant relationship is paramount in the research process. Openness and transparency in this regard are vital. In light of the questions and comments of the participants in the dialogue, the researcher may have to modify their protocol to be more responsive to their concerns and welfare.

4. 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 ensure that participants are aware that they can refuse to participate or withdraw at any time from the research without penalty or refuse to answer a question or questions during 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 participating.

5. Where there is a psychological or social intervention that is being tested that is 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 the benefits of the social intervention, which may induce individuals or communities to participate.

6. Informed consent must also be obtained not only regarding the collection of personal information and research-related data but also about the dissemination, disclosure, storage for future use, and sharing of such information. Research participants have the right to withhold consent concerning the dissemination or disclosure and storage for future use of such information, including, for example, statements made by participants, recorded interviews, photographs, and videos. They also have the right to know to whom such information will or may be shared. Their well-being ought to be the researcher's primary consideration in the dissemination or sharing, storage, and processing of research-related information. As mentioned in the general guidelines, even when participants have granted consent for the disclosure of their personal information, researchers must see to it that participants will not suffer harm (e.g., legal liabilities, reputational harms, uninsurability). Researchers may wish to refer ethical dilemmas or legal queries to the REC or others with expertise.

7. In situations where the participants have diminished capacity to decide for themselves, provisions 1–6 above shall apply to the legal guardian or legally authorized representative (*see sections on Research Involving Minors or Children and Research Involving Older Persons*) who is responsible for their best interests and welfare, without prejudice to the individual participant's right to provide informed consent should they be capable of doing so.

Waiver of Informed Consent

8. The informed consent process may be waived in specific research contexts, such as:

8.1. Archival research involving publicly available documents;

8.2. Research that uses the method of naturalistic observation (often described as the "covert" method) in data collection. Naturalistic observation does not necessitate informed consent if the activities or behaviors observed are public so that any person can observe them without violating principles of confidentiality or privacy. It ought to be emphasized that the data gathered through this method should be kept confidential, and the use of data should maintain the anonymity of those observed.

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 (if risks to participants are likely). Moreover, the use of this method requires that the researcher provide:

8.2.1. A thorough justification for its use;
8.2.2. A plan for how the data collected will be used; and
8.2.3. A mechanism to ensure confidentiality and anonymity of observed individuals and their data.

In some naturalistic observations, disclosure about the research data collection to the participants is done after data collection. In that case, informed consent concerns the use of collected data.

Waiver of Signed Informed Consent

9. Under the General Guidelines, informed consent is documented through the signature of the participant or their legally authorized representative (LAR) on the informed consent form (ICF). A documented informed consent may be waived (with the approval of the REC) if:

9.1. 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

9.2. 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

9.3. In cases where the documentation requirement is waived, the REC may require the researcher to provide participants with a written statement regarding the research.

10. Under certain circumstances, it is appropriate to obtain informed verbal consent. Participants unfamiliar with research 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, such as by a representative (who is not part of the research team) authorized by the participant or community. Alternative means of documenting consent, such as using initials, fingerprints, or voice recording, must be justified and approved by the REC.

Waiver of Some Elements of the Informed Consent

11. Some or all the elements in the informed consent may be waived or altered (with the approval of the REC) if all of the following conditions are met (*see Waiver of Informed Consent, page 21*):

11.1. The research presents no more than minimal risk;
11.2. The alteration will not adversely affect the rights and welfare of the participants;
11.3. The research cannot be practicably carried out without the waiver or alteration; and
11.4. The participants will be provided with additional pertinent information after their participation (whenever appropriate).

Withholding of Information

12. Withholding information in the informed consent process may be necessary to control biased responses of participants (i.e., demand characteristics; good subject phenomenon). This may be done if all the following conditions are present:

12.1. It is justified by the prospective scientific, educational, or applied

value of the study;

12.2. The risk is minimal, and the potential harm is reversible;

12.3. No equally effective design or method can be used; and

12.4. Debriefing is performed as soon as appropriate.

Vulnerability in Social Research

13. Social researchers must recognize the potential and actual vulnerability of their research participants, that they care for them, and that "the personal integrity of such individuals is respected" (Universal Declaration on Bioethics and Human Rights, art. 8). Such vulnerability may prevent (prospective) participants from making a decision that is in the participants' or their community's best interests and provide voluntary informed consent. Moreover, the contextual vulnerability of participants may more easily expose them to harm, exploitation, and manipulation. Hence, a researcher must design a protocol that shows an awareness of and compassion for such vulnerabilities, including measures that safeguard and prioritize the well-being and safety of vulnerable human participants, such as indigenous peoples, minors, differently abled persons, and women in poverty, and refraining from unduly coercing and influencing their research participation.

14. The table below shows the various categories of the potential vulnerability of research participants that are to be considered by researchers in obtaining informed consent:

Table 1. Potential vulnerability: Research ethics taxonomy (adapted from Lahman, 2018)

Potential Vulnerability	Researcher Question	Examples
1. Cognitive	Does the participant have the capacity to deliberate about and decide whether to participate in the study?	Persons with cognitive impairment, minors

2. Judicious	Is the participant liable to the authority of others who may have an independent interest in that participation?	Students, military and police personnel, persons deprived of liberty, employees
3. Deferential	Is the participant given patterns of deferential behavior that may mask an underlying unwillingness to participate?	Low-in-hierarchy workers, less educated/literate
4. Medical	Has the participant been selected because they have a serious health-related condition for which there are no satisfactory remedies?	Patients*
5. Allocational	Is the participant lacking in important social goods that will be provided because of their participation?	Poor, homeless, indigenous, and other marginalized groups
6. Infrastructural	Does the political, organizational, economic, and social context of the research setting possess the integrity and resources needed to manage the study?	Sites of disaster or political instability, where there is a lack of ethics oversight from mentors, colleagues, REC

7. Gender	Is the potential participant in a situation where their sex category or their sexual identity is a determinant of the allocation of power, opportunities, and privileges that impacts their capacity to protect themselves from risks of harm?	Women in poverty; LGBTQI+

** Those who are in ICUs and are terminally ill*

Research with Indigenous Peoples

15. The researcher must be aware of the special requirements and considerations in conducting research with and obtaining free and prior informed consent from indigenous peoples (IPs) pursuant to the Indigenous People's Rights Act (IPRA). 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 Involving Indigenous Peoples)

Consent of Minors

16. 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 by a third party who has no unresolved conflict of interest. (See Guidelines for Research Involving Minors or Children)

Other Groups Potentially Vulnerable to Undue Coercion and Influence (see Table 1)

17. 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:

17.1. *When students are "required" to participate in faculty research, be part of the subject pool, and in 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 participate in studies. The benefit of research participation shall not be so large as to remove students' freedom to voluntarily decide to participate. Their participation should only be allowed if it serves the purpose of achieving specific course objectives.

17.2. *When students are enjoined or required to collect data for faculty or a class or 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.

17.3. *Soliciting the participation of prisoners and other institutionalized persons or 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, to have their well-being prioritized, and to be treated fairly in it.

17.4. *When consent or permission is initially sought from individual gatekeepers, such as community leaders and officials or 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).

Community Research

18. 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.

19. The researcher shall conduct proper consultation with community leaders and stakeholders before initiating the research. If relevant, it must be closed to the community during consultations before data collection that observations will be done of particular public scenes during the research. If the research design requires 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.

20. In no case shall the researcher collect data through naturalistic observation if the community forbids it. There are communities (e.g., indigenous communities) that consider certain public activities (as defined above) to be sacred and certain behaviors of outsiders taboo.

21. The researcher shall recognize and respect the customary or culturally valued practice of decision-making in the community while noting permissible waivers or modifications of the informed consent process. Ideally, the giving of waivers and allowing modifications are to be done in dialogue with the community and their consent.

Beneficence and Non-Maleficence in Social Research

In addition to respect for persons, beneficence and non-maleficence are integral ethical principles in social research that involves human participants. Researchers are the ones who need and are indebted to them and not the other way around. Hence, research with human participants should be beneficial to them and their community. It must have a positive risk-ratio analysis. Adequate and necessary research-related care is to be provided to participants during and, if necessary, after the study to safeguard their welfare.

Management of Risks and Harms

22. Consent to participate in a study does not absolve researchers from

their obligation to protect their participants; rather, they shall ensure that risks or harms to the participants in their study are minimized as far as possible, particularly if the research deals with sensitive issues or topics, such as participants' sexual behavior or illegal activities. The determination of those risks or harms is preferably participatory, performed in consultation with participants and those with relevant expertise. The result of this consultative process might necessitate changes in the research design to better protect human subjects.

23. In research protocols where risk is not eliminated or mitigated, the benefits of conducting the study must clearly outweigh these potential risks.

24. Researchers ought to maintain the full confidentiality of all information and the anonymity of participants by instituting the necessary protection procedures in all research materials. "Participants should be informed of any potential limitations to the confidentiality of any information supplied" (UNESCO Code of Conduct Social Science Research no. 14) except when participants, after having been informed of foreseeable risks, consent to the disclosure, dissemination, storage for future use and sharing of their personal data and other materials collected during the research (e.g., photographs, recordings). Notwithstanding such consent, it is incumbent upon researchers to prevent foreseeable harm from befalling participants. As stated in the general guidelines, researchers are encouraged to refer ethical dilemmas or legal issues to the REC or other experts.

25. 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. The researcher is to avoid any undue intrusion into the lives of participants.

26. The protocol shall include referral and reparation strategies where there is potential or actual harm, no matter how low the likelihood or severity. The referral or reparation procedures must be concrete, specific, realistic, and not general statements in the protocol and the informed consent process or documents and must be included in the budget and

timeline of the study. When the research causes psychological stress to the research participants, there shall be provision for debriefing or counseling.

27. The researcher shall have the necessary expertise and competency to undertake the study (e.g., education, training, and experience in the use of the specific method and subject matter). Competency shall also include sociocultural sensitivity to the population and community under study and awareness of the ethical issues involved.

28. In case unforeseen situations arise during the study that requires its temporary or permanent cessation, researchers shall discontinue the study completely or resume it when the risk of harm is at a reasonable level after due consultation with participants, their community, and the REC. Researchers shall undertake appropriate measures to prepare the research participants or community for the exit of the study.

29. The researcher shall inform participants of any increased levels of risks or harms as the study proceeds and exercise the necessary prudential judgment that prevents immediate harm to them. The researcher shall also report those increased levels to the REC and await the REC's advice before continuing the study.

30. Researchers should consider the different dimensions or categories of risk beyond the physical or medical. Table 2 shows examples of risks and corresponding protection strategies that may be incorporated in a social science research protocol:

Table 2. Risk categories and protection strategies

Risk Category	Example of Risks	Examples of Protection Strategies
Physical	Fatigue	Inclusion of rest breaks in the protocol; supervision of a physical trainer
Social	Stigma	Procedures to safeguard the confidentiality of data; pseudonymization or de-identification of materials and data at the soonest possible time; campaigns and materials to reduce stigma

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 the confidentiality of data; referral protocol
Economic	Loss of job or advancement	Confidentiality of data (non-disclosure to the employer)

31. 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 their progress and final reports, to the REC.

32. 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

33. 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.

34. 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 and at the same time as the experimental variable, the withholding of the intervention to the control group shall only be for the duration of the experiment.

35. 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.

36. 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. It is advised that a benefit-sharing agreement be made between the researcher and the

participants. In cases when the research output is a communal item such as songs, healing rituals, or legends, the agreement may have to be forged with the community.

37. 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.

38. Potential legal repercussions in the research for the researcher or research participants shall be carefully identified in the study proposal, and steps are undertaken to mitigate or eliminate such repercussions. The researcher is to provide adequate legal assistance to research participants if they encounter legal problems because of their research participation.

Justice in Social Research

39. In a society marked by injustice in various forms and degrees, it is even more important that social research be characterized by justice and contribute to human flourishing (*eudaimonia*), particularly in the disadvantaged and marginalized sectors of society. Social researchers are expected to be in genuine solidarity with their research participants for whom they are responsible and without whom there is no research.

    39.1. The principle of justice demands that all those who will benefit from the study and its result be allowed to participate in and contribute to it and, in the process, share in the burdens and fruits of research.

    39.2. While it might be more expedient to invite human participants from particular sectors of society (e.g., the poor and other marginalized groups), researchers are to exercise fairness and equity in crafting their protocol and in the conduct of research.

    39.3. In the design and conduct of their study, researchers must always consider the rights of all stakeholders who are part of it.

It is important that in situations in which there is a conflict of interests between them, priority must be accorded to research participants, especially those who are vulnerable whose rights and interests need to be furthered.

39.4. Researchers should provide appropriate and just compensation to their research participants and reimburse them for reasonable research-related out-of-pocket expenses. If they are not provided compensation or reimbursement, it must be explained why in the protocol and the informed consent form. For participants who may not lose any cash income due to their participation in the research because they are not wage/cash earners (e.g., mothers) but whose life situation is such that their participation in the study will impose an additional burden on them (e.g., waking up earlier to complete the household chores and to attend the focus group discussion), the researcher must see to it that they are justly compensated.

39.5. While research is intended to generate new and various ways of understanding and interpreting our world, social research must contribute to the promotion and defense of justice in its diverse manifestations in research, in one's discipline, and in one's community. Constitutive of this task is the recognition that research participants are not mere objects of one's study, but they and their communities are research partners who are the researcher's co-producers of knowledge. As partners in knowledge production, their roles must be properly acknowledged.

39.6. In the interest of justice, when designing a protocol, researchers ought to consider not only the objectives of the research and its intended applications but also the possible use of one's research for unethical purposes, such as the stigmatization or discrimination against minority or vulnerable groups and provide an appropriate risk mitigation strategy (European Commission, 2018).

39.7. Researchers should consider and anticipate the effects or unintended consequences of their research on third parties. In

certain cases, researchers gain access to information that may have an impact on persons other than their participants and their community and may make them unreasonably exposed. The welfare of those parties must be considered vis-à-vis the research objectives as a matter of justice. If the information about those parties is deemed pertinent to the study and will be used by the researchers, it is necessary to also obtain the consent of those parties out of fairness to them. They must be accorded the opportunity to participate in it even if their participation is to be done in this manner.

39.8. The welfare and rights of third parties are to be duly protected in studies that are autoethnographic and autobiographical. While researchers are at the same time the participants of such studies, the protocols are to undergo a regular review process. For instance, it is inevitable that in autobiographical narratives, other persons and their personal stories will be mentioned in relation to the researcher's narrative. In this case, the REC ought to make sure that there is due regard for the privacy of individuals who become part of the researcher's story.

39.9. Researchers should inform their participants not to divulge information that are outside the scope of their study, and which appear to incriminate the participants so far as is reasonably practicable. This is intended to avoid the dilemma of the researcher whether to preserve the confidentiality or to disclose the information to authorities. Researchers must make it clear to participants of their intention and reasons for disclosure. “As a rule, criminal activity witnessed or uncovered in the course of research must be reported to the responsible and appropriate authorities, even if this means overriding commitments to participants to maintain confidentiality and anonymity” (European Commission, 2018). The decision to report a criminal activity that is inadvertently discovered during research must always promote justice and consider the common good. Due process is always to be respected.

39.10. As a matter of justice, research that is deemed unethical in a foreign country ought to be rejected in our own country. Local RECs are to ensure that protocols from foreign researchers and institutions are meticulously screened and evaluated to avoid the possible exploitation of local participants. Stringent ethical research standards are to be always applied to such protocols.

ETHICAL GUIDELINES FOR CLINICAL RESEARCH

Clinical research encompasses studies involving human participants designed and intended to produce knowledge for understanding disease, the prevention, diagnosis, treatment of illness, and health promotion. In this 2022 edition of the National Ethical Guidelines, guidelines for case reports have also been included. This is to guide researchers and REC members in writing and reviewing case reports.

In clinical research, the term "clinical" indicates that the study has moved up the development cycle from basic research (e.g., in-vitro laboratory or animal research) to one that can be done in humans, inclusive of interventional and observational studies. Although the term "clinical research" may encompass a broad category of studies with different designs, the focus of this section is on clinical trial research. 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 in human subjects intended to discover or verify, 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/**or** efficacy" (ICH-GCP, 2018). The terms clinical trial and clinical study are synonymous. Drug trials generally consist of phases I, II, III, and IV.

Clinical trials may also involve medical devices and in-vitro diagnostic medical devices (IVD). “Medical device” refers to any instrument, apparatus, implement, machine, appliance, implant, reagent for in-vitro use, software, material or other similar or related articles that is, intended by the manufacturer to be used, alone or in combination, for human beings for one or more of the for the specific medical purpose(s) of diagnosis, prevention, monitoring, treatment or alleviation of disease (orthopedic implants, intra-ocular lenses); alleviation of or compensation for an injury (devices used in rehabilitation medicine such as transcutaneous electrical nerve stimulator); investigation, replacement, modification, or support of the anatomy or of a physiological process (thermometers, insulin pumps); supporting or sustaining life (ventilators, pacemakers); control of conception (intra-uterine device or IUD); disinfection of medical devices (ultraviolet lamps); providing information for medical or diagnostic purposes by means of in vitro examination of specimens derived from the human body (glucometers); and which does not achieve its primary intended action in or on the human body by pharmacological, immunological or metabolic means, but which may be assisted in its intended function by such means (Global Harmonization Task Force Final Document GHTF/SG1/N071:2012).

The IVD, on the other hand, refers to a medical device, whether used alone or in combination, intended by the manufacturer for the in-vitro examination of specimens derived from the human body solely or principally to provide information for diagnostic, monitoring, or compatibility purposes. IVD medical devices include reagents, calibrators, control materials, specimen receptacles, software, and related instruments or apparatus or other articles and are used, for example, for the following test purposes: diagnosis, aid to diagnosis, screening, monitoring, predisposition, prognosis, prediction, determination of physiological status (Global Harmonization Task Force Final Document GHTF/SG1/N071:2012).

The clinical investigation of medical devices parallels those of drugs and involves assessing risks or hazards versus benefits. Although not yet implemented (as of September 2021), the guidance for registration of medical devices in the Philippines is found in AO 2018-002 entitled, “Guidelines Governing the Issuance of an Authorization for a Medical Device based on the ASEAN Harmonized Technical Requirements.” The definitions and risk classifications for medical devices and IVDs found in this document follow both the GHTF guidance and the ASEAN Medical Device Directive

developed through the ASEAN Consultative Committee on Standards and Quality-Medical Device Product Working Group (ACCSQ-MDPWG) (DOH AO 2018-002). These risk classification assessments are important to determine the anticipated hazards from using these medical devices. They can be used by both the investigators and RECs as a guide in evaluating risk-benefit ratios.

The classification system of medical devices used in the Philippines follows the scheme agreed on by the ACCSQ-MDPWG, which is rule-based and consistent with the international system as given by the GHTF SG1/ N015: 2006. The classification system considers the probability of harm due to several factors (e.g., whether the technology is regarded as mature; the device type is the source of many adverse event reports; the device's manufacturer has a long experience with the device and the technology it embodies, and the device user is a layperson). The classification rules also consider whether the device is life-supporting or -sustaining; is invasive and, if so, to what extent and for how long. Other considerations are if the device incorporates medicinal products or human/animal tissues/cells; is an active medical device; delivers medicinal products, energy or radiation; could modify blood or other body fluids; and is used in combination with another medical device (GHTF SG1/ N015: 2006). Table 3 shows the classification system of medical devices and some examples.

Table 3. Classification system of medical devices and some examples

Class	Hazard level	Examples
A	Low	Bandages, tongue depressors
B	Low-moderate	Hypodermic needles, suction equipment
C	Moderate-high	Ventilators, bone fixation plate
D	High	Heart valves, implantable fibrillators

The clinical investigation of medical devices aims to demonstrate safety and performance, as well as efficacy, when applicable. Thus, clinical trials on a medical device shall show that the device performs safely and follows 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, such as orthoses or braces) are deemed to have less risk than those that are

implanted or used inside the body (endoprosthesis or metal implants in orthopedics).

Quoting AO 2018-002, “medical devices strictly for research, clinical trial, exhibit, and/or donated brand new medical devices are exempted from Notification and Registration. However, the researcher, institution, and/ or user of such devices shall apply for a Certificate of Medical Device Listing.” Such applications shall be made with the Center for Device Regulation, Radiation Health, and Research (CDRRHR), the regulatory office under the Food and Drug Administration (FDA) of the Department of Health (DOH) that oversees the regulation of medical devices in the Philippines. This is already currently being enforced by the Philippine FDA CDRRHR.

Clinical trials on diagnostic procedures and preventive measures, including vaccines, raise similar ethical concerns, especially on the informed consent process and potential conflict of interest (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. The 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 in the future. It must be noted that a significant number of vaccine trials are done on children who belong to a vulnerable population group (*see section on Research Involving Minors or Children*).

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 the national ethical guidelines and other guidelines (ICH-GCP E6 R2, 2016; CIOMS, 2016; Declaration of Helsinki, 2013).

Clinical studies should have social value and their conduct adequately justified by the fact that they address one or more of the priority health needs of the country.

1. Investigators involved in clinical trials shall be governed by the principle of clinical equipoise. A state of clinical equipoise means that, based on available data, a condition of genuine uncertainty on the part of the clinical investigators 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 treatment strategies being tested since none have been established as preferable.

2. 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

3. The protocol shall at least contain the following:

    3.1. Administrative information about the study such as researchers or investigators, sponsors, monitors, other qualified medical experts, diagnostic laboratories, and research institutions involved;

    3.2. Background information regarding the study, relevant past and current research findings and references to such information and data, and potential risks and benefits;

    3.3. Background information on the drug under investigation, reason for the indicated route of administration, dosage, **duration** of treatment, population to be studied, a declaration regarding compliance with GCP, and regulatory requirements (in case of clinical trials under FDA oversight);

3.4. Objectives and purpose;

3.5. Study design, which substantially determines the scientific integrity of the study and reliability of the data and includes the following:

3.5.1. 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);
3.5.2. Primary and secondary endpoints to be measured;
3.5.3. Measures to minimize or avoid bias (e.g., randomization and blinding);
3.5.4. Trial treatments and investigational product's dosage, packaging, labeling, and storage (for clinical trials);
3.5.5. Nature of the placebo (if applicable);
3.5.6. Estimated duration of individuals' participation in the study;
3.5.7. Discontinuation rules for the participants and the study;
3.5.8. Treatment randomization codes maintenance and rules on breaking the code;
3.5.9. Procedures for accountability for the product being investigated, placebos, and comparators, if applicable; and
3.5.10. Other sources of data.

3.6. Selection and withdrawal of research participants, inclusive of criteria for inclusion, exclusion, and withdrawal;

3.7. Research participants' therapy or treatment and respective monitoring procedures;

3.8. Efficacy parameters, and methods and timing of measurement or ascertainment;

3.9. Safety parameters, methods, timing, and procedures for recording and reporting, as well as monitoring adverse reactions;

3.10. Safety measures for research participants when they withdraw or are withdrawn from the study;

3.11. Plan for data and statistical analysis;

3.12. Information describing direct access to study data and documents for monitoring, audit, ethical review, and regulatory inspections;

3.13. Ethical considerations;

3.14. Data management and record keeping;

3.15. Financing and insurance;

3.16. Dissemination and publication plan and procedures; and

3.17. Clinical trial participants' information sheet or brochure, if applicable.

Informed Consent

4. Informed consent of adult study participants, and assent of children and adolescent participants with their parents' or legally authorized representative's (LAR) informed consent shall be obtained before the conduct of the study.

4.1. See chapter on General Guidelines for the general guidelines on informed consent.

4.2. See section on Research Involving Minors or Children on guidelines on informed consent for minors or children.

Use of Placebo

5. As a rule, participants in the control group of a therapeutic or preventive intervention trial must receive an established effective intervention (CIOMS, 2016).

5.1. An established effective intervention exists when it is recognized by the body of medical professionals for the condition under study. It includes the best-proven intervention for treating, diagnosing, or preventing the given condition and interventions that may not be the best when compared to available alternatives but are nonetheless professionally recognized as a reasonable option (e.g., as evidenced in treatment guidelines).

5.2. In some cases, established effective interventions may need further testing, especially when there are reasonable disagreements among medical professionals and investigators. Clinical trials may be warranted when the risk-benefit profile of an intervention is not favorable, such that patients might reasonably forgo the usual intervention for the condition with the advice of their physicians.

5.3. A placebo may be used as a comparator when there is no established effective intervention for the condition under study or when a placebo is added to an established effective intervention (CIOMS, 2016).

5.4. Placebo may be used as a comparator without providing the established effective intervention to participants only if all the following conditions are satisfied:

5.4.1. There are compelling scientific reasons for using a placebo (Declaration of Helsinki, 2013; CIOMS, 2016);

5.4.2. Research participants are not subjected to additional risks of serious or irreversible harm because of not receiving the best-proven intervention (Declaration of Helsinki, 2013); and

5.4.3. Research participants give free and prior informed consent. and when there are changes in the knowledge about the trial intervention that could affect their decision

to participate, their participation is validated through a re-consent procedure.

Protocol Amendments

6. Any amendment(s) to the protocol shall be submitted to the REC and FDA for review and approval before implementation.

Medical Treatment versus Clinical Research

7. The principal investigator should provide strong justification for combining clinical research with medical care and assure that the study participants' participation will not adversely affect their health.

8. The difference between medical therapy and research should be clear throughout the conduct of a clinical study. The research participant should be made to understand that in a clinical trial, the investigational product (drug or device) is experimental and that its benefits are currently still being studied. On the other hand, the drug (or device) is already accepted by the medical community as safe and effective in medical treatment.

9. It shall be clearly defined in the informed consent which aspects of the clinical trial are part of the standard of care, and which are components of the study, and thus, experimental.

10. It shall be clearly explained to study volunteers that participation in the research will neither provide nor entitle them to better treatment (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. All clinical research shall comply with the necessary local regulatory requirements for the conduct of clinical trials. The DOH and the FDA have several AOs and circulars that define the processes involved in clinical trial applications, the criteria for their approval, and the regulations on the conduct of clinical trials. These include DOH AO 2020-0010: Regulations on the Conduct of Clinical Trials for Investigational Products (that supersedes AO 46-a and 47-a, AO 2006-021, 2011-0009, and FDA circular no 2012-007) and FDA Circular No. 2020-0029 Guidance on Applications for the Conduct of COVID-19 Clinical Trials.

14. The investigator(s) and sponsor shall be responsible for complying with all applicable regulatory requirements of the 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 preclinical 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 the Recruitment of Women of Reproductive Age in Clinical Trials

17. The proportion of women recruited into clinical trials has been historically low due to the potential for pregnancy, creating a knowledge gap regarding the use of drugs in this population. There is a need to prevent pregnancy in those who are sexually active to prevent potential harm to the fetus. On the other hand, mandated and required contraceptive methods (e.g., double barrier or combined oral contraceptives and intrauterine devices) may be out of proportion to

the risks. They may be burdensome, potentially violating the principle of respect for autonomy and beneficence (ACOG, 2015).

18. It is appropriate for investigators and sponsors, with the approval of the REC, to require a negative pregnancy test result as a criterion for participation in research when the research may pose more than minimal risk to the fetus.

19. Likewise, when it is anticipated that the research may pose more than minimal risk to a fetus, the informed consent process should involve a review of contraceptive options and their efficacy. Access to effective forms of contraception should also be provided. However, mandating the use of contraception among women who are not sexually active violates the principle of respect for persons; thus, these women should still be considered for inclusion in clinical trials.

20. Research among pregnant women should be performed only if relevant to their specific health needs during pregnancy, for the fetus, or pregnant women in general. Additionally, the clinical trial is supported by reliable evidence from animal experiments, particularly on the risks of teratogenicity and mutagenicity.

21. Researchers and RECs shall ensure that prospective pregnant participants are adequately informed about the risks and benefits to themselves, their pregnancy, the fetus and their subsequent offspring, and their fertility, of participating in clinical research.

Research on Medical Devices, Diagnostic Procedures, and Preventive Interventions

22. Randomized trials for medical devices are not usually indicated.

23. Review of clinical study protocols on medical devices shall include an expert consultant, such as a bioengineer or a biophysicist, who shall investigate the material and design, as well as the electrical safety of the device.

24. The research participant information sheet shall contain information on procedures to be adopted should the research participant decide to withdraw from the study.

25. Safety precautions in introducing a medical device (e.g., the potential for radiation exposure, puncture, or injury) should be clearly described in the protocol and followed.

26. Trials of critical medical devices such as implants that may present a potentially serious risk to the participant's health, safety, or welfare 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.

27. The follow-up period for medical device trials is longer than drug trials and may last for several years, especially for implantable devices.

28. 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 because of the 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

29. 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.

30. Clearance from the Philippine Nuclear Research Institute (PNRI) that the level of radiation from the radiopharmaceutical product is within the allowable limits for human use, shall be secured and submitted to the REC for consideration.

31. Measures to safeguard the health and safety of research participants and others who may be exposed to radiation shall be described in the protocol.

32. Adequate provisions shall be ensured for detecting pregnancies to avoid risks of exposure to the embryo.

33. RECs shall require that the informed consent document includes the information that participation will involve exposure to radiation, which may have an impact on significant others and possible genetic damage to their offspring.

Vaccine Trials

34. Women of child-bearing potential 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 because of failure of contraception shall be reported and monitored for abnormalities during a follow-up period determined as appropriate by the REC.

35. Live attenuated vaccines contain a version of the living virus that has been weakened so that it does not cause serious disease in people with healthy immune systems. However, they have the very rare potential to revert to pathogenic forms and cause illness in vaccinees or their contacts. For vaccine trials using live attenuated microorganisms, the researcher shall:

    35.1. Inform the participants and legal guardians about exposure to the specific infection for which the vaccine is being tested; and

    35.2. Ensure provision of the necessary care for the affected participants.

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).

37. DNA vaccines and vaccines developed using recombinant DNA technology shall have prior clearance from the Biosafety Committee of the institution where research will be done. If none, such shall be

referred to the National Committee on Biosafety of the Philippines (NCBP).

Research in an Emergency Room or ICU Setting

38. The well-being or safety of the critically ill patient shall be **of** paramount consideration in the emergency room or ICU setting. No research shall stand in the way of **administering the standard of care** to critically ill patients.

39. In cases where the research participant, by 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 before enrollment in the clinical study.

40. When the LAR is unavailable when the research participant is brought to the hospital, the principal investigator must exhaust all means to locate the LAR and document this process within the therapeutic window.

41. The protocol shall describe appropriate procedures to inform the LAR of the participant's inclusion in the study and their right to discontinue participation in the research at the earliest feasible opportunity.

42. Once the research participant's sensorium improves during management and can give informed consent, the researcher or investigator should seek consent from the research participant themselves on whether to continue with the study. If the research participant decides not to continue, they shall receive the standard treatment due to them.

43. In rare instances, the REC may grant exemption or waiver of the informed consent requirement, provided all the following conditions exist:

    43.1. The research participant has a life-threatening condition for which available treatments are unproven, lacking, or unsatisfactory;

43.2. Prospect of direct benefit to the research participants;

43.3. When research participants are unable to give consent (e.g., impaired sensorium), and no LAR is present or cannot be located;

43.4. The risks associated with the investigation are reasonable in relation to what is known about the emergent condition; and

43.5. 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.

Clinical Trials during Epidemics, Disasters, and Emergencies

44. Ethical considerations in clinical trials during epidemics, disasters, and emergencies are discussed in the section on Research During Disasters, Calamities, Epidemics, or Complex Emergencies.

Referral Fees

45. Payment of fees for the 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.

46. The recruitment process and possible payment of fees shall be subject to approval by the REC.

Publication of Results of Clinical Studies

47. 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.

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

49. 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.

Post-Trial Responsibilities of Sponsors and Investigators

50. The sponsor and investigator continue to have responsibilities to the study participant even after the conclusion of the clinical trial. While the focus has been on post-trial access to the investigational product, these responsibilities of the investigator and sponsor after trial close-out are broader in scope and purpose and are still part of their responsibilities as defined by ICH-GCP.

51. The Declaration of Helsinki, beginning in 2000, advanced the concept of making provisions for post-trial access for all participants who still need interventions identified as beneficial in a clinical trial (Declaration of Helsinki). These are especially important for certain diseases with no standard medical treatment or for emerging infectious diseases where the most effective vaccines or prophylaxis are unknown. These provisions should be stated in the protocol and should be disclosed during the informed consent process for the information of the trial participant.

52. Medical care of the study participant should continue even after trial close-out. Although there is no expectation that the investigator will assume the role of the participant's physician after the clinical trial, every effort must be made to allow a smooth transition from research to standard medical therapy in the appropriate health care setting. This may involve referring back to the primary care physician of the study participant with the full endorsement of the course and outcomes of the patient while on the clinical trial, to arranging referrals for appropriate follow-up care, including for subspecialty care if needed, referrals to social service, referral to another trial, or provision of alternative interventions to the investigational medication, and ensuring follow up and continued care for sequelae of serious adverse events. Transitioning back to medical therapy is even more critical for participants of clinical trials that are prematurely terminated for whatever reason, but

especially for those terminated for futility or lack of efficacy, or due to adverse drug reactions.

53. The sponsor and the investigator must inform study participants not only of their laboratory test results but of the study results, especially if it will have an impact on the management of the participant.

54. While archiving of essential documents related to the clinical trial is part of the responsibilities of both the investigator and the sponsor, it is a task that begins after trial close-out, and which typically continues for several years even after close-out as specified in the protocol. While it appears unimportant, archiving essential documents on-site or with reputable third-party document archiving companies is crucial to ensure the privacy and confidentiality of the study records and to prevent accidental destruction of paper files or digital copies of the essential documents. The length of time of archiving of essential documents, and the system of archiving need to be defined and decided on between the investigator and the sponsor as part of the agreements before site initiation.

Case Reports

55. Case reports are a significant platform for information exchange. It usually bridges the gap between patient management and clinical research. The stimulus to conceptualize, write, and publish a case report is dependent on the insight an individual case offers as to themes related to assessment, management, or outcome. The case report may be an impetus toward critical thinking, renewed patient approach, and stimulating clinical research.

56. Case reports are normally not reviewed by RECs. Ethical review of case reports is best delegated to the department concerned using the CARE Checklist (Appendix R). Only when a journal asks for an ethical clearance from the institutional REC shall the REC review and grant ethical clearance.

57. Well-described case reports usually include the following:

57.1. A rare or new, emerging disease;

57.2. Unusual or unexpected presentation of a disease;

57.3. Unusual, rare, or unreported adverse events following treatment;

57.4. Evolving or new disease associations; or

57.5. New findings regarding disease etiopathogenesis.

Ethical Considerations

58. Authors should not be only focused on the clinical content but likewise, be mindful of their professional obligation to the patient, which should not be compromised by academic gain. Important elements that will guide case report writing include "reciprocal information exchange, support, partnership, respect, and enablement" (King et al., 1996, p. 2).

59. Relevant ethical issues involved in case report writing are centered on informed consent and confidentiality.

60. A written and signed informed consent to participate in a case report must be voluntarily given by a competent patient after adequate disclosure of its objectives, benefits, and risks.

61. In cases where consent is not feasible from the patient, it should be asked from a legally authorized representative, guardian, or a recognized surrogate decision-maker. Assent/dissent rules likewise apply among case reports involving children.

62. It is good to note that altruism and the idea of being able to contribute to a body of scientific knowledge may be an important driver in cases of difficulty in obtaining consent.

63. In this digital age, access to medical information seems unrestricted and continuous. This should prompt us to preserve confidentiality and uphold the patient's right to privacy. In any case report, personal

identifiers including but not limited to name, initials, birth date, age, hospital, or other traceable information should be excluded.

64. Extra care should be employed when presenting ancillary data which may inadvertently contain personal identifiers/information.

65. Case reports showing physical findings, lesions, and other identifying marks, should focus on the objective findings to uphold the anonymity of the participants.

66. It is the author's responsibility to protect the patient's best interest through the shared responsibility of all stakeholders, including the institution and the journal/publisher. The following points will be helpful to prevent misconduct.

    66.1. Authors are reminded that there is a need for explicit informed consent. Our duty to uphold confidentiality is paramount.

    66.2. If feasible, the patient should be able to review the case report for possible editing, revision, or even removal of any compromising information.

    66.3. Local regulatory institutions (e.g., IRB), though not mandatory now, may provide guidance and oversight if necessary.

    66.4. Journals/publishers may request prior case report review before acceptance for publication.

To ensure the transparency, accuracy, and usefulness of case reports, David Riley, MD, and other international collaborators developed and published the CARE (CAse REports) guidelines in 2013 and 2017. Adopting the CARE guidelines (*see Appendix R*) will help authors decrease the possibility of bias, increase transparency, and provide a simplified approach to what may be best for patients and their respective circumstances.

ETHICAL GUIDELINES FOR INTERNET RESEARCH

The internet is a tool that provides a rich and fruitful site for social research. It presents manifold opportunities for researchers to examine human society, structures, interactions, and behavior. The ubiquity of the internet in individual and social lives and contexts such as a global pandemic wherein in-person interactions are limited make internet research more commonplace, if not necessary. "Internet research encompasses inquiry that:

- utilizes the internet to collect data or information, e.g., through online interviews, surveys, archiving, or automated means of data scraping;

- studies how people use and access the internet, e.g., through collecting and observing activities or participating on social network sites, listservs, websites, blogs, games, virtual worlds, or other online environments or contexts;

- utilizes or engages in data processing, analysis, or storage of datasets, databanks, and repositories available via the internet;

- studies software, code, and internet technologies;

- examines the design or structure of systems, interfaces, pages, and elements;

- employs visual and textual analysis, semiotic analysis, content analysis, or other methods of analysis to study the web and internet-facilitated images, writings, and media forms; and

- studies large scale production, use, and regulation of the internet by governments, industries, corporations, and military forces." (Markham & Buchanan, 2012)

In all kinds of internet research, the nature of the various venues and contexts (e.g., online interviews, special interest forums, social networking, blogs, and databanks) should always be considered since ethical issues arise

from and are dependent on their utilization. Ambiguity in determining risks arises from the virtual interaction between the researcher and the participant and their unfamiliarity with existing technologies. Moreover, there are limited means of gauging participant characteristics (e.g., age) and how participants respond to the study. In addition, some issues are associated with data and personal privacy, and access that are inherent in most internet activities.

There is "so much diversity across internet cultures, values and modes of operation" that it is unrealistic to expect a single set of guidelines to address every situation (Convery & Cox, 2012). "Ethical decision-making is a deliberative process, and researchers should consult as many people and resources as possible in this process, including fellow researchers, people participating in or familiar with contexts/sites being studied, research review boards, ethics guidelines, published scholarship (within one's discipline but also in other disciplines), and, where applicable, legal precedent" (Markham & Buchanan, 2012). What follows is an attempt to put forth basic principles that can guide researchers and RECs in internet research.

1. The following 7-point ethical checklist shall guide internet researchers to ensure that the welfare of both the respondents and researchers is safeguarded, and the integrity of the entire research is upheld (cf. Markham & Buchanan, 2012):

    1.1. *Validity*. Is the use of online technology or digital tools valid and appropriate in pursuit of the research objectives and methodology? Is the technology available during the conduct of the research? Will the participants have access to the technology?

    1.2. *Reliability*. How are the participants recruited? Is the use of remote referrals, virtual referrals, or using technology reliable? How fair is the recruitment of participants?

    1.3. *Transparency*: Do the participants know the purpose and the nature of the research? Do the participants know or expect that digital records are being kept (versus ephemeral or

impermanent data)? If online interviews will be stored for purposes of reference, do the participants give consent? Are the participants made aware of confidentiality, if applicable? Will the data be stored by a third-party service provider? If so, how will the data be protected, and how long will it be stored? If the data will be stored in a databank or repository, is there consent for the subsequent use of data? What are the provisions for shared data as regards consent and confidentiality?

1.4. *Anonymity and confidentiality*. Are the participants anonymous or identifiable? Are identities confidential or not? If not, are the participants made aware of it?

1.5. *Privacy*. Is the online behavior "public," or do respondents have reasonable expectations of privacy? How is privacy, anonymity, or confidentiality ensured? How does the protocol deal with differences in perception between the researchers and participants regarding public/private and sensitive/non-sensitive? How is the privacy of participants maintained, from recruitment (wherein personal information such as email addresses or social media accounts might be used) to data collected on online platforms, to the publication of results (e.g., can verbatim quotes be searched online)?

Should the researcher argue that the online behavior is "public" because it is publicly posted, the researcher should reflect on whether the person has reasonable expectations of privacy and whether informed consent should be solicited. The researcher is encouraged to read the reference cited by the National Privacy Commission in its Advisory Opinion No. 2017-41 (Office of the Privacy Commissioner for Personal Data [PCPD], 2013, as cited in NPC, 2017b).

1.6. *Prior consent*. If there is no anonymity, confidentiality, or privacy, how can the requirements for informed consent, if necessary, be fulfilled?

1.7. *Nonmaleficence*. Does the use of online technology present minimal harm to the respondents and their families,

communities, and organizations? Where there is potential harm, is it unintended, unavoidable, and proportionate to the potential benefits of using online technology? If the data from participants will be linked to them or their communities, will it cause harm? Are the researchers also safe? Are there adequate safeguards for vulnerable participants?

2. Data collection via the internet for studies ordinarily conducted in person shall be justified (versus other means). If a study involves more than minimal risk, researchers and the REC must ensure ample measures that protect the rights and welfare of the participants.

3. If individuals have reasonable expectations of privacy, confidentiality, anonymity, and safety (nonmaleficence), then the researchers ought to take specific and documented measures to inform the respondents and obtain their consent to use their data for research, with the attendant protection of their welfare.

4. Researchers must adhere to the applicable provisions of RA 10173 (Data Privacy Act of 2012) and its implementing rules and regulations regarding the collection, use and storage of personal information (*see section on Elements of Research Ethics*).

5. Researchers must not use any subterfuge in obtaining electronic addresses of potential respondents, such as collecting email addresses from public domains or under the guise of some other activity or using technologies or techniques to collect e-mail addresses without individuals' awareness (ESOMAR 2011, 2016).

6. Internet-based recruitment methods and materials should have the approval of the REC as a means of ensuring their ethical soundness. Researchers in their recruitment of participants are expected to respect the privacy of each participant and their potential vulnerability and use a contextually appropriate recruitment strategy.

7. Links to privacy policy statements on the online site and their terms of service must be posted prominently by researchers. Researchers are to ensure that participants sufficiently understand those policies,

particularly as they affect the participants' well-being and that they agree with them.

8. The researcher shall describe the technology chosen for the implementation of the research and justify the plan based on the sensitivity of the research.

9. The study team shall include a member familiar with technical issues concerning Internet security, including additional safeguards. If the study is to be conducted by an individual researcher, they must be familiar with internet security; or if they are not familiar with it, they must enlist the assistance of one who knows it. (See the Section Elements of Research Ethics for the Applicable Provisions of the Data Privacy Act of 2012)

10. Researchers must ensure there is a method to receive queries from participants. They are also to provide adequate assistance and referrals for research-related questions or problems encountered by the participants.

11. Researchers must take special care to treat online identities (personas or avatars) and their corresponding character names just like real ones. People care about the reputation of their personas and these aliases may be traced back to real-world names.

Informed Consent

12. Researchers should include all the required elements of informed consent as stated in the general guidelines when generating consent documents for online research. Participants should be particularly informed of the potential risks in the informed consent document, such as:

    12.1. Confidentiality during actual internet communication procedures cannot be guaranteed, although every reasonable effort will be taken.

    12.2. Although confidentiality will be kept to the degree permitted by the technology being used, no guarantee can be made regarding

the interception of data sent via the Internet by any third parties.

12.3. Data may exist on backups or server logs beyond the timeframe of the research project.

13. Informed consent for online research may be waived under the following conditions:

13.1. The information is publicly archived;
13.2. No password is required for archive access;
13.3. No site policy prohibits it;
13.4. The research is of minimal risk;
13.5. There is no aspect of the study which could cause or influence respondents to decline from participating; and
13.6. The protocol involves the type of research described in item 18 of this section.

14. For everything else not covered by 12, informed consent conveyed via electronic or digital means is required, such as a digital signature on an informed consent document (emailed or embedded in the platform, e.g., Google Form, Qualtrics, or other survey application). If electronic consent is not feasible, consent may be obtained with a signature on paper – returned to the researchers via surface mail, email, fax, or other means (e.g., a recorded verbal consent) that are acceptable to the participant, the researcher, and the REC.

15. The online consent form, if self-administered, should be written in a manner and language that is understandable by the prospective participants. It should be formatted to lead the prospective respondent through each element of the informed consent information. Agree or disagree nodes or ticks may be strategically placed after each critical element to help ensure that the individual understands or consents to each element.

As it is self-administered, the form could have a section wherein individuals can submit questions before consenting to participate. The researcher should provide their contact information so that the

prospective participant may also contact the researcher to ask questions before indicating consent.

16. The method of obtaining the informed consent must be justified by the researcher and approved by the REC (e.g., if via electronic/digital means such as a digital signature on an emailed document, an indication of consent embedded in an online survey platform via weblink, via signature on a print document to be mailed or faxed or photographed, or via a recording of verbal or written consent in a video or chat platform).

17. Prior consent must have been given by participants when recording material or data that is taking place in real-time (e.g., chatroom, online FGD, or interview). Consideration should be given to whether the act of recording potentially creates risks for the participants (if the study is recording information or activities that may present risks if inadvertently disclosed, such as illegal activities or socially undesirable statements). Researchers may use only those materials from participants who gave consent. Measures to protect participants' privacy must be in place.

18. Personal information about the participant must not be used for secondary purposes or shared with third parties without the participant's expressed consent.

19. Researchers who use apps and software to gather big data from the internet, especially social networking sites, personal spaces and blogs, and special interests' forums, are to obtain the consent of the authors insofar as it is reasonable and practicable. If no consent is obtained due to the nature of the study, there must be adequate safeguards that will protect the researcher and people's privacy and that the use of such apps and software is with the REC's approval.

20. Certain studies conducted on the Internet may involve covert processes wherein deception or withholding of information is deemed necessary by the researcher to obtain valid data. Examples may be studies of extremist or politically sensitive beliefs or socially unacceptable online activities (e.g., trolling). In such cases, researchers are to justify the necessity of the waiver of informed consent or the use of deception,

subject to the approval of the REC. Researchers must ensure suitable protection strategies for both researchers and participants.

21. Depending on the nature and objectives of the study, if appropriate, researchers are to share its results with their participants in a way that is intelligible and meaningful, and that does not compromise the participants. If warranted, researchers should obtain their feedback, which can be used to improve the project.

Internet Research involving Children and Young People

22. Soliciting the participation of minors shall be done with extreme care and only if truly necessary, 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 (nonmaleficence) and shall formally secure parental or guardian consent and the minor's assent/consent.

23. To ensure that respondents are not adversely affected because of participating in research, the following information must not be collected from children:

    23.1. topics generally regarded as sensitive
    23.2. personal information relating to other people (for example, parents, siblings)
    23.3. personal information unrelated to the objectives of the research (even information solicited to build rapport)

24. Questionnaires on websites aimed at children must require that the parent's consent be obtained first before collecting information from the child.

25. Reasonable steps must be taken to validate the parental consent by following up with an email, letter, or phone call, provided the parent or legal guardian gives this information.

Data Security

Researchers must consider additional data security provisions when conducting Internet-based research. All data must be protected as it moves along the communication pathways (e.g., from the participant to the server, server to the Investigator).

26. Researchers must provide information regarding the transmission and storage of the data in their REC application.

27. The level of security should be appropriate to the risk. Research involving sensitive topics may require additional protections.

28. If warranted by the nature of the research, 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, firewall, cookies, separation of data files for identifiers and responses, and registration requirement to gain access to a discussion group).

29. Internet protocol (IP) addresses are potentially identifiable; thus, if IP addresses are collected, proper confidentiality measures must be in place to protect the participant's identity (e.g., use of a password, encryption).

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 p. 95).

Epidemiologic studies are classified into descriptive and analytic studies. Descriptive studies describe the magnitude and distribution of health problems and provide hypotheses about the etiology of these problems. Analytic epidemiologic studies, made up of observational and experimental studies, are used to test hypotheses about the determinants of the health problem or the etiology of the disease. Moreover, analytic epidemiologic studies are also used to assess the effectiveness of public health strategies that promote health and prevent disease in population groups. Disease prevention strategies such as immunization of large numbers of susceptible populations could be evaluated using observational epidemiologic study designs.

A major part of epidemiologic research involves collecting data from individuals who will not benefit directly from promising public health interventions and often may not have a disease that needs treatment. Thus, there must be an 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 study participants' time and attention. They may encroach on a person'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.

In non-interventional or observational epidemiologic studies, consent procedures need not be as stringent as clinical trials of new drugs and treatment modalities. However, when the researcher proposes selective disclosure of information (e.g., 'blinding') to the participants, the REC takes a closer look at the protocol and decides whether such non-disclosure is justified.

Often, 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. (See section on Research Using Human Data and Samples from Biobanks, Registries, and Databases)

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, the 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 advocacy-driven epidemiology data.

Since the science and methods of epidemiology are rooted in public health, the issues on ethics in public health practice (e.g., surveillance, screening, outbreak investigation, contact tracing, vaccination) and ethics in public health research (e.g., etiologic studies, prevention effectiveness research) are common themes in the literature about public health ethics in general. In both public health practice and public health research, large amounts of data are usually collected and analyzed to characterize the target population for public health interventions or answer epidemiologic research questions. The tension between concerns over personal liberties and individual autonomy and public health perspective carries over from public health practice to public health research, which commonly employs epidemiologic research designs.

Requirement for Ethical Review

1. Epidemiologic studies shall undergo an ethics review before the start of the study. Exemption from a review is a decision made by a REC. (See section on Elements of Research Ethics)

2. The ethical review of an epidemiologic study shall consist of the same elements of review for other studies, namely: social value, scientific soundness, a fair selection of participants, a 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. Data collection 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, and the method of data analysis shall all be dictated by the objectives of the study and the intended users of the study results.

5. Explicit and detailed research protocols shall fully account for the requirements for scientific validity.

6. Through adherence to ethical principles, human participant protection precedes that of science and society.

Informed Consent

7. Researchers, in principle, shall obtain written informed consent from all research participants before 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 unrealistic or impractical, alternative methods of obtaining consent (e.g., verbal consent) shall be employed as discussed in Guidelines for Social Research.

9. Informed consent shall be obtained from parents or, in their absence, a legal guardian or legally authorized representative (LAR) for the 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 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 risk to the participants.

11. Researchers may request for waiver of the informed consent process if the process is impractical and the research procedures entail no more than minimal risk, for example:

    11.1. Collection of information in the public domain (i.e., published data). 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 anonymous data that no longer permits the identification of the individual; or

    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 Ethical Guidelines for Social Research). In some situations where a signed informed consent by the participant is not feasible, the researcher will ask the REC's permission for a third party to sign, as a witness, on behalf of the study participant.

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 to disseminate the results to those involved.

13. In general, if the information is obtained using a questionnaire and adequate information has been given to the research participant, there is no need for 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 to be used for research are not covered by the original consent, a REC shall decide whether renewed consent is needed or if the analyses may be done on anonymous samples. Details regarding the collection and storage of biological material are covered by the Ethical Guidelines for Genetics and Genomic Research.

15. There are some unresolved ethical issues, however. In biomedical research, the principle of informed consent is based on individual persons who are invited to participate in the research. In contrast, the interest of concern in public health is that of the public good. Will the spirit (or motivation) and the process of obtaining informed consent be different because of this fundamental difference? For example, in population genetic studies, which usually employ epidemiologic designs, will family consent be needed over and above the person's consent? Another related issue is in the use of randomized cluster design. Will individual participants' consent be needed or the consent of the entire cluster members? (*See section on Genetics and Genomic Research*)

Risks and Benefits

16. 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.

17. 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

18. 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.

19. Researchers shall properly manage and protect the personal data of all research participants in compliance with the Data Privacy Act of 2012 (*See Elements of Research Ethics*).

20. Data regarding income, personal habits, preferences, personal opinions, and political and religious inclinations, among others, may be considered sensitive and may require consent before collection.

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

22. Whereas the general population can benefit from the information required for timely control or prevention, in no case, however, shall the protection of privacy and respect for confidentiality be waived. Removing 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 must be notified, researchers must ensure that the risks of harm outweigh the benefits.

Sharing of Study Results with Participants

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

Compensation for Participants

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

Management of Conflict of Interest

25. Researchers shall disclose all potential and actual COI, including involvement in ideological advocacy related to the research,

financial interests, and funding sources when applying for ethical clearance, obtaining informed consent from participants, and publishing or disseminating research results.

26. When obtaining informed consent from research participants, potential or actual financial conflicts of interest shall also be disclosed.

27. Researchers shall avoid entering into contractual agreements that prevent them from publishing results in a timely manner.

ETHICAL GUIDELINES FOR RESEARCH INVOLVING MINORS OR CHILDREN

1. Definitions

    1.1. Children

        1.1.1. RA 9344 (Juvenile Justice and Welfare Act of 2006) and The United Nations Convention of the Rights of the Child define children as a “human being below the age of 18 years unless, under the law applicable to the child, majority is attained earlier.”

        1.1.2. RA 7610 (Special Protection of Children Against Abuse, Exploitation, and Discrimination Act) defines “children" as those persons younger than 18 years of age or those older but are unable to fully take care of themselves or protect themselves from abuse, neglect, cruelty, exploitation, or discrimination because of a physical or mental disability or condition.

    1.2. Minors are defined as those who have not reached the age of majority (< 18 years) as defined by Republic Act 6809 (An Act Lowering the Age of Majority from Twenty-One to Eighteen Years) (RA 6809, 1989).

2. The following features that speak of the uniqueness of the child as a research participant must be considered, particularly in drug trials. It should be realized that the child is not simply a small adult. These features include:

    2.1. Non-translatability and non-applicability of research findings from adults are due to:

        2.1.1. Differences in disease susceptibility

            2.1.1.1. Children are at risk for infectious diseases due to the immaturity of their immune system; thus, most vaccine-preventable

illnesses are more common among children.

2.1.1.2. Congenital illness and genetic conditions are often first appreciated upon birth or early childhood.

2.1.1.3. Some diseases predominantly affect children, such as dengue or Zika virus.

2.1.2. Children often being unwilling victims or collaterally affected in disasters and wars with the effects that could scar them for a lifetime;

2.1.3. Children being affected by or may be the victims of family or sexual violence, poverty, or crime; and

2.1.4. Children as a class being susceptible to malnutrition and developmental disorders.

2.2. Differences in physiology and pharmacokinetics

- stage of development
- nutritional status
- pathology

2.3. Heterogeneity of the population

2.3.1. There are several birthweight categories, each with different disease susceptibilities.

- ELBW (< 1000 g)
- VLBW (< 2000 g)
- LBW (< 2500 g)

2.3.2. There are different gestational age categories with varying clinical risks and prognoses.

- Preterm (< 37 weeks)
- Term (3–42 weeks)
- Post term (> 42 weeks)

2.3.3. There are different child developmental stages with their unique developmental, and among adolescents, social issues.

- Neonates (0–28 days)
- Early infancy (28 days to 12 mos.)
- Late infancy (12–24 mos.)
- Pre-school (2–5 yrs.)
- Primary school (6–11 yrs.)
- Adolescents (12–18 yrs.)

2.4. Vulnerability

2.4.1. Young children are incapable of understanding the consent assent process.

2.4.2. Children may have a situational vulnerability, such as victims of violence, war, or crimes.

2.4.3. Children have a relational vulnerability to adults.

3. Existing guidelines regarding children as research participants are concerned with the responsibilities of the persons, institutions, and authorities involved in biomedical research. These include the WMA Declaration of Helsinki, the ICH-GCP guidelines, the EU directives on the implementation of GCP, the CIOMS guidelines, and our National Ethical Guidelines.

Gil (2004) suggests that in addition to existing guidelines, the following principles should be considered in doing research among children.

3.1. Aim of clinical studies

3.1.1. The aim of studies should focus on clinically or socially relevant conditions affecting children. Children should not be used as research objects on behalf of adults.

3.1.2. Children should not be involved in research that serves only scientific interests, especially if the research has no benefit to them.

3.2. Integrity of the child and respect for autonomy

3.2.1. The Convention of the Rights of the Child guarantees child protection. The protection of the child's integrity must be considered in all life stages.

3.2.2. Children need special protection because of their vulnerability.

3.2.3. To respect the child's autonomy is to involve them in the assent process whenever possible.

3.2.4. Involvement of the child in the assent consent process is developmentally determined and will differ for different populations and cultures. In keeping with the child's capacity, the present guidelines for assent include the following:

- < 7 y/o – no need for assent
- 7 to < 12 y/o – verbal assent
- 12 to < 15 y/o – simplified written assent
- 15 to < 18 y/o – the minor can co-sign the consent signed by the parents

3.2.5. According to CIOMS (2016), if children reach the legal age of maturity during long-term studies, their consent to continued participation should be obtained.

3.2.5.1. Children less than 12 y/o, who during the research turn older than 12 but younger than 15 years, should sign an assent form.

3.2.5.2. Children aged between 12 and 15 years, who during the research turn older than 15 years, should co-sign the consent form signed by their parent or LAR.

3.2.5.3. Children younger than 18 years, who during the research turn 18 y/o, should sign a newly administered consent form (apart from what was signed by their LAR or parents).

3.2.6. In general, the refusal of a child or adolescent to participate or continue in the research must be respected unless continued participation in the research is in the best interest of the child, considering their medical condition.

3.2.7. The child's dissent should be upheld and respected.

3.3. Study design: Observational research vs. Interventional research

3.4. Benefits vs. risks

3.4.1. The goal of research among children should be to improve the welfare of the child or to reduce suffering.

3.4.2. The predicted benefits must always outweigh the recognizable risks of participation.

3.4.3. The risk must be minimized by all available means.

3.4.4. Should the objectives be realized through observational studies, this should be preferred over interventional studies.

3.5. Investigator qualifications in investigational provisions

3.5.1. Only studies that are properly planned and conducted by competent researchers are ethically justified. The study should be conducted or

supervised by child experts such as pediatricians whenever possible.

3.5.2. Study protocols and study designs should be child-specific and not simple modifications of study protocols originally designed for adults.

3.5.3. Clinical trials and other interventional studies should be carried out in a facility that provides a child-friendly atmosphere.

3.6. Timing of the involvement of children in clinical trials (Gill, 2004):

3.6.1. For diseases exclusively affecting children, trials involving children may be carried out even without previous adult exposure.

3.6.2. For diseases mainly affecting children or graver in children or having a different natural history in comparison with adults, trials are needed at an early stage following evidence of efficacy in adults

3.6.3. For diseases occurring in both adults and children with no or limited treatment, trials are needed at an early stage following evidence of efficacy in adults.

3.6.4. For diseases occurring in adults and children for which sufficient treatment exists, trials in children should follow the completion of adult trials.

3.7. Minimizing risks

3.7.1. Adequate pre-clinical toxicity studies and safety data from adult studies should be available.

3.7.2. The sample size should be the smallest to affect the least number of participants but be large enough for statistical inference.

3.7.3. Doses used for clinical trials should be the lowest therapeutic dose.

3.7.4. The number and extent of interventions (especially invasive) should be minimum.

3.7.5. The methods for laboratory tests should use the smallest blood sample volumes possible.

3.7.6. The study should be reviewed and approved by an ethics committee with the necessary expertise in childcare (e.g., the presence of a pediatrician or developmental psychologist).

3.8. Minimizing discomforts

3.8.1. Every effort must be made by research institutions and staff to minimize pain, discomfort, and fear through preparations, play facilities, and a child-friendly environment.

4. In reviewing research involving children and minors, the following assessment items should be reviewed by the members of the Research Ethics Committees.

4.1. The investigator and the study team must be qualified to conduct of research among children. These qualifications may be assessed by reviewing the resumé. The proponent is qualified by his education, training, and experience.

4.2. In therapeutic trials, the reviewer should note the results of existing studies done among adults. These can be assessed by reviewing the investigators' brochures.

4.3. The social value of the study considers the burden of illness, equipoise, and whether it addresses an important unmet need.

4.4. The risk-benefit ratio should be favorable, and the benefits should far outweigh the risk considering that the child is vulnerable.

4.5. The reviewer should pay particular attention to risk mitigation procedures, monitoring details, and withdrawal.

4.6. The reviewer should ensure that the assent consent is comprehensive and written in a language that will be understood, considering the age of the children to be recruited.

ETHICAL GUIDELINES FOR RESEARCH INVOLVING OLDER PERSONS

The Philippines needs to prepare for the burgeoning population of older persons. 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. Health status and functional capacity vary among the young-old (60 to 69 years), middle-old (70 to 79 years), and the oldest-old (80 years and older). 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. Thus, 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, and those who are home-bound, may be inadvertently excluded from participating in research, leading to recruitment bias.

6. Socio-economic demographic characteristics may render older persons more vulnerable and 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, who will potentially benefit from the knowledge generated shall be represented in the research, regardless of the venue of care.

Informed Consent

8. Researchers must be careful to clarify the purpose of the study to address participants' desires for a 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 lookout for cognitive, psychiatric, and functional problems 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. If the capacity for informed consent is doubtful and depending on the research objectives and outcomes to be measured, a cognitive assessment shall be done. Several tools may be used to determine decisional capacity. Current screening tools to assess cognition, such as Folstein's MMSE (score of 27/30 and higher) and the clock drawing test (score 4/4), may be too long, require payment, or subscription fees. Shorter versions that are free and locally validated may be used. The researcher may also use the following guide to determine competency:

11.1. Level 1: the research participant knows that they are faced with a choice;
11.2. Level 2: the research participant can make a reasonable choice compared to that of an average person;
11.3. Level 3: the research participant is aware of the emotional consequences of their positive or negative choice;
11.4. Level 4: the research participant can provide reasons for their choice; and
11.5. Level 5: the research participant can understand the meaning of the information and the treatment situation.

No single tool is sufficient in determining the ability to consent. Based on history and assessment, the researcher's judgment is of utmost importance.

12. In the absence of capacity or competency to provide informed consent, a legally authorized representative (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 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 the potential for adverse drug events, which is especially relevant in clinical trials.

15. The protocol shall include adequate safeguards that mitigate the risks and 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 benefit the research participants directly.

Dissemination of Research Output

19. The researcher must ensure that the research participants (with particular attention to those who are institutionalized, homebound, or who have communication and mobility problems) are informed of the study results.

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

ETHICAL GUIDELINES FOR RESEARCH INVOLVING PEOPLE LIVING WITH HIV AND AIDS

After four decades of intensive work on the epidemics of the human immunodeficiency virus (HIV) infections and the acquired immunodeficiency syndrome (AIDS), interest in conducting and funding global, regional, and local research on HIV and AIDS avidly continues. The Joint United Nations Programme on HIV and AIDS (UNAIDS) 2021 global report has shown significant improvement in the number of persons living with HIV (PLHIV) on affordable, accessible, and quality antiretroviral treatment (ART), which in turn is estimated to have averted 16.2 million deaths since 2001. Most remarkably, the number of new HIV infections has gone down in almost all countries except for a handful, including the Philippines (DOH Epidemiology Bureau, 2021). The UNAIDS report (2021) has convincingly shown that many countries worldwide have triumphantly achieved the 2020 targets set by the United Nations in 2016, thus further fueling the commitment to scientific efforts, particularly research.

To review, in 2016, the United Nations (UN) called the world to the challenge of ending the AIDS pandemic through the 90-90-90 targets. In recent years, we have grown accustomed to being benchmarked to this 90-90-90 system, also called the HIV Continuum of Care. The UN argued that control of the HIV epidemic does not only mean that we need to reach, find, and test the PLHIVs. If found to test positive, we should also be able to link the PLHIVs to proper holistic care, foremost of which is to receive the ART promptly.

When the 90-90-90 system was first introduced in 2014, it was described as "too ambitious and unachievable." But if we are to envision a world ending the HIV epidemic by 2030, we needed to reach the 90-90-90 targets by 2020. 90-90-90 means:

- By 2020, 90% of all people living with HIV will know their HIV status.
- By 2020, 90% of all people with diagnosed HIV infection will receive sustained antiretroviral therapy.
- By 2020, 90% of all people receiving antiretroviral therapy will have viral suppression.

Now that most countries have achieved the 90-90-90 targets, the new target has become 95-95-95 (UNAIDS, 2015). However, NHSSS (2020) of the DOH reports a growing number of HIV fueled by a legal and policy environment that is unfriendly to evidence-based policies and interventions proven to help prevent HIV transmission.

Researchers shall be aware of and abide by the Republic Act (RA) 11166, which is the "Act Strengthening the Philippine Comprehensive Policy on Human Immunodeficiency Virus (HIV) and Acquired Immune Deficiency Syndrome (AIDS) Prevention, Treatment, Care, and Support" promulgated in 2018. This new HIV law in effect repealed RA 8504, or the "Philippine AIDS Prevention and Control Act of 1998," after 20 years of its legal existence. This is the much-anticipated amendment to the outdated AIDS law.

To ensure and facilitate compliance with the RA 11166 provisions, the Implementing Rules and Regulations (IRR) of RA 11166 was signed on July 12, 2019. The IRR is a demonstration of the strong commitment of the country to end the HIV epidemic. Key provisions of RA 11166 address critical bottlenecks in the HIV Program in the Philippines.

The new HIV law removed the age-related barrier to testing, and young people aged 15 years and older can now undergo an HIV test without parental or guardian consent. This will facilitate the expansion of HIV services among young key populations (YKP) and reach the high-risk men having sex with men (MSM) and transgender women (TGW). Section 29 of RA 11166 states that "any young person aged below 15 years who is pregnant or engaged in high-risk behavior shall be eligible for HIV testing and counseling with a licensed social worker or health worker. Consent to voluntary HIV testing shall be obtained from the child without the need of a guardian." HIV testing is now also a routine procedure of prenatal care to prevent HIV infection from mother to child during pregnancy, labor, and breastfeeding.

RA 11166 will also accelerate access to free HIV treatment and related illnesses, as the "law embeds HIV/AIDS in universal health care by tasking PhilHealth to develop a revised benefit package including medication and diagnostics for in-patients and out-patients."

Researchers must also be aware that RA 11166 ensures the protection of PLHIVs' basic human rights that include affordable access to health services without the fear of being discriminated against.

HIV-AIDS Research Agenda

Through the years, HIV research has provided evidence that has guided strategies and policies of successful countries in paving the way to reverse increasing HIV trends and save lives. Most frequent, relevant, and critical research topics include but are not limited to:

- determining ways to improve access to effective HIV services, including HIV testing;
- discovering new ART options;
- establishing efficacy and acceptability of pre-exposure prophylaxis and potential vaccines to prevent HIV;
- evaluating strategies to provide quality linkage to HIV follow-up and care consistent with the 90-90-90 approach; and
- describing HIV and epidemiologic trends;
- identifying risk factors including socio-behavioral, cultural, and other epidemiologic concerns; and
- end of life issues.

Ethical Issues in HIV AIDS Research

Research in HIV and AIDS continues to present challenges, particularly a long list of ethical issues related to improving care while protecting human life and vulnerability and preserving the dignity of PLHIVs. This is especially true in the Philippines — where the trend of new HIV infections continues to rise and is starkly different from other countries; where resources are limited, leading to many international collaborations; and where the problem of stigma and discrimination remains a pervading issue in many health facilities and societies.

1. Defining and assuring the provision of the standard of care

While there is no cure for the condition, HIV disease can be managed by treatment regimens using a combination of at least three ARV drugs. Current

ART, if consistently taken, is efficacious in suppressing viral replication and allows the PLHIV's immune system to recover and regain the capacity to fight off opportunistic infections and some cancers. Since 2016, the WHO has recommended that PLHIVs be provided with lifelong ART, including children, adolescents, adults, pregnant and breastfeeding women, regardless of clinical status or CD4 cell count (WHO, 2016). The WHO (2021) reported that by June 2021, 187 countries had already adopted this "Treat All" strategy, covering 99% of PLHIVs globally. The WHO also recommended a rapid ART initiation for all people living with HIV, including offering ART on the same day as a diagnosis to those who are ready to start treatment. By June 2020, WHO also reported that 82 low- and middle-income countries are already adopting this policy. In the review of Phanuphak and Gulick in 2019, ART is the current standard of HIV care. Available ARVs are potent, convenient, generally well tolerated, and durable, leading to a normal life expectancy for PLHIVs.

Standards of care and treatment refer to the medical and health-related services package that research participants can expect to receive during a study by Rennie and Sugarman in 2010. The different domains of care and treatment include care and treatment for those screened but failing to meet study inclusion criteria due to a pre-existing medical condition; care and treatment provided for research-related reasons; care and treatment provided to participants for medically significant findings occurring during the study participation; and care, treatment, or monetary compensation for research-related injuries.

On the other hand, the term "standard of prevention" has been more aptly defined by the HIV Prevention Trials Network (HPTN) (Rennie and Sugarman, 2010). HPTN is a global collaborative network that has been conducting clinical and behavioral studies on non-vaccine interventions to reduce the transmission of HIV for decades. The HPTN defines the "standard of prevention" as the package of HIV prevention products or services offered to those who participate in HPTN research.

1.1. Investigators must be familiar with the standards of care and prevention of HIV.

1.2. Research teams must initially make a thorough investigation of standards of care and treatment at study sites.

1.3. The protocol shall provide at the very least equivalent services if the standards are adequate and seek to enhance local standards if they are unacceptably low.

1.4. Research participants at risk of exposure to HIV shall have access to effective means to protect themselves from acquiring the virus. The "prevention package" should consider providing access to HIV voluntary testing and counseling, HIV and STI risk reduction education, and provision of male and female condoms.

2. Assuring robust methodologic designs of HIV/AIDS vaccine trials, microbicidal trials, and prevention of parent-to-child transmission (PPTCT) trials, especially in resource-limited countries

2.1. Adopt The World Medical Association's latest release of the Declaration of Helsinki in July 2018, particularly as it may pertain to research on HIV.

2.2. As the debate about the role of placebo in treatment arms of interventional trials in HIV may persist, investigators must be guided by the specific provisions on the Use of Placebo (See section on Clinical Research), which states: "The benefits, risks, burdens, and effectiveness of a new intervention must be tested against those of the best-proven intervention(s), except in the following circumstances…"

2.3. The design of the study shall be reviewed for its technical merits.

2.4. The design is sufficiently rigorous that the results will be valid and generalizable.

2.5. The sample size must have been generated with reasonably acceptable assumptions based on currently available data.

2.6. Clear endpoints must have been identified.

2.7. Clinical trials on new agents for treatment or prevention must have some basis from preliminary laboratory and animal research.

3. **Addressing the vulnerability of participants**

The Philippines is one of the very few countries still disturbingly experiencing a rapid rise in new HIV infections (UNAIDS, 2021; NHSSS, 2021). Additionally, while the overall reported national HIV prevalence rate remained and continues to remain below 1%, identified vulnerable populations showed an alarming higher prevalence rate in recent years. The DOH, through its Epidemiologic Bureau (EB), releases the Integrated HIV Behavioral and Serologic Surveillance (IHBSS) reports every two years to update stakeholders and the public about what is happening to key populations (KP) and how interventions affect their risks for HIV infections. The IHBSS (2018) reports worrisome HIV prevalence among KPs, including MSM, TGW, persons who inject drugs (PWIDs), and sex workers. These KPs have thus been implicated as the key drivers in the steep rise of new HIV infections in our country. Though prevention and testing services are available, uptake among these KPs remains low: reported that only about 60% of MSM and about 40% of TGW accessed prevention services in Global Fund-supported sites in 2016. Testing coverage and yield among these KP groups also remained low.

3.1. Standards of care for treatment shall be offered to KPs who are found to be PLHIVs during the trial if they are not yet on adequate treatment. They shall also be linked to care.

3.2. All vulnerable groups and individuals should receive specifically considered protection.

3.3. Medical research with a vulnerable group is only justified if the research is responsive to this group's health needs or priorities and the research cannot be carried out in a non-vulnerable group. In addition, this group should benefit from the

knowledge, practices, or interventions that result from the research.

3.4. The potential for vulnerability should be carefully evaluated in the clinical research context for each participant.

3.5. Asking about specific aspects of a person or the circumstances that might render participants vulnerable serves as a basis for ethical and effective clinical study implementation.

3.6. Pre-empting possible causes of vulnerability can improve protection while avoiding unnecessary barriers to participation, stereotyping, and even stigmatization.

3.7. Most PLHIVs have specific physical, psychological, social, and spiritual needs, and a patient-centered approach may address their vulnerabilities.

4. **Recruitment and obtaining informed consent process**

Many PLHIVs are concerned about keeping their diagnosis a secret that they may not want anything to do with any research activity. Fear of stigma and experiencing discrimination may be so intense that they resist any kind of participation in any other activity which may identify them as PLHIV. On the other hand, they may feel that they are so dependent on their physician that they may agree to anything their doctor says. If their physician suggests that joining the trial may be a good idea, PLHIVs may consider this an order rather than an invitation and agree without any question. They may also think that not agreeing may jeopardize their access to treatment, and therefore, they may be pressured to sign the consent. In addition, patients' trust in their doctors and nurses may lead them to agree to participate in research without critically reviewing information about the trial. Health care providers themselves frequently overestimate the benefits of experimental interventions and participation in clinical trials

4.1. Recruiting PLHIVs to participate in research shall be done with care so that the potential study participant clearly understands what they agree to be part of.

4.2. The protocol shall describe the recruitment process, in detail, including mechanisms to avoid double counting through the interlocking of area groupings.

4.3. In non-interventional or observational studies, where the written consent may increase the possibility of identifying the person with HIV and become a permanent record, verbal informed consent can be done if it is witnessed and properly documented with appropriate and specific codes.

4.4. Special attention shall be given to the potentially sensitive nature of the information extracted from the research participants and, if applicable, the necessity of undergoing an HIV test.

4.5. It is important to determine the participant's willingness to be informed of the test result, its reportability, and the implication on their sexual partners and lifestyle if found positive.

4.6. The research participant must also be informed that they are free to withdraw from the study anytime.

4.7. Whenever possible, the person explaining the study and getting the informed consent is not the primary HIV physician of the PLHIV to reduce the potential for confusion regarding the roles of the health provider and investigator.

5. **Maintaining host country and community consultation, especially for international collaborative research initiatives**

The importance of community engagement is regarded by Rennie and Sugarman (2010) as both intrinsic and instrumental. The involvement of the communities in research expresses respect for local communities and enhances the ability to conduct and complete HIV prevention research.

5.1. Researchers shall meaningfully involve communities in all relevant phases of research see section on Ensuring Quality Research.

5.2. Research sponsors/funding agencies shall identify the country's and or community representative/s to set the boundaries of collaboration.

5.3. Community and host country members and researchers need to explore each other's perspectives and concerns through joint discussions.

5.4. Identify ways to maintain communication between researchers, community representatives, and members of community advisory boards.

6. **Pre- and post-test counseling**

As stipulated in Republic Act (RA) 11166 and its IRR, pre- and post-test counseling shall be implemented as part of the HIV testing process.

7. **Assuring privacy and confidentiality**

Researchers shall adhere to the guidelines on privacy and confidentiality outlined in the General Guidelines.

8. **Addressing stigma and discrimination**

Bullying and discrimination of people living with HIV based on actual, perceived, or suspected HIV status are prohibited. Their right to fair employment and livelihood, protection and confidentiality, and peer-led counseling, support, and case management are guaranteed under the law. RA 11166 also addresses stigma through education and awareness not only to prevent the spread of the disease but also for de-stigmatization.

9. **Research benefits**

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

10. **Use of research data**

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 cultural bias.

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. Concerning persons with disabilities (PWDs), the UN Convention on the Rights of Persons with Disability has made it clear that these human rights include respect for persons' inherent dignity, individual autonomy, and independence. In the 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 (RA7277) as amended by RA 9442, disabled persons are those persons suffering from restrictions or different abilities, because 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 a 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, the depth of insensitivity to the PWD situation and the representation of this population in the collection of data spells the difference. PWDs are classified as vulnerable participants, and the informed consent process shall ensure freedom from manipulation and coercion, considering this population's special needs.

1. The well-being of the PWDs participating in research, involved in, or affected by the research process shall always be promoted. RECS should have consultants who are PWDs or experts in PWD research (e.g., medical team or allied health professionals involved in PWD research or medical management).

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 PWD's 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 research have the right to make their own decisions regarding participation in the research process.

Participation of PWDs in Research

5. For research involving humans to be truly representative, PWDs should be equally eligible to join 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 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), preferably from the National Council on Disability Affairs (RA 10070), before conducting any research with this population.
    8.1. Sensitivity training should include measures on how to deal with trauma-related disabilities, especially if it crops up during the research (interview) process:

        8.1.1. Be able to identify signs of distress.
        8.1.2. Ensure immediate termination of the interview should signs of distress manifest during the process.

8.1.3. Ensure that appropriate counseling support is provided in case trauma or stress is expressed by the research participant.

Facilitating Participation of PWDs in Research

9. The researcher shall endeavor to address the needs of research participants with visual, hearing, speech, cognitive, or other physical impairments to facilitate participation in research as follows:

    9.1. Use of large print materials or audiotape 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 (e.g., wide doors, PWD accessible, chairs) during interviews or focus group discussions (FGDs).

    9.5. Consideration of the respondent burden, specifically the possible limited stamina of research participants,s by allowing frequent breaks in the interview process. This should be stipulated in the research protocol as well.

    9.6. Every effort to uphold research participant privacy should be promoted. Apart from the researchers and the study team, carers of PWDs included in the research are bound to uphold the duty of confidentiality.

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 UNIFORMED PERSONNEL

Members of institutions involving uniformed personnel include the military, police force, coast guards, and those in the fire protection units.

Guideline No. 15 of the 2016 CIOMS classifies this group as vulnerable research participants since they are in a subordinate relationship. They have a culture of almost absolute obedience to authorities, potentially conflicting with the right to participant autonomy in research decisions. In this context, research may be expected to accord substantial consideration to the nature of the hierarchical or superior-subordinate relationship among the uniformed personnel.

1. The involvement of uniformed personnel in research framed within the above tradition must be justified by any of the following reasons:

    1.1. The study addresses a need of uniformed personnel.

    1.2. The study will provide direct benefit to them.

    1.3. The risk entailed is minimal. In assessing the level of risk, the REC shall compare the proposed research activities to those experienced by a typical civilian in determining and mitigating risk levels. Thus, the REC shall exclude the unique demands on the uniformed personnel in the performance of their duties, such as exposure to combat, intense physical training, exposure to the elements, or prolonged pain.

    1.4. More than minimal risk research on the uniformed personnel and research involving classified information of national security concern, although rare, may be allowed only if the following conditions are met:

        1.4.1. The research will directly benefit the uniformed personnel.

1.4.2. The lead researcher is a uniformed personnel with expertise in health or the research topic of concern.

1.4.3. The research protocol shall not involve undue physical, psychological, cognitive, or emotional harm to the participants.

1.4.4. The protocol is approved by the Secretary of National Defense or the National Chief of Police.

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. However, unit commanders shall approve the participation of their subordinates when research activities occur during duty hours or might interfere with the subordinate's performance even when the research activities are done during off-duty hours.

4. Officers and senior non-commissioned officers shall be recruited separately from their subordinates.

Informed Consent

5. Special protection must be accorded to the uniformed 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 be in their official uniforms when recruiting and obtaining informed consent.

Compensation for Joining a Research

7. Compensation is not allowed if the funding source is from a government agency.

8. Compensation may be allowed if the funding agency is from a non-government entity. The amount shall be comparable to current local rates.

Safety Monitoring

9. If the research involves more than minimal risk, an independent research monitor shall be appointed by the funding agency and approved by the REC.

International Collaborative Research

10. Before REC review, all research conducted by foreign investigators and institutions shall seek from the following offices:

    10.1. endorsement letter from their respective embassies

    10.2. certificate of approval from the Philippines' Secretary of National Defense and the Secretary of Foreign Affairs

ETHICAL GUIDELINES FOR RESEARCH INVOLVING INDIGENOUS PEOPLES

There are challenges in the use of mainstream standards or guidelines when indigenous peoples (IPs)/indigenous cultural communities (ICCs) are involved as research participants. The composition, standards, and procedures of research ethics committees (RECs) pose problems when indigenous beliefs, knowledge systems, and practices are not adequately acknowledged and considered. Existing research ethics guidelines need to be inclusive of and interpreted within the context of IP worldviews.

The PHREB and the National Commission on Indigenous Peoples (NCIP) agreed on a Memorandum of Understanding in 2016 (Appendix D) that described the level of coordination in the ethical review of research conducted in IPs/ICCs. It specified that the research protocol must first undergo a preliminary evaluation by a REC. 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 the basis for issuing the final ethical approval (*see Appendix F*).

Oversight Considerations

1. In deliberations on research involving IPs/ICCs by a REC, the following considerations shall be included:

    1.1. Social, economic, political, and cultural needs of the IPs/ICCs and their various indigenous political structures IPs;

    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, such as the:

1.3.1. Indigenous and Tribal People's Convention, 1989 (No. 169);
1.3.2. Convention on Biological Diversity (CBD), 1993;
1.3.3. Indigenous Peoples' Rights Act (IPRA) (RA 8371), 1997;
1.3.4. United Nations Declaration on the Rights of Indigenous Peoples (UNDRIP), 2007; and
1.3.5. Organic Law for the BARMM (RA 11054), 2018, and the establishment of a monitoring mechanism to ensure that the guidelines are complied with.

1.4. Access to a member, advocate, or representative of IPs/ICCs who has a good understanding of the nature of indigenous knowledge and their means of expression and who has a good standing and is acceptable to the IP being studied;

1.5. Respect for the right to self-determination of the IP;

1.6. Recognition of the members of IPs/ICCs as partners with equal rights in the research process; and

1.7. Compliance with the review procedures of local RECs and the National Commission of Indigenous Peoples (NCIP), the primary government agency that "shall protect and promote the interest and well-being of the ICCs/IPs with due regard to their beliefs, customs, traditions, and institutions" (IPRA Sec. 39).

Informed Consent

2. Research involving IPs/ICCs must comply with standard elements of free and prior informed consent (FPIC), "the consensus of all members of the ICCs/IPs to be determined in accordance with their respective customary laws and practices, free from any external manipulation, interference, and coercion, and obtained after fully disclosing the intent and scope of the activity, in a language and process understandable to the community" (IPRA Section 3g), including a memorandum of agreement with the community, as needed.

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 to proceed with the second.

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, and consensus taking, where members freely participated, the community approval may be regarded as representing the members' decision. In this case, the group's decision strengthens individual decisions rather than violates individual autonomy. The process of obtaining both the community's and the participant's consent must foster the unity and harmony of the community.

5. Community consultations are required for approval to conduct the study before approaching individual members for consent, and the community's efforts to build consensus must always be respected. Community consultations will provide the opportunity for the researcher to learn culturally appropriate ways of soliciting individual consent, and at the same time, to explain the rationale for individual consent. It may happen that the community itself will decide on the selection of individuals who will be part of the study. 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 and shall be reasonably comprehensive in accordance with customary laws.

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). The MOA should include provisions about the researcher's rights when performing their research, the rights of IPs/ICCs regarding research materials, and the expectations of the IPs/ICCs that the researcher will respect their traditions and culture.

8. "Access to biological and genetic resources and indigenous knowledge related to the conservation, utilization, and enhancement of these resources, shall be allowed within ancestral lands and domains of the ICCs/IPs only with a free and prior informed consent of such communities, obtained in accordance with customary laws of the concerned community" (IPRA Sec. 35) and with the approval of the NCIP, and after undergoing ethical clearance from a local REC.

9. Samples, genetic or material, collected and taken from ICCs/IPs before the current guidelines and pertinent laws and without their FPIC should only be used in a study with the consent of the IP community. It is unethical to use such samples, knowing that they were obtained without FPIC.

Competence of the Researcher

10. To be familiar with the culture and preferably with the language of the indigenous people who are to be studied, the researcher is expected to engage in an appropriate social preparation phase. They shall approach the IPs/ICCs, learn their culture, seek informed consent, develop a culturally sensitive research design, and conduct a study that does not violate its tradition while respecting individual autonomy. A researcher ought to be sensitive to the impact of their presence in the community and be respectful of their values, beliefs, and practices.

11. The researcher shall identify knowledgeable community members who are persons of integrity whom they will consult for specific research problems. Still, they will have to be confirmed by the IPs/ICCs and, if necessary, the IPs/ICCs will suggest alternative informants.

12. The 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.

13. The researcher shall protect the confidentiality of research materials and results, including those deemed proprietary by the community.

14. Researchers shall familiarize themselves with the procedures for pre-termination. In consultation with the IPs/ICCs, a researcher shall pre-terminate a research project when the welfare and rights of the participants are compromised.

15. An IP researcher who studies their own community should have no unresolved conflict of interest. They shall follow their community's customary laws and processes in the preparation and conduct of the study. Like other researchers, they are expected to uphold the highest ethical standards in safeguarding their community's welfare, customs, and traditions. They shall obtain the necessary REC clearance and coordinate with the NCIP about their study. [In situations where there is a conflict between IP researchers or their community and the NCIP, they are encouraged to engage in dialogue to arrive at a mutually acceptable agreement that prioritizes the welfare of IP participants and their community.]

Respect for Traditions

16. The researcher must demonstrate knowledge and appreciation of the traditions of IPs/ICCs through the development of a culturally sensitive research protocol.

17. The researcher shall respect sacred places and rituals, including the communities' right to conduct rituals, as part of the decision-making process of IPs/ICCs regarding whether to allow the study.

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

Addressing Vulnerability, Risks, and Safety

19. Risks and harms to non-IP populations shall be included in the risk-benefit assessment.

20. Special attention shall be given to the vulnerability of IPs/ICCs. Procedures for informed consent and arrangements for benefit sharing must consider this vulnerability.

21. Researchers shall exercise care in designing and conducting their research and in disseminating research information that could be used by vested interests in exploiting IPs and the resources in their ancestral domains or violating their traditions. Researchers are to ensure that their research contributes to the challenge of making IPs less vulnerable to changes in our social, economic, and political landscape and be empowered in the process. As a safeguard, the community should consent to the research dissemination plan, which includes the information disseminated and to whom it is disseminated.

22. Since IP identity and ways of life are intimately related to their land, risks to biodiversity must be critically examined, specifically whether the study poses risks of destruction of the biodiversity or alteration of the ecology in IP land. Researchers ought to be aware of and sensitive to the adverse effects of environmental degradation on IPs.

23. The study shall consider requirements for the protection of biodiversity already contained in the Guidelines for Herbal Research and other pertinent legislation. Any flora and fauna research among IPs/ICCs should always be with their consent and be beneficial to their community. The study must demonstrate respect for the intimate relationship between the IPs/ICCs and the land and be consistent with promoting ecological integrity.

Benefit Sharing and Ownership

24. The research plan shall include an explicit description of access and benefit-sharing and describe how the researcher will ensure that the community has access to or gets a fair share of whatever benefits will accrue from the study.

25. Information about access and benefit-sharing shall be disclosed during community consultations and solicitation of individual consent.

26. Access and benefit-sharing agreements shall be formalized as stipulations in a contract or memorandum of agreement between the IPs/ICCs and other parties.

27. Research shall comply with Philippine laws on the transport and protection of indigenous materials, which should occur only with the consent of the IPs from whom those materials originate or are taken.

28. Results of the research project shall respond to the needs of the IPs/ICCs and be presented in a manner that is useful and accessible to its members in a language fully understandable to the community. The research results shall be presented to the community members before publication or presentation in various research fora, with their comments taken into consideration in the development of the final report, which shall be validated and approved by the community.

29. If communities, or parties other than the study community, make an ownership claim on the knowledge (and the benefits) from the study, the researcher shall undertake separate consultations and negotiations with these parties or communities. "When disputes involve ICCs/IPs, customary laws and practices shall be used to resolve the dispute" (IPRA Sec. 65).

30. 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, institutions, or individuals who can assist them in ensuring their rights in the agreement.

31. 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.

32. IP/ICC ownership of traditional knowledge shall be acknowledged in any report in any medium.

Role of the Research Ethics Committee

33. A REC that processes the ethical clearance of research involving IPs must have an adequate understanding of the application of the instruments cited in the "Oversight considerations" section of this specific guideline. If necessary, the REC shall invite an expert to assist in reviewing the study.

34. The expertise of the REC could be enhanced by the recognition and participation of IP/ICC representatives who genuinely embody the interests of and are acceptable to the indigenous peoples to be studied. Recognition and participation are key given the marginalized situation of IP/ICC. Therefore, the study needs to ensure that the role of the IP/ICC representative as knowledge co-creator is acknowledged and respected.

35. 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.

36. To preempt any possible misconduct, the PHREB shall coordinate with the NCIP to ensure the integrity of the obtainment of the FPIC.

Approval of Protocol Amendments

37. Any change in the approved protocol shall undergo the approval process of the REC, the NCIP, and the ICC.

Sanctions against Violators

38. If a researcher violates the protocol, their MOA with the IPs/ICCs, and the trust of their IP research community and participants, sanctions may be imposed on them by the REC after due consultation with the offended party. In extreme cases, the researcher will be blacklisted from conducting research involving IPs/ICCs.

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 a 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.

The World Health Organization has also declared its support for integrating Traditional Medicine (TM) into national health care systems by helping member states develop their national policies on TM/CAM (Complementary and Alternative Medicine). Aside from this, the WHO has also developed standards, technical guidelines, and methodologies for research into herbal products used during the manufacture of TM/CAM products.

These legislated objectives and the support of the WHO 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.

Many modern medicines have been derived from plants, such as digitalis, vinblastine, and metformin. Thus, research on plant material as a source of new drugs is still relevant today.

There are several approaches to studying plant material to develop new drugs:

a. Ethnomedical approach
b. Taxonomic approach
c. Phytochemical approach
d. Random approach
e. Information managed approach

The development of botanical products may lead to the following types of drugs:

a. Bioactive compounds isolated from plants for direct use as medicines, e.g., digoxin. These are classified as Drugs and shall follow all regulations and ethical requirements of conventional drug development.

b. Bioactive compounds with structures that themselves may act as lead compounds for more potent compounds, e.g., paclitaxel from *Taxus* species.

c. Crude herbal extracts/preparations as botanical drugs, e.g., green tea extract.

d. Herbal extracts/ingredients developed into modern formulations such as syrups, tablets, and ointments and are classified as herbal medicines. They must abide by Phil FDA AO 2004 172s Guidelines on the Registration of Herbal Medicines.

Unlike conventional drugs, herbal medicine candidates are composed of many compounds. These constituents may offer a therapeutic advantage of additive or synergistic effect. The evaluation of herbal medicine candidates does not require purification to be known or single chemical constituents (WHO 2005). For these herbal medicine candidates, to analyze the active ingredients, it is recommended to analyze one or more hypothesized active ingredients, analyze a chemical constituent that constitutes a considerable percentage of the total ingredients, and make a chemical fingerprint of the total ingredients. The last two mentioned are surrogates for analyzing the unknown constituents of herbal medicine.

Drug discovery and herbal medicine studies involve collecting plant samples in communities. When herbal research involves medicinal plants from indigenous cultural communities found only in ancestral domains, the researcher must be aware of the appropriate procedures for securing ethical approval (See section on Research Involving Indigenous Peoples). Researchers must consider the impact of these activities on the environment and biodiversity, indigenous peoples' rights, and their proprietary community claims. Thus, the individual is not the only

participant in this context, but a complex family and community network is involved. For any research that involves ancestral domains and IKSPs, the NCIP must be involved, and the REC must look for this in the protocol.

Some traditional and herbal medicine advocates are convinced that herbal products can be used without subjecting them to the same rigorous scientific evaluation (e.g., a requirement for pre-clinical trials) required in Western medicine. It is argued that the current universal scientific procedures and standards do not apply to remedies with a long history of use and have been accepted by communities. Long time or widespread use of an herbal preparation suggests but does not assure that traditional medicines have a favorable risk-benefit ratio. It should not be assumed that because the herbal products are "natural," they are "harmless and safe." Pre-clinical studies should still be performed to determine their toxicity and provide information on adverse effects on specific organ systems.

Thus, despite all the arguments against treating research on herbal medicines differently from Western Medicine, the safety and well-being of participants in herbal research must remain paramount over the desire of any researcher to prove their effectiveness. Thus, as espoused by many international instruments, basic ethical guidelines are applicable. The TAMA guides the formulation of these ethical guidelines as its policy framework and the ICH-GCP Guidelines for its scientific and quality underpinnings

1. In research that aims to validate a traditional herbal preparation's therapeutic or diagnostic value, there shall be proof of a long history of using 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 for the research proposal. The research proposal must incorporate documents supporting its putative actions and traditional use in the community. If the knowledge comes from an indigenous community, it must be used with their permission and with due respect for their cultural sensibilities. Proof of its use may be both in 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.

2. The geographic area, plant maturity at the time of collection, and the method of its preparation must be clearly described. Formulation of herbal medicines (as with synthetic medicines) may be proprietary information, and RECs should respect confidentiality.

3. Research in herbal remedies shall include standardization of the preparation and identification of markers to ensure that the studied and assessed ingredients are the same. This method must be followed throughout the conduct of research.

4. Herbal medicine candidates, regardless of the drug discovery approach, must undergo Phases I and II clinical trials before Phase III clinical trials for its registration (See Figure 1)

   One major difference between plant materials/extracts and synthetic drugs is heterogeneity. A plant with the same scientific name may have several varieties. Also, the plant compounds present may vary due to different factors, including temperature, climate, and type of soil, thus affecting the pharmacologic activity and adverse effect profile. Therefore, data submitted to assess the benefit/risk ratio must be SPECIFIC to the variety being studied and not data from other countries.

   4.1. Phase I studies shall require the inclusion of the following information in the protocol:

   - description of the plant, genus species; region and country of origin;
   - plant processing;
   - amount of herbal component;
   - list of excipients/diluents;
   - type of product (e.g., tablet, capsule) and its method of manufacture;
   - analysis of putative active ingredients 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, microbes, toxins, etc.;
- results of dissolution studies;
- storage conditions and stability over the length of the trial.
- acute toxicity study- LD50, NOAEL, Maximum tolerated dose, Toxidromes- same variety, batch (not from data from other countries)
- pharmacologic effects in animals, in vivo, and in vitro
- bioassay when applicable
- non-mutagenicity- Ames' test, micronucleus test
- subchronic toxicity data for 90 days, for products intended to be used for more than ten days
- chronic toxicity for mice- 9 mos.; rat for 12 mos.; minimum would be completed 50% of required chronic toxicity duration; for products intended to be used for more than 30 days

4.2. Phase II studies shall include the following information in the protocol:

- All that is required for Phase 1
- For products intended to be used for more than ten days subchronic toxicity data for 90 days
- For products intended to be used for more than 30 days – chronic toxicity studies for mice –9 months; rat for 12 months; minimum would be completed 50% of required chronic toxicity duration
- A favorable benefit-risk ratio based on the above information must be evident.
- Information on clinical safety parameters from the Phase 1 trial, including:
    - lack of neurologic symptoms, evidence of lack of allergic reactions; lack of arthritis or myalgias, gastrointestinal evidence of tolerability; normal liver function tests, normal kidney function tests, normal values of albumin,

glucose, cholesterol, amylase, lipase, normal electrocardiography, and blood pressure

4.3. Phase III studies shall include the following information in the protocol:

- All that is required in Phase 1 and Phase 2
- Efficacy data from Phase 2 trials

Uncertainty regarding the herbal preparation or product adulteration, interactions between herbal remedies and other entities, minimal toxicity data, and incomplete prior dose-finding, if present, must be clearly disclosed to all concerned, particularly in the informed consent process.

5. Participation of Traditional Healers

Cultural settings and expectations must be considered in the proposal's review, inviting a traditional healer or a known scholar of herbal medicines in the REC. The REC needs to make sure that the proposal has given due respect to customary laws and respect for the rights of IPs as regards traditional knowledge. If the traditional healer is to be invited, the REC is to make sure that their participation in the review is with the blessings (consent) of the IP community. The traditional healer is the community's steward of indigenous knowledge.

6. Research Design

Randomized controlled trials are still the gold standard, especially for Phase 3 clinical trials.

As in trials for other drugs, a placebo may be used as a comparator when there is no established effective intervention for the condition under study or when a placebo is added to a based effective intervention (CIOMS, 2016).

6.1. The effectiveness of herbal preparations may not only be measured with improvements in health or the 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.

6.2. Although the 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. Specific procedures for monitoring adverse events or toxicity should be specified in the protocol.

6.3. Blinding in herbal research may be challenging because of the difficulty in preparing control galenicals/decoctions indistinguishable from the tested herbal preparation. In this case, it is acceptable to "blind" the health status assessor or evaluator to support objectivity.

7. Transport

7.1. No indigenous materials used in the research may be transported outside the country without the informed consent of the IP leader and elders from the community where it is sourced. Thus, the material transfer agreement (MTA) should have the signatures of the IP leader, the elders, and the government agency or institution.

7.2. Researchers shall comply with the MTA if plant products or herbal preparations will be tested outside the country. (See section on International Collaborative Research)

7.3. A memorandum of agreement (MOA) regarding benefit sharing and patenting conditions, especially for indigenous plant products, shall be set as early as the planning stage of the research. The said MOA should be favorable to the IPs

and must truly benefit from any financial gains which may result from the research.

7.4. 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 (IPOPHL).

8. Safeguarding Indigenous Knowledge

With the approval of the NCIP and the consent of the indigenous community, the rich knowledge about indigenous herbal plants in a community must be documented, appropriately recorded, and archived for posterity. Its use in research ought to be with the community's consent, and its provenance should be duly acknowledged. Any use of indigenous knowledge about herbal plants that prove to be financially profitable should benefit the indigenous community

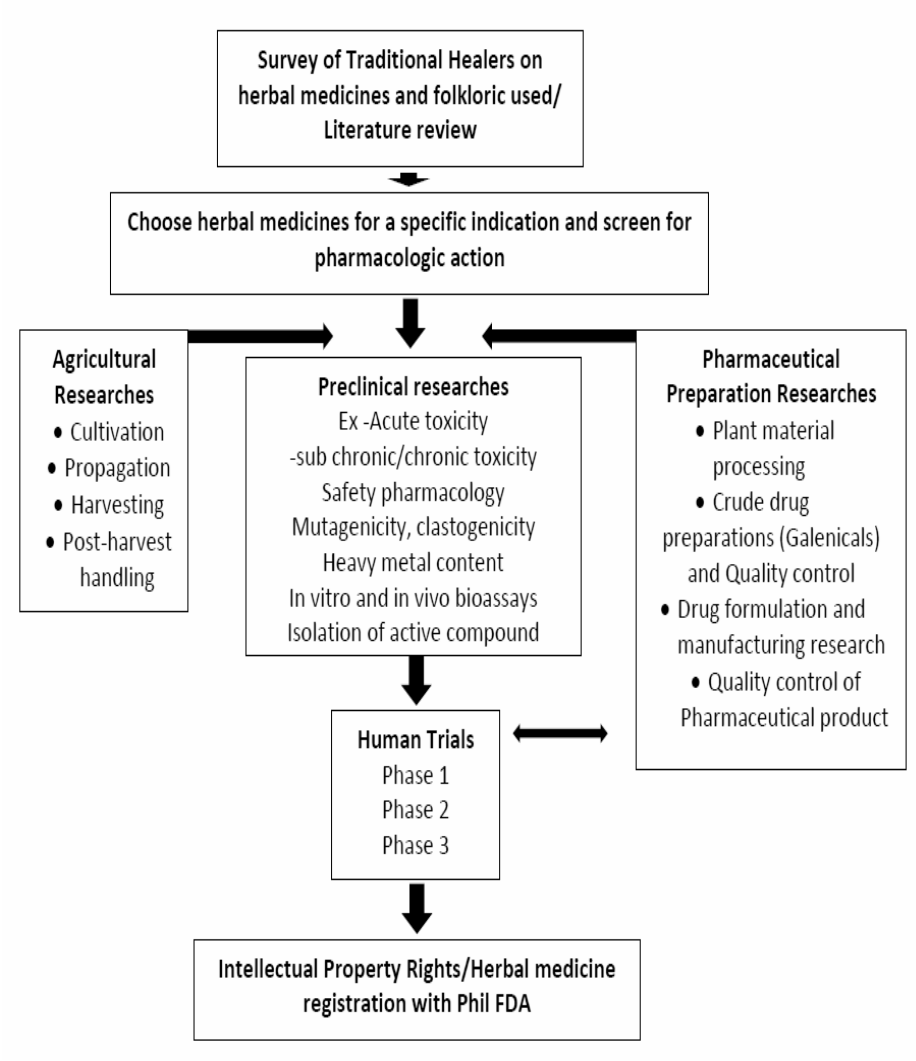


Figure 1. Algorithm of Herbal Medicine Drug Development

ETHICAL GUIDELINES FOR RESEARCH IN TRADITIONAL AND ALTERNATIVE HEALTH CARE

Worldwide, there is a continuing popular interest in and utilization of complementary traditional and alternative medicine health care (TAHC). In the Philippines, promotion of the utilization of TAHC is embodied in the Traditional and Alternative Medicine Act of 1997 (RA 8423). This act 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 TAHC 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 TAHC modalities could be promoted for widespread use.

Traditional medicine has a long history. It is the sum total of the knowledge, skill, and practices based on the theories, beliefs, and experiences indigenous to different cultures, whether explicable or not, used in the maintenance of health as well as in the prevention, diagnosis, improvement, or treatment of physical and mental illness.

The terms "complementary medicine" or "alternative medicine" refer to a broad set of health care practices that are not part of that country's tradition or conventional medicine and are not fully integrated into the dominant healthcare system. They are used interchangeably with traditional medicine in some countries (WHO, 2019).

According to the National Center for Complementary and Alternative Medicine (NCCAM; now NCCIH or National Center for Complementary and Integrative Health) in 2011, CAM non-mainstream medical therapies include the following:

- Biologically-based therapies such as dietary supplements, herbal products, animal products, and aromatherapy;

- Manipulative body-based methods such as massage, acupressure, chiropractic, and osteopathic manipulation;

- Mind-body interventions such as meditation, prayer, mental healing, art or music therapy;

- Energy therapies such as qi gong, reiki, therapeutic touch, pranic healing, electromagnetic fields methods; 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 TAHC therapies, for most, there are key questions that have yet to be answered through well-designed scientific studies. For example, whether these therapies are safe and 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 three generations for traditional medicine or at least one generation for complementary medicine.

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 used.

Use of Randomized Controlled Trial Design

4. In contrast to mainstream medicine, TAHC modalities focus on beneficial effects (e.g., quality of life) rather than efficacy. In this context, study designs other than randomized controlled trials should be acceptable.

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

Blinding

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

Safety

7. The study shall ensure evidence of safety and that the experimental arm will not worsen the patient's condition by the delay in administering mainstream 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.

Intellectual Property Protection

9. Where applicable, the intellectual property rights of the traditional knowledge owner shall be protected, as provided in the law.

ETHICAL GUIDELINES FOR RESEARCH INVOLVING ASSISTED REPRODUCTIVE TECHNOLOGY

Research involving Assisted Reproductive Technology (ART) is arguably under the category of Reproductive Health research, which is in the theme of Research to Enhance and Extend Healthy Lives of the National Unified Health Research Agenda (NUHRA 2017-2022). In fact, what is specifically mentioned under the category of Reproductive Health is "studies on the acceptability and effectiveness of family planning commodities and other interventions for family planning and sexually transmitted infections (STI) prevention." Although the current NUHRA is due for review and update after 2022 and thus might re-classify ART as a specific part of Reproductive Health, the ethical principles of justice and social value should give perspective in allocating research resources in this field. Nevertheless, ethical guidelines for research involving ART are never irrelevant.

Research involving assisted reproductive technology (ART) includes, among others, studies on ovulatory (ovulation) rates, ejaculatory efficiency, sperm quantity and quality, fertilization success, embryo viability, and fallopian tube and uterine hospitability. It may also involve studies on the psycho-socio-cultural, economic, legal, and religious aspects of reproductive technology. Research in the field of reproductive health, in general, also encompasses gender issues.

Research in ART is ethically complex because research participants, 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. Thus, 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 2019, and the Philippine Society of Reproductive Endocrinology and Infertility (PSREI), in their 2016 guidelines, mandated a set of requirements for medical hospitals, clinics, centers, and other facilities where assisted reproductive techniques or technologies and related research can be conducted.

Additionally, the same guidelines emphasized that clinical and biological research in assisted reproductive technology should be carried out only under the supervision of a qualified and certified practitioner. Adequate and up-to-date training in the technical aspects and sensitivity to ethical and other issues of using technology for assisted reproduction must have been acquired by said practitioner.

The following are the considerations notably applicable to Reproductive Health Research:

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

2. The research protocol must not include prohibited or unacceptable practices because they are deemed contrary to accepted policy and public morals. These include the following:

    - Surrogacy, a method of assisted reproduction where intended parents work with a gestational surrogate who will carry and care for their babies until birth;

    - Gamete donation (egg/sperm donation), a procedure that enables those who wish to have children but who cannot produce or use their own gametes (sperms or eggs) to use gametes provided by others in attempts to procreate; and

    - ART services outside the context of marriage.

3. Obtaining informed consent from the potential participants must consider the following: 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 conflict of interest.

    3.1. Information sheets for research projects must be separate from and can be read independently of the written

information provided to a patient during 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, and the attendant risks, must be discussed with the research participants and their partners, and consensual decisions should be arrived at in the light of institutional practices and religious considerations.

3.4. Informed consent for the use of excess human gametes or human genetic material outside of those originally stated in the protocol must be obtained from all concerned persons, e.g., research participant and partner. Such use, e.g., future research, must be stated in specific terms, avoiding general open-ended statements.

3.5. The participants in the 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 research protocol should include long-term follow-up procedures to monitor the outcomes of the ART.

6. Researchers must disclose any financial interests in the research in the protocol to be submitted to the REC.

7. Conscientious objections must be appropriately recognized.

7.1. If any person 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 they object.

7.2. Clinics or research facilities must also ensure that a person or trainee is not disadvantaged because of a conscientious objection.

ETHICAL GUIDELINES FOR RESEARCH IN MENTAL HEALTH

A quick survey of current research in mental health revealed a wide variety of research projects, such as the National Survey for Mental Health and Wellness (2020–2021), anthropological studies on mental illness, and common language for mental health symptoms and manifestations. Other ongoing studies are clinical drug trials, including pharmacogenomics, the determination of the effectiveness of psychosocial interventions in drug abuse and post-traumatic or aftermath of violent experiences like the covid-19 pandemic coupled with the rising incidence of suicide, the establishment of a national clinical registry for mental illness, the derivation of a Filipino diagnostic manual for mental illness, and various association and causative genetic studies. Programs that support the mental health of healthcare workers, students, and Filipinos in general, in response to the COVID-19 pandemic and its consequences are also being developed. Mental health research involves 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 clinical and non-clinical studies involving different disciplines (e.g., anthropology, psychology, sociology, psychiatry, genetics and neuroscience, nutrition, pharmacology, philosophy). It is conducted in various settings, including hospital laboratories, health care facilities, free-standing clinics, schools, and 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, unique issues challenge mental health research in the Philippines. Most of the clinical or behavioral scales used in mental health research and clinical drug/diagnostic trials have been developed, validated, established, and licensed in Western countries. It must be encouraged that these measuring scales should be locally validated to address cultural and conceptual differences for the global application of the results of the studies.

Methodology

1. The researcher shall develop ways and means other than blinding

to promote the 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.

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. The exclusion of certain groups of individuals because of their lack of access to information on ongoing research or clinical drug trials is a form of inequity and a potential selection bias. Interested participants with poor insight can participate in a study through a proxy consent (legally authorized representative, LAR). If the participant is not psychologically fit to give consent for a clinical drug trial, a LAR can be a proxy, but the participant must also give his consent. If the LAR agrees to make the patient participate in a research study but refuses to join, the patient should not be forced to sign an informed consent form. When their insight improves, efforts can be applied to obtain the individual's informed consent.

4. If the participant is illiterate, the sponsor must provide other means that will facilitate understanding of the clinical trial process, like the use of new strategies to improve communication with patients, including the use of videotapes or animated cartoon illustrations.

5. Informed consent is a continuing process, and the mental health researcher must base their assessment of the decisional capacity of the potential participant 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 informed consent during moments of rationality.

8. Researchers must clarify the purpose of the study to address participants' desires for a therapeutic outcome, social contact, or practical help.

9. Confidentiality is the responsibility of the person to whom this private information was given. However, when the right to safety of another individual is infringed, the policy of the 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 justify breaching the participants' privacy.

10. In clinical trials, the participant's identity must be established through a valid government-issued identification card, passport, or birth certificate. A copy of this document must be inserted together with the signed ICF. This must be strictly observed to protect institutionalized patients and avoid "professional" clinical trial participants who enroll in more than one site for monetary gain.

    Since this is a vulnerable population, the institutionalized participant must have a relative or a guardian during every clinical trial visit to confirm abnormal findings, new physical examination findings, or observations and ensure that the participant consents to continue their participation.

11. Investigators involved in clinical drug trials for the 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 their 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

therapy regimen is clearly described and is included in the protocol for both the control and the experimental treatment. 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 the 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. Community-based research must always include benefits to the community, e.g., Community Mental Health Promotion Seminar/Psychoeducation.

17. As much as possible, unless the study objectives 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, local government unit, and police authorities shall be done before its implementation to protect both the researcher and the participant.

18. Deliberation should be done for the use of pseudonyms, or the removal of links between names and data, for participants whose illegal activity may be revealed or discovered in research.

ETHICAL GUIDELINES FOR RESEARCH ON COSMETICS

In 2003, the ASEAN nations, including the Philippines, agreed to harmonize the requirements for cosmetic products putting into force the ASEAN Cosmetic Directive by 2008 (ASEAN, 2003). The ASEAN Cosmetic Committee (ACC), established by the ASEAN member states, meets twice a year to give advice or update guidelines on any matter of a scientific or technical nature in the field of cosmetic products. Thus, it behooves the researcher to check the latest minutes of the meeting of the ACC for an updated list of substances or compounds that should not be used as components of cosmetic products.

In this 2003 ASEAN agreement, cosmetics is *"any substance or preparation intended to be placed in contact with various external parts of the human body (epidermis, hair system, nails, lips, and external genital organs) or with the teeth and the mucous membranes of the oral cavity with a view exclusively or mainly to cleaning them, perfuming them, changing their appearance and/or correcting body odours and/or protecting them or keeping them in good condition"* (ASEAN, 2003, p.18). Philippine FDA registration of cosmetic products does not require clinical trial data except in cases where claims (e.g., sun protection factor [SPF] levels) require substantiation.

These guidelines shall be applicable to research in the development of cosmetics and the use of cosmetics.

These guidelines are not meant for research in cosmetic surgery that generally investigates the efficiency and safety of surgical techniques and the prevention and management of surgical complications.

Social Value

1. Cosmetic research shall not promote a specific ideology of "beauty" that disparages the characteristics of the Filipino.

2. The proposed cosmetic product shall adhere to the definition of cosmetics above. It shall not be presented as treating or preventing disease in humans, nor does it permanently restore, correct, or

modify physiological function by exerting a pharmacological or immunological action.

Quality and Safety of the Cosmetic Product

3. The proposed cosmetic product shall not contain ingredients banned in the ASEAN Cosmetic Directive.

4. A certificate of compliance with Good Manufacturing Practice (GMP) shall be obtained for the cosmetic product

5. Safety reporting from consumers and cosmetic and dermatology practitioners shall be promoted to build a useful database for adverse reactions to cosmetic products, including soaps.

6. Before any participant is exposed to the test product, all safety information regarding the product and its ingredients shall have been assessed and the corresponding proofs presented.

7. The researcher shall check the possible presence of antibiotics, banned ingredients, and restricted ingredients (e.g., colorants, preservatives) for proper reporting and decision-making.

8. 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

9. Inclusion and exclusion criteria shall consider different skin conditions, allergic reactions, occupation of the participant, and past experiences with cosmetics. Pregnancy and breastfeeding may be confounding factors in the study because of the different hormonal dynamics of women in these physiological states.

Avoidance of Risks

10. The protocol shall include all precautions to be taken (e.g., exposure to sunlight, wetting and drying, and possible interactions with other commonly used cosmetic products) to avoid the occurrence of adverse events.

11. Cosmetics to be tested on the face, neck, or scalp shall be most carefully evaluated for risk of serious adverse reactions.

Privacy and Confidentiality

12. Care must be taken in protecting the participants' privacy, especially regarding documentation by taking pictures that involve the face. Additionally, researchers are reminded that moles and other skin marks are identifying.

Withdrawal from the Study

13. A participant who withdraws from a research study 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 during visits and provided with the appropriate medical care in accordance with REC-approved procedures.

Clinical Care and Compensation of Participants

14. In case of an unexpected/adverse skin reaction, the investigator/researcher shall assess the severity of the reaction, complete the required safety report, and start the appropriate therapy promptly.

15. Investigators shall ensure that research participants who suffer an injury because of their participation are entitled to free medical treatment for such injury and financial or other forms of assistance that would compensate them proportionately for any resultant impairment.

Qualification of Researchers

16. Principal investigators or lead proponents in cosmetic research shall be limited to those trained in accredited dermatology residency or fellowship programs by authorized organizations.

ETHICAL GUIDELINES FOR GENETICS AND GENOMIC RESEARCH

Genetics refers to the study of genes and their role in the inheritance of traits and diseases. On the other hand, genomics is the study of all a person's genes, referred to as the genome, including interactions of those genes with each other and with the environment. Research on genetics and genomics offers opportunities to develop newer, more precise diagnostics and novel targeted therapeutics. The goal is to use the knowledge gained through research to discover ways to better diagnose, treat and prevent disease. Genetic and genomic research encompass gene discovery, genetic diagnosis of rare monogenic disorders and common complex genetic conditions, pharmacogenetics/pharmacogenomics, gene-based targeted therapies, epigenetics, stem cell therapy, gene therapy, and genome editing.

Human biological samples for genetic research include samples that are sources of DNA, RNA, and protein such as tissues from biopsies, aspirates, scrapings, and body fluids such as blood, saliva, ocular fluids, stools, and other excretions. These samples are often stored in biobanks and anonymized for future use. However, there are ethical issues unique to genetic and genomic research. The genetic information stored in genes is very personal to an individual, his family, and even an ethnic group.

Common ethical challenges in genetic and genomic research include informed consent, privacy, and confidentiality (e.g., re-identifiability and data breach), storage/biobanking from future use, community engagement, data sharing, and return of research results as well as incidental findings.

Use of Human Samples or Human Materials

1. Human biological samples shall be collected, processed, used, and stored only for the following research purposes:

    1.1. Therapeutic and non-therapeutic genetic research (i.e., epidemiological, prognostic, population-based genetic studies, anthropological or archeological studies);

    1.2. Development of drugs, biomedical devices, molecular

diagnostics, and medical technologies;

1.3. Forensic medicine, in which case use of samples shall be in accordance with domestic laws and consistent with laws on human rights; and

1.4. Other reasons of public interest (e.g., genomic biosurveillance, identification of victims of mass disasters).

Informed Consent

2. Prior, voluntary, informed consent for research participation by someone competent to do so shall be obtained for the collection of biological samples, human genetic, genomic, transcriptomic, proteomic, metabolomic, metagenomic data, and their subsequent processing, use, and storage; without inducement relating to the offer of financial or personal gain.

3. Research participants shall be provided full and comprehensible information in a language the participant can understand about the following:

    3.1. Background information on the study with a clear explanation of genetics;
    3.2. Procedure;
    3.3. Risk and benefits;
    3.4. Privacy and confidentiality, especially in protecting the participant's identity;
    3.5. Voluntary nature of participation;
    3.6. Withdrawing from the study;
    3.7. Data which includes an explanation of the difference between the physical sample and the data generated from it; and
    3.8. Storage who (custody), where (local or foreign institution), up to when (in years), and disposal of samples

4. 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.

5. Research participants shall be recruited as individuals, rather than as a family group, and shall consent as individuals.

6. In cases where identities of groups or communities can be linked to genetic biomarkers in a study, permission or endorsement may be obtained from an elected or recognized leader responsible for permitting the participation of the group or community. For specific guidance on genetic studies involving indigenous peoples or indigenous cultural communities, refer to section on Research Involving Indigenous Peoples.

7. Consent shall be obtained for biobanking and future use of samples for genetic research with a clear opt-out option.

8. Informed consent is not required to re-use samples that are anonymized and cannot be linked to a person's personal information, a community, or an institution. Any sample that can be linked to any of this information mentioned is not considered an anonymized sample.

   All second- and third-party use of biological samples are restricted to anonymized samples. Such use requires ethical approval. Limited, non-identifying demographic information may be retained on the sample.

9. For stored biological samples, see the section on Research Using Human Data and Samples from Biobanks, Registries, and Databases.

10. If informed consent is withdrawn, samples shall be irreversibly unlinked from the data. All identifiers shall be destroyed and disposed of, following the guidelines on Research Using Human Data and Samples from Biobanks, Registries, and Databases.

Genetic Studies among Indigenous Peoples

11. International and national laws and regulations on respect for

human rights and privacy and protection from exploitation shall guide genetic studies involving indigenous people's groups. (See section on Research Involving Indigenous Peoples). An ethical review must occur in both the host and the sponsoring institutions in externally sponsored research.

Requirement for Genetic Counseling in Clinical Genetics

12. Genetic research protocols that involve the disclosure of results of genetic testing shall be accompanied by pre- and post-genetic testing counseling.

Privacy, Confidentiality, and Security

13. 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.

14. Results of genetic and genomic research that seek to discover the association of biomarkers with disease and are exploratory, in general, are not disclosed to individual research participants. However, genetic research can produce information beyond the aim of the research that may have clinical implications or may be of personal interest to the study participant. There is no consensus on when it is appropriate to return results, what types of results should be returned, and how to return results. In the absence of consensus guidelines, the protocol for ethics approval shall include plans for disclosure of individual research results and incidental findings that may be 'actionable' (actionable is defined as an associated action to reduce the risk of a disease or treat the disease). The informed consent shall state clearly how investigators will handle incidental findings and how this shall be communicated during the informed consent process.

15. In case the disclosure of genetic information becomes unavoidable,

such information shall be dealt with sensitively during genetic counseling.

16. Researchers shall ensure that the results of genetic testing done in the research process are protected from access by third parties.

17. Genetic information from genetic research shall not be released to any other person, 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

18. The research participant's right to privacy (researcher's duty for confidentiality) continues after the participant's death, so 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 Specimens

19. The researcher shall ensure that the handling and preservation of biological samples shall be in accordance with standard scientific procedures and local laws and policies. There are available local guidelines, such as the Guidelines on the Use, Retention, and Storage of Residual Dried Blood Spots from Newborn Screening (DOH AO 2012-0017).

20. Disposal of stored biological specimens shall be done in accordance with standards for handling biohazardous and infectious materials.

21. Documents on 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) as agreed upon at the level of the institutions. The terms of the MTA must comply with applicable Philippine laws. In the case of clinical trials, an MTA is needed if the sponsor is taking samples out of the country for processing in their

laboratory in another country.

22. The respective institutions shall determine the retention time for stored biological samples in accordance with the applicable provisions of the Data Privacy Act of 2012 (RA 10173). This must be declared in the informed consent form. An official institutional policy is recommended.

23. All specimens in a biobank must be accompanied by a copy of the consent agreement signed by the donor.

24. No specimen shall be removed from a biobank for research purposes without an approved research protocol.

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

    25.1. The researcher and the other research groups are collaborating on research that has been approved by their respective RECs and shall be governed by IRB Reliance Agreements.

    25.2. In health-related research protocols involving three or more sites, a harmonized review can be conducted through the Single Joint Research Ethics Board (SJREB) organized by the Department of Health.

    25.3. The genetic material and information are provided in a manner that ensures participants cannot be identified.

International Collaborative Genetic Research

26. A Material Transfer Agreement (MTA), a contract between two parties involved in a research project, shall specify exactly the nature of work to be done on materials given by one party to the other. The specifications shall include:

26.1. materials to be transferred;

26.2. exact work to be done on the materials;

26.3. conditions of storage of the materials, including details on building access and security;

26.4. persons involved with the samples, typically the heads of research groups and all the members of their group;

26.5. duration of the collaboration;

26.6. an agreement about data sharing and collaboration in analysis; and

26.7. procedures for agreeing on any other work not covered in the current MTA.

ETHICAL GUIDELINES FOR RESEARCH ON STEM CELL AND CELL-BASED THERAPY

Research in human stem and cell-based therapy holds enormous potential for contributing to an understanding of fundamental human biology. Research in this area may lead to potential novel treatments and a cure for many diseases. Cell-based therapy (CT) is the transplantation of human cells to replace or repair damaged tissue or cells. Some of the cells used include hematopoietic (blood-forming) stem cells (HSC), skeletal muscle stem cells, mesenchymal stem cells, lymphocytes, dendritic cells, and pancreatic islet cells. Potential applications of cell therapies include treating cancers, autoimmune diseases, urinary problems, and infectious diseases, rebuilding damaged cartilage in joints, repairing spinal cord injuries, and improving a weakened immune system. Hematopoietic stem cell transplantation (also called bone marrow transplant) is the most frequently used cell therapy for blood cancers and hematologic conditions.

While stem cell-based treatments have been established as a clinical standard of care for some conditions, such as hematopoietic stem cell transplants for leukemia and epithelial stem cell-based treatments for burns and corneal disorders, the scope of potential stem cell-based therapies has expanded in recent years due to advances in stem cell research. Stem cells are primordial cells that have the potential to develop into many different cell types in the body during early development and growth.

The rapid advances in stem cell research and genome editing technologies have created high expectations for the promise of regenerative medicine and gene- and cell-based therapies. As the field advances, it is essential to rigorously evaluate the safety and effectiveness of each potential new intervention. The primary goals of stem cell research are advancing scientific understanding, generating evidence for addressing unmet medical and public health needs, and developing safe and efficacious therapies for patients.

The following are examples of cells that are used in cell-based therapy research.

1. Dendritic cells (DCs), named for their probing, 'tree-like' or dendritic shapes, are responsible for initiating adaptive immune responses and hence function as the 'sentinels' of the immune system. Paul Langerhans first described DCs in human skin in 1868 but thought they were cutaneous nerve cells. DCs are bone marrow (BM)-derived leukocytes and are the most potent type of antigen-presenting cells. DCs are specialized to capture and process antigens, converting proteins to peptides presented on major histocompatibility complex (MHC) molecules recognized by T cells. They can also be propagated in vitro from BM and blood using various combinations of growth factors, such as granulocyte macrophage-colony stimulating factor (GM-CSF) and Flt3 ligand. DCs are heterogeneous, e.g., myeloid and plasmacytoid DCs. Although all DCs are capable of antigen uptake, processing, and presentation to naive T cells, the DC subtypes have distinct markers and differ in location, migratory pathways, detailed immunological function, and dependence on infections or inflammatory stimuli for their generation. During the development of an adaptive immune response, the phenotype and function of DCs play a critical role in initiating tolerance, memory, and polarized T-helper 1 (Th1), Th2, and Th17 differentiation.

2. Hematopoietic stem cells are immature cells that can develop into all types of blood cells, including white blood cells, red blood cells, and platelets. Hematopoietic stem cells are found in the peripheral blood and the bone marrow.

3. Induced pluripotent stem cells (iPS cells) are immature cells generated from an adult (mature) cell, which have regained the capacity to differentiate into any type of cell in the body.

4. Limbal stem cells, also known as corneal epithelial stem cells, are stem cells located in the basal epithelial layer of the corneal limbus.

5. Mesenchymal stem cells are multipotent adult stem cells present in various tissues, including the umbilical cord, bone marrow, and fat tissue. Mesenchymal stem cells can self-renew by dividing and can differentiate into multiple tissues, including bone, cartilage, muscle and fat cells, and connective tissue.

General Principles

The National Ethical Guidelines on Stem Cell Research has considered the guidelines of several international stem cell and research organizations that were deemed applicable to the local research environment.

1. As with all clinical research, clinical trials of stem cell-based interventions must follow internationally accepted principles governing the ethical conduct of clinical research and the protection of human participants.

2. Key requirements include regulatory oversight, peer review by an expert panel independent of the investigators and sponsors, management of ethical issues including fair subject selection, informed consent, patient monitoring, and adherence to standards of quality of products used.

3. The scientific and ethics oversight process must assess the scientific rationale and merit of research proposals, the relevant expertise of the researchers, and the ethical permissibility and justification for the research.

4. The processing and manufacture of any product must be conducted under scrupulous, expert, and independent review and oversight to ensure as much as possible the quality and safety of the cells.

Responsibilities of Clinical Researchers

5. Cell-based clinical researchers shall assess:

    5.1. the biological characteristics of the cells to be used in clinical trials;

    5.2. whether these cells have been developed with appropriate manufacturing standards; and

5.3. the preclinical data on their use in animal and other models for evaluating their safety and efficacy; and any early clinical data, if available, which address safety issues in the short and medium-term and continued observation for long-term effects.

6. Cell-based clinical researchers shall

6.1. provide with utmost clarity the potential benefits of participating in the trial with stem cells since patients (research participants) may have recourse to reasonable therapeutic alternatives;

6.2. protect the confidentiality of the research participant's health data;

6.3. monitor research participants for long-term health effects;

6.4. provide a clear, timely, and effective plan for adverse event reporting; and

6.5. offer a clinical plan to provide treatment for toxicity, including treatment of tumors that might arise. This plan might include compensation for research-related injuries.

Voluntary Informed Consent

7. Informed consent is particularly challenging for clinical trials involving highly innovative interventions.

7.1. Informed consent must be obtained from potential human participants or their legally authorized representatives. Re-consent of participants must be obtained if substantial changes in risks or benefits of a study intervention are identified or alternative treatments emerge during the research.

7.2. Informed consent should include the following:

7.2.1. background and rationale of the research;

7.2.2. when novel stem cell-derived products have never been tested before in humans and researchers do not know whether they will work as hoped;

7.2.3. tests required in the study;

7.2.4. source of the cells so that their values are respected, and be given the option of not participating in the study if stem cells were derived in a way inconsistent with their beliefs and values;

7.2.5. other standards of care treatment options, potential short- and long-term risks and side effects of the research, and potential benefits; and

7.2.6. the possible irreversibility of a cellular transplant should be explained clearly since cell-based interventions may not leave the body and may continue to generate adverse effects for the patient's lifetime.

7.3. Patients shall be allowed ample time to ask questions and decide to participate in the research.

7.4. Patients shall be informed of the cost of the treatment. 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 regarding which component is research and which component is clinical care.

7.5. If human cells and tissues are procured from a minor or adult who lacks the decision-making capacity to provide informed consent, consent must be provided by a parent, legal guardian, or another legally authorized person. Whenever feasible, the assent of the minor or decisionally incapacitated adult is also strongly encouraged.

7.6. Research ethics committees shall ensure that informed consent documents accurately portray these uncertainties and potential risks and explain the experimental nature of the clinical study.

Donors of Cells

8. Researchers shall ensure that potential donors or their legally authorized representatives adequately understand the stem cell-specific aspects of their research participation. The following issues need to be emphasized and clarified with the donor:

8.1. The importance of donating, the rationale of the research, and how the cells will be collected;

8.2. The cells and cell lines may be subject to storage. If possible, the duration of storage should be specified;

8.3. The donation is made without restrictions regarding the choice of the recipient of the transplanted cells except for directed altruistic donation;

8.4. The potential risks of donating;

8.5. The donor will be screened for infectious and possibly genetic diseases; what types of genomic analyses (if any) will be performed and how genomic information will be handled;

8.6. A disclosure that any resulting cells, lines, or other stem cell-derived products may have commercial potential and whether any commercial and intellectual property rights will reside with the institution conducting the research;

8.7. Disclosure of medical and other relevant information that will be retained, and the specific steps that will be taken to protect donor privacy and confidentiality of retained information, including the date at which donor information

will be destroyed, if applicable;

8.8. The donor will be allowed ample time to decide and ask questions; and

8.9. The donor will not be pressured to donate or receive any compensation.

9. In the case that human cells and tissues are procured from a minor or adult that lacks the decision-making capacity to provide informed consent, consent must be provided by a parent, legal guardian, or another legally authorized person. Whenever feasible, the assent of the minor or decisionally incapacitated adult is also strongly encouraged.

10. Stem cells that are retrieved from the umbilical cord blood, cord materials (Wharton's Jelly), placenta, and other birth materials after delivery shall require informed consent from the donor (the woman or the couple concerned, as applicable), including information on possible present and future uses of the cells for research and treatment.

Use of Aborted Fetuses and Pre-implantation Embryos

11. 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.

Manufacture of Cells

12. There should be steps taken to ensure the quality (consistency, purity, and potency) and safety of cellular derivatives generated from stem cells and tissues.

13. All reagents and processes should be subject to quality control systems and standard operating procedures to ensure the quality of

the reagents and consistency of protocols used in making the cellular products administered to participants and patients.

Components in Culture or Preservation of Cells

14. Human or chemically defined components should be used in the culture or preservation of cells whenever possible. All reagents used in manufacturing stem cell-derived therapeutics should be of the highest quality available.

15. Criteria for process and release specifications should be developed during the regulatory review process. Release criteria for stem cell-based interventions should utilize qualified or validated assays that assess the identity, purity, sterility, activity, and potency of the product.

Risk-benefit Analysis

16. Risks should be identified and minimized, unknown risks acknowledged, and potential benefits to participants and scientific understanding estimated. Researchers should be able to justify research with human subjects in terms of likely risk and benefit based on evidence from preclinical studies and the published literature.

Monitoring and Reporting of Adverse events

17. Investigators should report adverse events, including their severity and potential causal relationship with the experimental intervention.

18. Given the potential for transplanted cellular products to persist indefinitely and depending on the nature of the experimental stem cell-based intervention, participants should be advised to undergo long-term health monitoring.

19. Additional safeguards for ongoing research participant privacy should be provided.

20. Participant withdrawal from the research should be made orderly to promote physical and psychological welfare.

Conflict of Interest

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

22. Institutional COI exists when the institution promotes stem cell experimental therapy as an iconic project that defines the institution's aspirations for public recognition. The REC must avoid the coercive influence of administrative officials and insist on its independence in decision-making.

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. These biological samples include blood, saliva, urine, semen, breast milk, cells, tissues, molecules extracted from these, and other human-derived materials. Biobanks are an important resource in biomedical research, especially genomics, transcriptomics, proteomics, and metabolomics. Through biobanks, researchers can access biological samples and data from a large number or a cohort of people that ordinarily would have needed much more time and resources to collect. Genome-wide association studies and other 'omics'-based research that require thousands of individuals can be done using biobanks. However, biobanks have raised privacy issues, the validity of informed consent processes, and the 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 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. Proposals for establishing Human Biobanks, Registries, and Databases (HBRD) of samples collected for research shall be subject to ethics review by a duly constituted research ethics committee.

2. The purpose, both current and for the foreseeable future, of the HBRD shall be 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.

3. The governance and custodianship of the HBRD shall ensure its long-term security and sustainability, especially when funding support is terminated or its nature changes. Every proposal for establishing a biobank, registry, or database should describe plans for the continuing custodianship or disposal of human biological materials or data in the event of transfer or termination of the biobank, registry, or database.

4. The HBRD custodian shall perform the following functions:

    4.1 Formulate HBRD governance structure and the responsibilities of its management, and make such information publicly available;

    4.2 Ensure that sufficient professional staff and resources are available to operate effectively; and

    4.3 Create guidelines on who will have access and how access to samples or data can be granted.

Data Privacy Act of 2012

5. The processing (e.g., storage, use, disposal, sharing, or disclosure) of the sensitive personal information contained in biobanks, registries, and databases shall comply with the applicable provisions of the Data Privacy Act of 2012.

    5.1. The HBRD custodian shall be responsible for ensuring the protection of the rights of data participants as provided for in the law.

Informed Consent

6. During the consent process for collecting and storing specimens or data, participants shall be informed of specific terms of future, secondary, or third-party uses of their samples or data. Information provided to participants shall include plans for the continuing custodianship or disposal of human biological materials or data in the event of transfer or termination of the biobank, registry, or database.

7. If subsequent use of specimen or data is not consistent with the original informed consent, new consent shall be obtained from the participant.

    7.1. If the person concerned has expressed a wish not to be contacted, that should be respected.

    7.2. If the attempt to contact the person concerned proves unsuccessful, these biological materials should only be used in the research project subject to an independent evaluation of the fulfillment of the following conditions:

        7.2.1. evidence is provided that reasonable efforts have been made to contact the person concerned;

        7.2.2. informed consent is given by an appropriate legally authorized representative (LAR), or a waiver of consent is obtained from a REC;

        7.2.3. the research addresses an important scientific interest and is in accordance with the principle of proportionality (Refer to the Data Privacy Act of 2012);

        7.2.4. the aims of the research could not reasonably be achieved using biological materials for which consent or authorization can be obtained; and

        7.2.5. there is no evidence that the person concerned has expressly opposed such research use.

8. The informed consent document shall include information on whether specimens or data will be made available for allowable non-research purposes.

9. During the consent process, the participant shall be informed 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

10. Stored human biological materials or data shall be promptly de-identified and coded in accordance with data privacy standards. Access to the code shall be limited to those who will also be legally accountable for breaches of privacy and confidentiality.

11. 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

12. 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 a REC.

13. 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.

14. Human biological materials and data shall only be transferred when the recipient has adequate standards regarding privacy and confidentiality. Use of information and materials for marketing purposes is not allowed.

15. A Material Transfer Agreement (MTA) shall be made between institutions involved in a collaborative project that will use the stored human samples or data.

16. Researchers shall only have access to human biological materials or data 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 the new research.

17. Except when required by law or for public safety and national security purposes, 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. Information protection is guaranteed even when the custodian is no longer employed in the institution that houses the databank or biobank.

ETHICAL GUIDELINES FOR RESEARCH ON EMERGING TECHNOLOGIES

Emerging technologies refer to new technologies just coming into existence or the continuing development of existing technologies with new applications (Rotolo et al., 2015). They are usually reserved for technologies that create are expected to create significant social and or economic impact. Nanotechnology, nanomedicine, biosimilars, artificial intelligence (AI), and augmented reality are emerging bio-related technologies included in this section.

Artificial Intelligence and Augmented Reality

Artificial intelligence is defined as "the ability of a digital computer or computer-controlled robot to perform tasks commonly associated with intelligent beings. The term is frequently applied to developing systems endowed with the intellectual processes characteristic of humans, such as the ability to reason, discover meaning, generalize, or learn from experience (Copeland, 2020). AI can be applied in health care and research to diagnose, prevent, and prognosticate diseases, morbidity or mortality risk assessment, drug development, disease outbreaks and surveillance, and health system management and planning.

Virtual and augmented reality, on the other hand, are two distinct but related areas under the category of "mixed reality." Users interact with a new world entirely using a headset (virtual reality) or face-to-face but with digital information overlaid on the real world (augmented reality). Major research themes in virtual and augmented reality are diagnostic and surgical procedures, and rehabilitation for neurodegenerative and mental health disorders.

The emergence of artificial intelligence and mixed reality has introduced several ethical, social, legal, and cultural issues. These technologies, while not new, have emerged in popularity in recent years because of the democratization of computational resources, access to personal devices, and expansion of the Internet. Virtual and augmented reality is presently unregulated, and there is little to no protection for its users. As a result, the

potential for abuse and mishap is high. Because they are unregulated, many of these technologies are released for public consumption without undergoing ethical reviews.

Nanotechnology and Nanomedicine

Nanotechnology involves "*research and technology development at the atomic, molecular, or macromolecular levels, in the length scale of approximately 1 to 200 nm range, to provide a fundamental understanding of phenomena and materials at the nanoscale and to create and use structures, devices, and systems that have novel properties and functions because of their small size and/or intermediate*." (http://www.nano.gov.html/facts/whatIsNano.html).

By taking advantage of quantum-level properties, nanotechnology allows control of the material world at the nanoscale, providing how systems and materials can be built with exacting specifications and characteristics. Thus, nanotechnology enables manipulating molecular-sized materials to create new processes and products. The major research objectives in nanotechnology are the design, modeling, and fabrication of molecular machines and molecular devices.

Nanomedicine is the application of nanotechnology for medical purposes. There are three major areas where nanotechnology can be applied in medicine: the diagnosis of diseases (nanodiagnosis), controlled drug delivery (nanotherapy), and regenerative medicine. The fourth area of application is emerging called theranostics, where diagnostics and therapy are combined in the same system that holds both the imaging and therapeutic agents. Potential applications can include improved imaging techniques, improved transport across biological barriers, nanodevices for tracking therapeutic interventions and targeted destruction of tumor cells, killing bacteria, tissue repair, and immune enhancement.

The emergence of nanotechnology has numerous social, environmental, legal, cultural, ethical, religious, philosophical, and political implications. In research involving emerging technologies, there shall be an assurance that the product will be available and affordable to the population where the participants were chosen if found effective and safe.

Similar Biotherapeutic Products or Biosimilars

A biosimilar or similar biotherapeutic product (SBP) is a biopharmaceutical product similar to a licensed biologic product or reference biotherapeutic product (RBP) in terms of quality, safety, and efficacy. While there may be some differences between the clinically inactive parts of the SBP and the RBP, there should be no clinically meaningful differences in the biosimilar product's safety, purity, and potency. The development of biosimilars involves emerging technologies, especially recombinant DNA technology. Examples of this group include high molecular weight hormones, products derived from blood and plasma, allergens, and products of genetic engineering.

Under a research management framework, studies involving emerging technologies that will affect the human condition should undergo the rigor of review by competent reviewers who ensure that the technologies to be developed are safe and that their intended benefits outweigh the risks to the research participants.

General Guidelines

The development of these technologies and products requires compliance with Good Manufacturing Practice (GMP) and stringent biological product development requirements.

1. Guidelines for GMP shall be clearly set for specific emerging technologies. For hardware and devices, the guidelines for Good Manufacturing Process shall be adopted before their application to human participants. For software, the ACM Software Engineering Code of Ethics and Professional Practice shall be observed. If these technologies will be used for human participants, and there are potential risks, Good Clinical Practice guidelines should be adopted.

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 to introduce 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 biological products or devices of emerging technologies shall be done.

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

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

Ethics in Artificial Intelligence and Mixed Reality (Virtual and Augmented Reality) Research

7. The principles of transparency, justice and fairness, non-maleficence, responsibility, and privacy hold even with artificial intelligence research.

8. Software developers should release for peer review the underlying equations and anonymized datasets they used for internal validation. These include but are not limited to characterizing the data sources and the nature of the content (period covered, geographic scope, and demographics). The researchers should enumerate the possible biases (such as race, sex, ethnicity, economic status, religion,) in these datasets and express their inability to ascertain if there are any. Artificial intelligence is limited by the sources of data fed to it. These data sources, which could be skewed towards specific groups of people in a known area over a period, may, in turn, transfer these biases to the resulting algorithms.

9. In their reports and publications, researchers must share information about (a) the populations used upon which the algorithms were trained, (b) the health issues the algorithms can

best answer, and (c) the erroneous conclusions the algorithms may introduce. Clinicians who use AI in practice should be informed of these caveats and warnings.

10. The main ethical challenges in terms of virtual and augmented reality implementation include privacy (when participants are identified through facial recognition) and non-maleficence (when participants exhibit mental and social side effects or develop unrealistic expectations through reality distortion and manipulation).

11. Researchers, developers, and ethics boards must critically examine their design, the ability and intention of the technology, and their desired outcomes (PASE 2012 Ethical decision tree).

12. The adoption of ethical codes of conduct by researchers can serve as preliminary control for the protection of participants. By adhering to these codes, the ethical practice of researchers can be assured through the whole spectrum of emerging technology research from inception to development to implementation. The ACM Software Engineering Code of Ethics and Professional Practice, Good Manufacturing Practice, and Good Clinical Practice are examples of these codes.

13. AI and mixed reality research should be registered and examined by an ethical review board to minimize risks. These boards must have at least one member knowledgeable about computer science or software development, especially the inherent risks involved in the process.

14. Researchers and developers should provide full, accessible, and understandable disclosure to the participants to limit ethical concerns. This includes explaining the benefits and risks to the participant or end-user in a language that they can understand.

15. Like other research, AI and mixed reality researchers and developers must fully disclose to potential research participants or their representatives the purpose of the technology, processes, benefits,

risks, alternatives, confidentiality protections, unintended consequences, and other information the participant would require to decide whether to participate.

Ethics in Nanotechnology

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

17. 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 in the research facility.

18. Safety standards shall be set for all stages of research involving nanomaterials.

19. The disposal of nanomaterial waste products should be managed through the institution's chemical waste program.

20. A nanotechnology researcher shall provide a credible account of the technology's benefits, costs, and risks.

Ethics in Nanomedicine

21. Before nanomedicine products can be used to diagnose, prevent, or treat disease, they must first undergo extensive pre-clinical and clinical testing.

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

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

24. 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.

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

26. The researcher shall inform a potential research participant, or their 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.

27. 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.

28. If a nanosensor is incorporated in the investigational drug (IND) to monitor compliance and outcomes, and if an external wireless device is worn by the participant that will pick up the signals from the nanosensor in the IND, researchers should disclose to the participants or LAR the following:

    28.1. where the electronic device shall be connected (e.g., internet, hospital network, or other medical devices);
    28.2. that the signals shall be encrypted;
    28.3. the risk of breach of confidentiality; and
    28.4. a potential cyber security threat.

29. 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

30. Manufacturers of biosimilars shall conduct all phases of clinical studies to promote drug safety and efficacy. In particular, the studies must address immunogenicity concerns.

31. Based on total quality, safety, and efficacy data, the innovator biological product shall be the reference or comparator for head-to-head studies with the SBP in a relevant research population.

32. 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.

33. Because the inherent differences between an SBP and an RBP may involve a greater risk-to-benefit ratio for specific research participant populations (e.g., stem cell donors) than for others, extrapolation shall be implemented on a case-by-case basis.

34. Owing to the limited clinical database available during the approval of an SBP, it is essential 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 ENVIRONMENTAL HEALTH RESEARCH

Environmental health focuses on the physical, chemical, and biological aspects peripheral to individuals and the interconnected factors influencing a person's behavior. It encompasses the assessment, prevention, mitigation, and control of environmentally related attributes that are capable of negatively affecting human health. Additionally, it also delves into the impact of individuals on the environment (WHO, 2011).

The Stockholm Declaration Principle 1 states that "man has the fundamental right to freedom, equality, and adequate conditions of life, in an environment of a quality that permits a life of dignity and well-being, 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 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, to ensure healthy lives and promote well-being for all at all ages, and one of its targets to substantially reduce the number of deaths and illnesses from hazardous chemicals and air, water, and soil pollution and contamination by 2030.

The core areas of concern in environmental health and are the topics of inquiry in environmental health research are:

- Air Quality
- Chemical Safety
- Climate Change
- Emergency Preparedness
- Food Safety
- Healthy Housing
- Infectious Disease and Vector Control
- Injury Prevention
- Occupational Safety and Health
- Radiation

- Soil Quality
- Solid Waste Management
- Toxicology
- Water Supply and Sanitation

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

Study Design

1. The study design shall ensure the provision of effective environmental health interventions for research participants if warranted by the situation.

2. Environmental health research involving children shall consider their unique susceptibility to certain toxicants that is different from adults. Children shall not be treated like they are little adults.

3. The study design must include procedures for researchers to report the environmental health concerns to relevant government agencies/authorities to take appropriate action. This can consist of adequate relocation when there is a possibility of contamination in environmental monitoring.

4. The study design should not cause changes in behavior that may cause harm to a participant during the conduct of the study. The informed consent process should therefore ensure that participants

understand that the study's goal is to observe and measure the participant's exposures as they carry out their daily activities.

5. The study design must include procedures for managing wastes generated from the research in accordance with existing regulations and guidelines for waste management.

Community Participation

6. The participation of the community shall be encouraged in preparation of the research agenda through a community assembly or consultation. This process will enable the community to deliberate and explore the pros and cons of the research to facilitate informed decision-making and ensure that the research is responsive to the community's needs.

7. Community empowerment and local government action shall be ensured before community-based environmental monitoring or health research.

8. The research protocol shall describe the communication strategy that will ensure a better understanding of the culture and expectations of the community.

9. 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.

10. Researchers should continuously engage with the community and be willing to revisit their procedures and study design in response to community concerns and, if necessary, revise them accordingly.

Informing Third Parties of Research Activities

11. When study participants are involved in personal sampling that includes time spent in other settings, the researchers must inform or request permission from appropriate authorities.

12. The potential impact of third-party knowledge of research activities on confidentiality and risks for the study participant should be considered. Study protocols should be structured to minimize these potential risks. In addition, the risks and mitigation measures, and limits on the ability to provide or protect the confidentiality, should be explained in the informed consent process.

Research involving Housing-related Health Hazards

13. The protocol shall ensure that intrusion into the privacy of residents is minimized. If field investigations are conducted in homes, the researchers may access private information that is not part of the study. The investigators must protect the privacy of their subjects and keep this information confidential unless there is evidence of hazards that can potentially cause imminent or serious danger.

14. The vulnerability of communities in poor-quality housing shall be recognized and protected.

15. In poor housing communities, undue influence to participate because of financial and material incentives shall not be allowed.

Confidentiality of Participation

16. Researchers must consider if disclosing an individual's participation in the study can create potential harm or distress.

17. The protocol should include strategies to minimize the risks of causing harm or distress to the study participants due to disclosure of participation.

18. The informed consent process should help the study participants understand the extent to which the confidentiality of participation can be ensured and the possible risk of disclosure.

Sharing of Results with the Community

19. Research results shall be shared with the community unless results are not definitive and ambiguous. This can involve the disclosure of levels of biomarkers and environmental toxicants. During longitudinal studies with repeated measurements over time, the researchers should ensure the provision of results to research participants and the community as the study proceeds. Appropriate health hazard and risk communication strategies should be developed for this purpose.

20. Researchers should ensure the confidentiality and privacy of study participants if reporting of study results to third parties is being considered or is required. Aggregated data or a summary of research results can be presented. The informed consent process should clarify under what conditions and how research results will be disclosed to third parties who are sources of the environmental health issue, government agencies/authorities, and policymakers, among others.

Use of Biobanks in Environmental Health Research

21. Environmental health research concerning biobanks shall include a mechanism in its protocol to address the following:

    21.1. Respect for the decision of participants from whom specimens were collected, who participated as children or through their parents and have now become adults, to withdraw their specimens from the biobank;

    21.2. Management of incidental findings, especially false positives with putative psychological implications; and

    21.3. Transparency in the handling of the financial aspects of the biobank.

Management of Conflict of Interest

22. Potential conflicts of interest among researchers or study participants should be identified at all stages of the research, most especially during the planning stage. The presence of any of the following indicators shall require a declaration of COI to the REC by the researcher or expert (adapted from the National Academy of Sciences, 2009).

    22.1. employment and consulting within the past four years, such as being employed by an interested party or providing a professional opinion on an environmental issue in court or to a government agency;

    22.2. research support, which additionally, requires submission of an account of support for the expert's own research and that of their unit, including supplies and equipment; or

    22.3. financial interest such as ownership of stock, and other securities, business interest, and patents or intellectual property related to environmental health concerns.

        22.3.1. All sponsors of the research should be identified.

        22.3.2. The protocol should include measures to disclose and address potential conflicts of interest.

        22.3.3. Concerns about perceived conflicts of interest need to be identified and discussed with the REC, community, and other stakeholders to determine how they should be avoided.

ETHICAL GUIDELINES FOR RESEARCH DURING DISASTERS, CALAMITIES, EPIDEMICS, OR COMPLEX EMERGENCIES

Emergencies and disasters broadly refer to sudden occurrences or events brought about by natural or human-induced hazards, which may disrupt the normal way of life in such areas or communities (Loughborough University, 2011). The impact of emergencies and disasters can have acute or lingering physical, psychological, social, and economic effects on individuals or groups.

In the Philippines, prevention and mitigation, preparedness, response, and recovery efforts for emergencies and disasters form an integral part of the country's policy framework dating back to the Commonwealth era (Commission on Audit, n.d.). The country's geographic location and sociopolitical milieu heighten its vulnerability to risks arising from emergencies and disasters (DOH, 2018; UN Office for Disaster Risk Reduction and the Asian Disaster Preparedness Center, 2019). In 2018, for instance, the country was ranked third among countries globally in terms of disaster risk, taking into account exposure to natural hazards and societal vulnerability (Bündnis Entwicklung Hilft, 2018).

Research related to emergencies and disasters has been identified as a critical component of the Philippines' disaster risk reduction and management plan (National Disaster Risk Reduction and Management Council, 2020). While the framework situates research under the thematic pillars of prevention, mitigation, and preparedness, there is growing recognition that some research questions can only be adequately answered in emergency contexts, making doing research during emergencies an ethical imperative (WHO, 2020). However, this need to generate evidence that can inform the development and implementation of response efforts, however, has to be carefully balanced with ensuring that the immediate needs of affected groups and communities are met and are not compromised (SAMHSA, 2016). Ethical issues related to research during emergencies and disasters include, among others, identifying and addressing risks and vulnerabilities related to study participation among populations who have been exposed to stressful situations; ensuring the safety of researchers conducting studies in emergency contexts and

settings; weighing resource allocation for research and response efforts; sharing of data and results in a timely manner to influence emergency-related interventions and initiatives; and conducting rapid and quality ethics review during an unprecedented event that may require urgent data collection (SAMHSA, 2016; WHO, 2020).

This guideline distills and localizes existing international guidelines for research conducted during emergency and disaster situations. At its core, the guidelines were formulated to align with the ethical standards that research must meet in an emergency context, namely: scientific validity; social value; collaborative partnership; reasonable risk-benefit ratio; fair and voluntary participation; independent review; and equal moral respect for participants and affected communities (WHO, 2020). Further, these guidelines were formulated following the principle borrowed from the "all-hazards" approach to emergency management (Gregory, 2015). It provides guidelines that can be applied to most, if not all, situations where research during emergencies and disasters may occur as it is quite impractical, not to mention cumbersome, to anticipate particular ethical issues that may arise from specific hazard and context combinations. This determination is best left to the wisdom of reviewers and RECs. The Nuffield Council on Bioethics' (2020) ethical compass may be a useful heuristic when thinking through ethical dilemmas arising in emergencies (Figure 2).

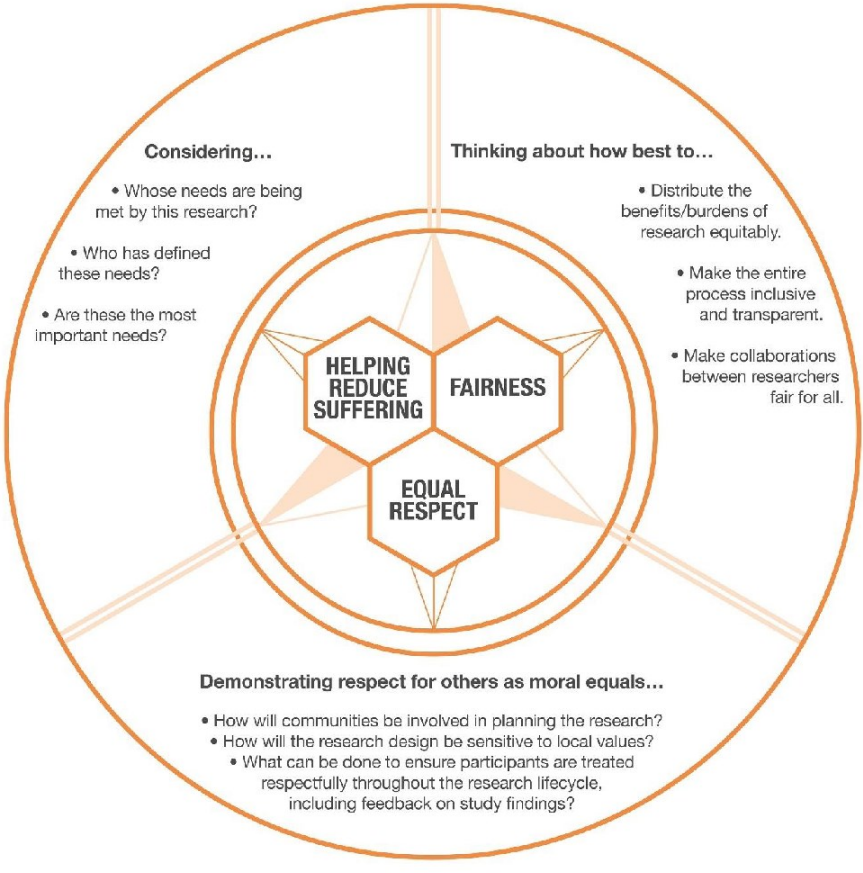


Figure 2. Ethical compass thinking through ethical dilemmas arising in emergencies

From "Research in global health emergencies: ethical issues short report," by the Nuffield Council on Bioethics, 2020, p. 7 https://www.nuffieldbioethics.org/assets/pdfs/RGHE_Short_report_web_version1.pdf. © Nuffield Council on Bioethics, January 2020. Reprinted with permission.

Specific Guidelines

Social Value

1. The assessment of the social value of research during emergencies and disasters shall include consideration of the following points: (a) the proposed research addresses the needs of affected

communities, (b) the study cannot be conducted in a more stable setting, and (c) conduct of the study will not impede response efforts.

1.1. Research during emergencies and disasters shall give particular attention to the unique needs, priorities, and special concerns of affected individuals and communities and their specific cultural, religious, racial, and ethnic affiliations. By doing so, the pursuit of answers to the study questions may also bring about services and opportunities appropriate and acceptable to these individuals. As such, the research proposal must explain how its objectives relate to the priorities and interests of the community.

1.2. A dissemination plan specifying mechanisms for timely sharing of research results with relevant agencies that may aid in the design or implementation of response initiatives or interventions shall be included in the protocol.

1.3. Research in disaster areas shall be justified if proponents can demonstrate that the study objectives cannot otherwise be achieved if the research is done in a more stable setting or period. The protocol should indicate the justification for the timing of the conduct of the research in the selected study site.

1.4. Research in an area affected by an emergency or disaster should not impede or unduly compromise response efforts. This means that the resources necessary to conduct the research should not take away resources required for response or the continuous delivery of routine public health services.

1.5. The protocol shall include provisions to address the risks to the study team conducting research in the context of emergencies and disasters, including exit strategies and project close-out activities. The research budget shall have a corresponding line item that shall account for the risk management activities specified in the protocol.

Community Engagement

2. Researchers should respectfully engage with stakeholders in the study community or area throughout the whole research process, if feasible, to ensure that the research addresses local needs and that practical and pragmatic implementation issues are addressed.

    2.1. In place of incorporating community engagement as part of the current research project, researchers may instead specify in the protocol any recent community stakeholder engagement initiatives conducted (i.e., as part of another project/program) to demonstrate familiarity with the community's situation and their cultural beliefs and practices. This could take several forms, such as, but not limited to, (a) preliminary mapping or scoping exercise, (b) needs assessment, (c) meetings with formal office holders and informal influencers, or (d) local researcher or community member involvement in the research team.

    2.2. Where feasible or required by existing statutes or regulations, a statement of support or endorsement from the community, community representatives, and relevant government agencies may be submitted by researchers to the REC to demonstrate support for their proposed research.

Scientific Soundness

3. Research conducted during emergencies and disasters must have a scientifically sound research design, which will yield results that can address the research questions or objectives. However, such research design should be informed by the context in which the research is conducted.

    3.1. The soundness of a proposed research approach should be judged based on its appropriateness to the research questions or objectives, as well as pragmatic and practical implementation considerations, and not simply on utilizing the "best," "ideal," or "preferred" method. The specific

guidelines relating to different methods and methodologies should be consulted when scrutinizing research proposals to be conducted during emergencies and disasters.

3.2. Consistent with the spirit of community engagement, research designs should also be context-appropriate and locally acceptable. Thus, a discussion of the research approach should form part of the research team's community engagement strategy.

Qualification of Researcher/s

4. In addition to the qualifications of researchers stated in the General Guidelines, the research team for studies during emergencies and disasters should include a member, either as Principal Investigator/Lead Researcher or Co-Investigator/Co-Researcher, who has prior experience in carrying out studies in such context. Proof of such experience/capability should be highlighted in the researcher's curriculum vitae.

Fair Selection of Research Participants

5. Participant selection and the exclusion of particular population groups shall be justified by considerations of scientific soundness, social value, and benefit-risk ratio.

5.1. The research protocol shall specify the criteria for and manner of participant selection, recruitment, and retention, and this should be aligned with current practice in the discipline, the aims and purpose of the research, and the benefits and risks of the study, as well as practical and pragmatic considerations.

5.2. Automatic exclusion of vulnerable groups from a study during emergencies and disasters is discouraged. Instead, researchers shall consider the benefits and risks for the group or sub-group in question in the context in which the research is being proposed.

5.3. When involvement of vulnerable groups is warranted, the researchers shall specify mechanisms to protect such

vulnerable groups or mitigate the impact of their vulnerability during the study. The specific guidelines for research among different population groups should be consulted, where relevant, when scrutinizing research proposals to be conducted during emergencies and disasters.

Benefits and Risks

6. The benefits and risks to study participation, including exposure to experimental interventions, are justified and equitably distributed.

    6.1. The research protocol shall contain a clear and unambiguous statement on direct benefits to the participants and the community, which shall be a primary consideration in assessing a research proposal. This, however, does not preclude possible indirect benefits of the study, such as enhancing or developing an intervention or program for affected communities or populations.

    6.2. The research team must specify in the proposal potential risks and negative events that may arise because of research participation (e.g., psychological risk in the form of repeat traumatization of affected individuals; security risk for people in armed conflict) or that may transpire during data collection (e.g., the discovery of acts or omission that may be contrary to law). The proposal should also indicate measures to prevent these events (e.g., use of homogenous groups during group interviews or discussions for people involved in security-sensitive situations) and mitigate their impact on the study participants (e.g., referral for psychosocial intervention).

    6.3. The research budget shall have a corresponding line-item that shall account for the direct benefits (if any) and interventions for risk management specified in the protocol.

Informed Consent

7. The informed consent process shall reflect the best and most

sensitive approach that can be achieved in the context of an emergency and disaster, and any waiver of informed consent is justified.

7.1. The consent of individual participants shall be secured before research participation. The research team shall identify any factor that may prevent potential participants from providing voluntary and free consent and provide appropriate mechanisms to address these.

7.2. Individual research participants should be informed of any plans for sharing or future use of data or samples collected from the research during emergencies and disasters. The relevant guidelines on data protection and reuse, as well as biobanking, shall apply.

7.3. Requests for waiver of informed consent, or the waiver or alteration of any element of consent, shall be assessed by the REC to comply with the relevant requirements outlined in the General Guidelines.

7.4. The informed consent document, as well as the informed consent process, must clearly distinguish between the roles of researchers, health researchers, health providers, and volunteer workers, as confusion among potential participants may be heightened in the context of an emergency or disaster.

Ethics Review

8. Consistent with the General Guidelines, research during emergencies and disasters shall undergo ethics review by an independent and competent REC. Such scrutiny, however, should be adapted as necessary to the context without compromising the quality of the review.

8.1. RECs should incorporate in their SOPs procedures for emergency response ethical review that will allow for rapid assessment of proposals during emergencies and disasters. This includes, among others, using flexible means of

communication and deliberation outside of the regular face-to-face meetings and the option of participating in joint reviews with other RECs (*see, for instance, PHREB Resolution No. 20-003 dated 15 Oct 2020*).

8.2. Where feasible, RECs may consider pre-review of a preliminary protocol document developed before an anticipated emergency, followed by review and approval, during or after the emergency, of a final protocol contextualized to the specific study site(s). A preliminary protocol will contain elements on the research background, rationale, objectives, methodology, outcomes, informed consent procedures, among others. On the other hand, the final protocol will contain more detailed information and considerations on the location(s) and context-related aspects such as communities' vulnerability, community engagement, and the standard of care.

8.3. RECs will also need to assess the data and sample sharing plan for the study. Given the rapidly evolving nature of emergencies and disasters, a preliminary plan that outlines the broad approach to data and sample sharing may be initially acceptable. Researchers, however, should be required to submit a more concrete and detailed data and sample sharing plan after a specified period.

Special Considerations for Clinical Research during Emergencies and Disasters

9. This section outlines the special consideration for conducting clinical research during emergencies and disasters.

9.1. The well-being or safety of the study participant shall be of primary consideration in conducting research in the context of disasters, calamities, epidemics, and similar complex community emergencies. As provided in statement 1 above, the conduct of research should not impede, compromise, or stand in the way of the response efforts being given during these circumstances, especially in the administration of the

standard of care to the persons who have been harmed by these disasters, calamities, or epidemics.

9.2. Especially for infectious disease epidemics, there may be a need to conduct clinical research to rapidly generate the evidence needed to support novel interventions when there are no known treatments, such as drugs or vaccines. Consistent with statement 8 above, RECs need to perform rapid screening of protocols and, subsequently, quick but competent reviews that maintain the same high-quality standards. To this end, RECs may need to revise and adapt their SOPs to allow for flexibility and greater efficiency in their methods and allow for greater coordination with all relevant stakeholders.

9.3. The same principles for doing clinical research apply during epidemics, calamities, and disasters, but special attention must be given to the following areas (in addition to those already mentioned above).

9.3.1. *Social value.* Considering the provisions of statement 1 above, doing clinical research during emergencies and disasters must be justified, especially due to the typically difficult circumstances that research participants find themselves in.

9.3.2. *Scientific soundness*. All clinical research must have a sound design and methodology, whether done in the usual clinical setting or under the more difficult circumstances of epidemics and disasters. In the latter though, research designs may have to be modified from the usual parallel-group designs where the interventions are fixed from the beginning to the end of the clinical study. For example, more adaptive trial designs for novel or repurposed drugs have been seen in clinical research for COVID-19. Adaptive designs allow for greater flexibility in conducting clinical trials by

utilizing results accumulated in the ongoing trial to modify parameters of the trial protocol in accordance with pre-specified rules, adaptation schedules, and processes. (Pallmann et al., 2018) Modifications may include changes in dosage, sample size, drug undergoing trial, patient selection criteria, and combinations of interventions. Some trials even have processes that regularly allow the dropping and addition of therapies and even patient groups or subgroups as more information is gathered.

9.3.3. *Fair selection of study participants and risk-benefit ratio.* While protection of study participants is always paramount, this sometimes leads to the unnecessary exclusion of vulnerable individuals. The principle of fair selection of study participants implies that even persons considered to be vulnerable can be included if the specific research question being answered by the protocol applies specifically to them, as they are also typically the ones who are placed at greatest hazard during disasters or epidemics. An assessment of the risk and benefit ratio of participation for these vulnerable populations should always be done, and specific protection or risk management given as applicable.

9.3.4. *Informed consent process*. The site for performing the clinical research in these circumstances may be more informal or done in the community setting. However, this should not compromise the comprehensiveness, privacy, and confidentiality of the informed consent process. The investigator may need to consider what is practical and be sensitive to the prevailing realities, especially during disasters. Waiver of informed consent, when appropriate or applicable, should be justified.

9.3.5. Dissemination plans should be clear and specific at the outset. There may be a need to quickly use the research results to generate further research or rapidly translate the results to community interventions or clinical applications to individual patients.

ETHICAL GUIDELINES FOR HEALTH POLICY AND SYSTEMS RESEARCH

Health policy and systems research (HPSR) is an emerging field of inquiry that "seeks to understand and improve how societies organize themselves in achieving collective health goals, and how different actors interact in the policy and implementation processes to contribute to policy outcomes" (Alliance for Health Policy and Systems Research, n.d.).

HPSR is multidisciplinary, addresses issues at various geopolitical levels (i.e., sub-national to global), and is ultimately research on, of, and for policy (Gilson, 2012). The central issues of HPSR include health systems, health system development or strengthening, health policy, and health policy analysis. Thus, HPSR is not defined by a specific methodology but by the type of questions it attempts to answer.

The end goal of HPSR is to describe and analyze how health policies and health systems, alongside health determinants, interact and result in health outcomes. The value of HPSR stems from the recognition that strong health systems are essential in achieving global health targets (i.e., Sustainable Development Goals) and that health agencies and organizations require evidence to inform and influence policies and actions in the health sector (Bennett et al., 2018; Peters, 2018).

Locally, the term "health policy and systems research" was adopted by the Department of Health (DOH) and the Philippine Council for Health Research and Development (PCHRD) sometime in 2017 through the launch of the *Advancing Health through Evidence-Assisted Decisions with Health Policy and Systems Research (AHEAD-HPSR) Program*. It provides grant support for individual and organizations conducting research in priority areas, and the *DOH Health Policy and Systems Research Fellows*, a training opportunity for young professionals who are interested in HPSR. However, HPSR was possibly introduced much earlier in the country, as there is admittedly some overlap with other nomenclature such as "'health systems research" and "health services research" (Mills, 2012), which the local research community has already used even before 2017 (e.g., Health Systems Research Management program in 2013 of the DOH and PCHRD). Other government

agencies and non-government organizations also commissioned studies that fall within the HPSR field but have not explicitly used the HPSR nomenclature (e.g., PhilHealth STUDIES [Strengthening the Thrust for Universal Health Care through Data, Information, and Knowledge Exchange Systems] program, which is a collaboration between the Philippine Health Insurance Corporation and PCHRD).

Several ethical issues have been identified concerning the conduct of HPSR, including in low- and middle-income countries (Hyder et al., 2014; Luyckx et al., 2017; Pratt et al., 2017). These include, among others, the overlap between practice and research and the identification of the research intervention; the role of the funding agency, which in most cases is the state requesting evaluation of its program; different individuals/groups to whom risks and benefits may accrue; and sustainability of interventions beyond the study period. Research ethics committees primarily trained in the review of clinical research may also find it challenging to reorient their biomedical framework to accommodate HPSR studies (Hyder et al., 2014; Pratt et al., 2017). Based on the "*Ethical Considerations for Health Policy and Systems Research"* (World Health Organization, 2019), this ethical guideline addresses these HPSR issues.

At the outset, it must be emphasized that the specific guidelines listed below are intended to supplement the General Guidelines discussed in earlier parts of this volume. The provisions of the General Guidelines apply to HPSR, and these specific guidelines should be read and interpreted with the General Guidelines in mind. Research ethics committees should also bear in mind that articulation of the ethical considerations in HPSR is a relatively new initiative, which means that this area of research ethics will continue to evolve in lockstep with the continuing development of HPSR in general.

Specific Guidelines

Ethics Review

1. The protocol for a proposed research under HPSR is subject to ethical review by a competent research ethics committee. Where doubts exist as to whether an activity is research or not, researchers should seek a written determination from a REC.

1.1. Practice and research elements often overlap in HPSR, and there is often difficulty distinguishing between these two. For these guidelines, *research* shall be understood to mean "research involving human participants" and will follow the definition provided under the General Guidelines. In addition, activities with *research* will typically be under the control of a researcher. In contrast, *practice* refers to parts of routine delivery of care under the control of the Department of Health, a healthcare organization, or an individual practitioner. As these guidelines only apply to research involving human participants, broadly construed, practice elements are not subject to oversight by the REC but by another agency or body.

1.2. Consistent with government regulations, the following definition of public health practice from the Department of Health is hereby adopted: "refers to the conduct of governmental activities that protect the public's health, including performing oversight functions for these activities" (DOH Administrative Order No. 2020-0061).

1.3. In case of doubt as to whether an activity is research or not, research ethics committees may refer to the criteria proposed by the Council of State and Territorial Epidemiologists (Hodge & Gostin, 2004) in distinguishing between public health practice and research (Table 4). A checklist for distinguishing is included as Appendix S.

Table 4. Essential characteristics of public health and practice

Public Health Practice	**Research**
• Involves specific legal authorization for conducting the activity as public health practice at the federal, state, or local levels	• Involves living individuals • Involves, in part, identifiable private health information • Involves research subjects who are selected and voluntarily participate

• Includes a corresponding governmental duty to perform the activity to protect the public's health	(or participate with the consent of their guardians), absent a waiver of informed consent
• Involves direct performance or oversight by a governmental public health authority (or its authorized partner) and accountability to the public for its performance	• Supported by principles of bioethics that focus on the interests of individuals while balancing the communal value of research
• May legitimately involve persons who did not specifically volunteer to participate (i.e., they did not provide informed consent)	
• Supported by principles of public health ethics that focus on populations while respecting the dignity and rights of individuals	

Conflicts of Interest

2. Actual or potential conflicts of interest, including the role of the funding agency, should be disclosed by the researcher to the REC, which is tasked to ensure the study's independence and disclosure of results.

    2.1. HPSR is typically commissioned and funded by health departments or other agencies to evaluate the performance of the agency's programs or projects. Funding agencies will also usually reserve the right to authorize or approve the dissemination of research findings. In these instances, an actual or potential conflict of interest may arise as these decisions may result in financial, legal, or reputational issues that may accrue to the funding or commissioning organization. In these instances, researchers should disclose such conflict of interest, and RECs should scrutinize the adequacy of plans to ensure the independence of the study and disclosure of results.

Scientific Soundness and Participant Selection

3. In weighing benefits and risks, it is essential to accurately determine the study intervention and the level to which it is applied, the procedures for data collection, and who the research participants are.

    3.1. In HPSR, study interventions may take the form of health education, the introduction of a new service, reorganization of care delivery, or the introduction of a new policy. Such interventions may be applied to the individual patient, healthcare provider or a cluster (e.g., an entire organization or community). There are also instances in which a study may involve no intervention, such as in evaluating a routine program or service. Accurate identification of the study intervention is important for analyzing the potential benefits and harms of the study.

    3.2. Because HPSR is not a specific methodology, data collection for HPSR studies may take the form of policy document review, data abstraction from records/reports, administration of a questionnaire, observation, or conduct of interviews and focus groups. Data may also be collected and analyzed at the individual or group levels. In either case, accurate identification of data collection procedures for research is important for the analysis of the potential benefits and harms of studies. The specific guidelines relating to different methods and methodologies should be consulted when scrutinizing HPSR studies.

    3.3. Participants in HPSR studies include stakeholders at the level of health systems (i.e., policymakers and decision-makers), organization (e.g., executive and managerial staff), or individuals (i.e., health providers, patients or service users, healthy individuals in the community). As provided under the General Guidelines, the definition of a *research participant* holds for HPSR studies. To ascertain who should be classified as a research participant, researchers and RECs should consider whether the “manipulation, intervention,

observation or other interaction" is direct or not and the degree to which the interests of individuals are meaningfully affected by such actions. Further, the specific guidelines for research among different population groups should be consulted, where relevant, when scrutinizing HPSR studies.

Informed Consent

4. Informed consent must be obtained from all research participants. Procedures for consent must be tailored to the specific aspects of the study to which a participant will be exposed. Waiver of consent may be granted by the REC where an HPSR study fulfills the criteria for such waiver.

    4.1. The general rule for HPSR studies is that it is generally presumed that informed consent must be obtained from research participants, consistent with the principle of respect for persons and as contemplated under the General Guidelines.

    4.2. One novel aspect of HPSR studies, however, is that different groups of research participants may require varying consent procedures, especially in cases where such individuals or groups are exposed to different aspects of the study. For instance, the intervention may be at the organizational level (e.g., change in insurance fee structure), but health outcomes data will come from patients. While the basic elements of consent and general information about the study will be the same, the details of the disclosure may differ by group.

    4.3. Where individual consent may pose a pragmatic challenge to the conduct of an HPSR study that seeks to achieve a socially significant end (e.g., testing of a new policy at the organizational or community levels, collection of data from large groups of individuals), the researcher should make a case for waiver of informed consent. The REC should determine whether all the ethical requirements for waiver of informed consent, as provided under the General

Guidelines, are fulfilled. Further, when a request for a waiver for consent is granted, the REC may require that relevant stakeholders in the health system or institution be notified that a research study is being conducted. Notification may include advertisements, media announcements, or letters to patients/individual community members.

Permission for the Conduct of Research

5. Gatekeeper permission may be necessary when conducting research among groups. Such permission, however, does not supplant informed consent from individual research participants.

    5.1. As mentioned in the preceding paragraphs, HPSR studies may involve groups or clusters, such as health systems, organizations, and communities. In these instances, gatekeeper involvement in study approval may be required (e.g., health officer for a health system, local chief executive in a community, executive officer in an organization). This may be especially true if it is likely that study results will substantially affect the group's interests, provided that such a gatekeeper has the authority to provide such permission. On the other hand, gatekeepers should not unduly withhold such permission for the conduct of an HPSR study based on fear of potential disclosure or discovery of poor practices and performance in the group setting but should instead view the study as an opportunity to improve the quality of care or service being provided by the group. Gatekeeper permission, however, does not weaken or replace the requirement for informed consent from individual participants.

Community and Stakeholder Engagement

6. Researchers should communicate their community and stakeholder engagement strategy to the REC.

    6.1. Community and stakeholder engagement forms an important part of the research process, where potential

participants, communities, and relevant stakeholder groups are consulted at the earliest opportunity on the design and conduct of research and the dissemination of the research results. This should especially be considered in instances when the research is likely to have a substantial impact on group or community interests. The process of community and stakeholder engagement will, among others, help identify the impact of a study on these groups and minimize risks related to the study.

Privacy and Confidentiality

7. Researchers and RECs should consider the risk of stigmatization of practitioners or organizations due to the results of studies and should put in place adequate protection of data from multiple sources and on various entities.

    7.1. The protection of privacy and confidentiality in HPSR studies may be complicated using multiple data collection methods sourced from different levels. This is especially relevant in cases where HPSR studies may reveal poor performance or health outcomes. In all instances, researchers and RECs should consider the risk of stigmatization of practitioners or organizations due to the results of studies.

Benefits and Risks

8. The potential benefits of any proposed HPSR intervention (if any) should be justified, and the risks of data collection procedures are justified and minimized.

    8.1. Weighing the benefits and risks of an HPSR study is complicated since group interventions may affect not only individuals but also communities, organizations, and systems. Further, a study's potential benefits and harms may not be the same for all participants, who may be involved in different aspects of the study.

    8.2. Any proposed study intervention should be consistent with competent practice in the relevant field of study. Contextual, more than clinical, equipoise is a more relevant

consideration. A health intervention, proven effective in another setting, may be evaluated for its effectiveness in another setting where evidence of effectiveness is lacking. In the absence of evidence, the REC may need to seek expert opinion about the study intervention.

8.3. The involvement of individuals or groups in a control condition should be justified. There should be no reasonable impediment for participants assigned to the control condition to receive effective care or programs to which they would have access. Caution should be exercised in using augmented controls (compared to usual care) as "their use is not required by clinical equipoise, and they may bias the study towards a null result."

Vulnerable Population

9. Researchers should provide additional safeguards when involving vulnerable populations in HPSR studies (i.e., the study hypothesis justifies the inclusion of vulnerable populations, and research procedures with no direct benefit are not of more than minimal risk).

9.1. Some HPSR studies are designed specifically to address the social causes of vulnerability, such as those aiming to address health care disparities in communities. In these circumstances, community, and stakeholder engagement discussed previously may help to address the impact, both beneficial and harmful, of research involvement of such vulnerable populations.

9.2. In addition, however, employees of organizations that are the subject of HPSR studies may also be considered vulnerable populations, as they are in hierarchical institutions and may feel pressured to participate in research, especially an organizational gatekeeper has already approved it. A possible mitigation strategy is the recruitment of participants in the absence of supervisors. Further, the organization should not be informed about

who among their employees or staff agreed or refused to participate in a study.

Dissemination of Findings

10. Researchers should communicate to the REC any plans to ensure the sustainability of any HPSR interventions that are proven effective, including disseminating findings to relevant state agencies.

    10.1. As explained in the introductory section to this guideline, the end goal of HPSR is to strengthen health systems through the generation of research evidence, making sustainability a key feature of HPSR. Researchers, however, should not be unreasonably burdened with such commitment as the responsibility for large-scale and long-term implementation of effective interventions rests with the State. At the minimum, however, researchers should communicate with the REC how they intend to share such research findings with relevant policymakers and decision-makers of state agencies.

ETHICAL GUIDELINES FOR RESEARCH USED IN HEALTH ECONOMICS AND OUTCOMES RESEARCH

Health economics and outcomes research (HEOR) refers to a "multidisciplinary field that combines aspects of health economics with the methods of outcomes research in the evaluation of the impact of health care interventions on patient well-being, population health, and health system efficiency" (Santos et al., 2017, p. 1230). The methods of HEOR are closely related to clinical trials, observational studies, real-world research studies, and market research. They can utilize primary participant data (including data from wearables), observational data, patient charts, secondary database review, data mining, social media scraping, and evidence synthesis (Appendices 3 and 4, ISPOR Code of Ethics 2017). HEOR is intended to complement the traditional clinical development information of efficacy, safety, and quality to support healthcare decision-making, specifically in health technology assessment (HTA) (Holtorf et al., 2012).

In the Philippines, HTA was initially a function lodged under the Philippine Health Insurance Corporation, whose primary focus was developing reimbursement policies for medical claims (De Rosas-Valera, 2009). This was later institutionalized as a unit under the Department of Health (DOH) by virtue of Republic Act No. 11223, or the Universal Health Care Act, and DOH Administrative Order No. 2020-0041, and its function broadened to guide policies on fund allocation and coverage decisions in support of universal health care. This development is expected to lead to an increase in HTA-related studies, particularly those on HEOR; hence the Ad Hoc Committee decided to include a specific guideline on HEOR in the National Ethical Guidelines.

As previously mentioned, HEOR relies on a broad methodologic base and utilizes a variety of data sources, some of which are already adequately covered by the General Guidelines and the other specific/special guidelines in this volume. This present section will, thus, focus on ethical considerations specific to HEOR not mentioned elsewhere.

Specific Guidelines

Scientific Soundness

1. Researchers should observe transparency when reporting methodological choices in protocols submitted for review by the REC.

    1.1. For all types of research, protocols should specify the hypothesis and research design, the justification for these (including their relative value over alternatives), and mechanisms for recognizing and minimizing all types of bias (Statement 31, ISPOR Code of Ethics 2017). All departures from the a priori analysis plan should be disclosed and justified (Statement 36, ISPOR Code of Ethics 2017).

    1.2. For research involving the analysis of a database initially collected for another purpose (e.g., administrative databases and other large datasets), protocols should include the following: (a) a description of approaches, methods, and technologies used to ensure data completeness and validity, including any software package(s) that will be used for data analysis (Statement 25, ISPOR Code of Ethics 2017); and (b) disclosure of any known or potential source of bias in the data that can affect the results (Statement 24, ISPOR Code of Ethics 2017).

    1.3. For modeling studies (e.g., decision-analytic models, extrapolation of costs and benefits from a clinical trial), protocols should specify the following: (a) the estimates used for key parameters; (b) the logic used in selecting estimates (including sources/references); and (c) whether and how sensitivity analysis will be used to explore the impact of parameter choice (Statement 27, ISPOR Code of Ethics 2017).

    1.4. For studies that combine research data (i.e., adding data to an existing database by linking relevant information from another source), protocols should specify, among others, the source/s of data to be linked, the appropriateness of combining data from these sources, mechanisms to ensure integrity and authenticity of data during linkage, and whether such linkage is permitted by the database owner or administrator (Statement 29, ISPOR Code of Ethics 2017; Santos et al., 2017).

1.5. Researchers should possess the necessary qualifications (i.e., education, training, and experience) to perform the procedures outlined in the protocol or submit evidence of collaboration with individuals (e.g., consultants) who are qualified to do so (Statement 25, ISPOR Code of Ethics 2017). These qualifications should also show evidence of current knowledge of general and locally relevant, research practices in the discipline (Statement 7, ISPOR Code of Ethics 2017).

1.6. Where feasible and allowed by contractual obligations with the sponsor, protocols for clinical, observational, and economic research should be registered prospectively in relevant databases (e.g., ClinicalTrials.gov) to ensure transparency and minimize study biases (e.g., misrepresentation of prespecified analyses) (Statement 26, ISPOR Code of Ethics 2017).

Privacy and Confidentiality

2. Researchers are duty-bound to uphold the confidentiality of the personal data of research participants. They should establish mechanisms to reduce the likelihood of breaches of participant privacy throughout the research process (Statement 9, ISPOR Code of Ethics 2017).

2.1. The security of personal data collected as part of the research should be maintained. Thus, in addition to the General Guidelines on data protection, protocols should specify data access limits and control systems to ensure data confidentiality when stored or transmitted electronically (Statement 29, ISPOR Code of Ethics 2017).

2.2. For research involving secondary data, protocols should state the approaches, tools, and technologies used to store the data and maintain patient privacy/confidentiality and de-identification (Statement 28, ISPOR Code of Ethics 2017).

2.3. For research involving the analysis of a database initially collected for another purpose, the protocol should specify if data to be

accessed by researchers are already de-identified. If these contain personally identifiable information (i.e., when database linkage is contemplated), any additional safeguards to maintain the privacy and confidentiality of the data participants should be indicated.

2.4. Researchers should specify in the protocol any plans for offering access to anonymized, group-level data used in their research (e.g., to other researchers or journal reviewers; to panels involved in healthcare decision-making or advising healthcare decision-makers) and the nature of such access (e.g., full access vs. confidential review) (Statement 30, ISPOR Code of Ethics 2017).

Consent for and Access to Secondary Data

3. Researchers should provide documentation that prior permissions have been secured when secondary data sources initially collected for another purpose will be used for a study (Statement 22, ISPOR Code of Ethics 2017). These include the protection of participants' data privacy and informed consent for secondary use of data (Santos et al., 2017).

3.1. A principal assumption of these guidelines is that the secondary database used in the research was legally and ethically constructed. Researchers must conduct a due diligence process on the data source before use if doubt or concern exists regarding how the database was generated [Santos et al., 2017].

3.2. Researchers should ensure that the original data holder, or the database administrator, has a lawful basis to process personal data (i.e., compliant with Republic Act 10173 or the Data Privacy Act of 2012) and can contractually transfer personal data to other parties without seeking additional explicit permission of the data participant (Santos et al., 2017).

Conflicts of Interest

4. HEOR will typically receive funding from organizations or stakeholders, whether in the government, commercial, or non-profit sectors, with interests in specific findings (Santos et al., 2017). Researchers should, therefore, (a) identify the sponsor/s of their research (Statement 32, ISPOR Code of Ethics 2017); (b) disclose potential or actual conflicts of interest (Statement 30, ISPOR Code of Ethics 2017); (c) specify any limits

of information disclosure/dissemination as part of the researcher's contractual obligations to sponsors (Statement 44, ISPOR Code of Ethics 2017); and (d) report the role of sponsors and funders in the research (*cf.* Statements 43 and 58, ISPOR Code of Ethics 2017).

Stakeholder and Patient Engagement

5. Researchers should engage with patients and patient organizations/patient advocacy organizations before, during, and after conducting research (Statement 54, ISPOR Code of Ethics 2017). Engagement and collaboration are intended to, among others, ensure that the study topic and outcome measures/endpoints are relevant to patients and their families; strengthen aspects of the study design (e.g., site selection and participant recruitment); and translate research results (Santos et al., 2017).

Ethics Review

6. The researcher should obtain prior ethical approval for the planned research from a competent REC (Santos et al., 2017).

    6.1. When reviewing protocols involving secondary data or big data analysis, RECs will need to engage experts in data science, bioinformatics, and cybersecurity, among others, either as members or as consultants (Lenca et al., 2018).

    6.2. For RECs that review a substantial number of proposals involving the use and analysis of a database initially collected for another purpose, sensitization, at the minimum, or formal training in the technical, methodological, ethical, and epistemological issues and challenges of evaluating proposals involving large databases should be strongly considered (Lenca et al., 2018).

ETHICAL GUIDELINES FOR INTERNATIONAL COLLABORATIVE RESEARCH

International collaborative research refers to a scientific undertaking that involves the participation of investigators or researchers whose primary affiliations are from different countries or jurisdictions. The scientific undertaking can be funded by foreign or local funding or a combination. It can be a clinical trial or any partnership that will involve a local researcher or investigator that contributes local data or knowledge from local sources. There are different forms of international collaborative research. Type 1 is an International Study Group working on a global phenomenon. The Study Group is composed of country representatives, each of whom contributes local data toward a better understanding of a global phenomenon. Type 2 is a multi-country research group working on a specific disease endemic in the Philippines. In this arrangement, patient clinical data and biological samples are sourced in the Philippines and shared with foreign collaborators. Type 3 involves mostly clinical drug trials where a foreign pharmaceutical company sponsors the clinical trial of an investigational new drug. 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 in international collaborative research have constantly been raised, such as:

- 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; and
- no formal collaborative agreement among countries or foreign and local institutions.

The persistence of these issues has been partly due to the different interpretations of existing ethical guidelines and the varied perspectives and thinking of sponsors, funders, and collaborators from developed and developing economies.

One other major issue is 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 will 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. The involvement of patients in international research collaboration raises hope, thus implying greater disappointment and frustration in research failure.

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. (KFPE, 2018):

- 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 adopted in addressing ethical issues in international collaborations/ Clinical trials are taken up in the Guidelines for Clinical Research.

Setting the Agenda Together

1. Filipino researchers shall consider local capacities and needs in developing the agenda, especially in an international study group or research consortium.

2. Filipino researchers shall be deeply involved in setting the research agenda, especially in multi-country collaboration focusing on the specific disease or where clinical data or biological samples are sourced locally and shared with foreign investigators.

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. Openness to constructive criticism shall be an important indicator of maturity in collaborative interaction.

4. The technical review shall be the responsibility of an international panel, but an ethical review must be done at the local level. The involvement of Filipino research participants requires ethical review by a PHREB-accredited REC.

Creating Transparency

5. The partnership shall develop comprehensive SOPs that guide processes and indicative activities to promote transparency in all transactions and decisions.

6. The informed consent form shall contain all the elements of informed consent (*see section on Elements of Research Ethics*). It must indicate the specific research protocol, the proponent's name, source of funding, procedures involved, and the site of research data collection.

7. Local laws, rules, norms, and regulatory requirements shall always be upheld and shall be included in the SOPs/protocols of the study.

Clarifying Responsibilities

8. A set of terms of reference shall be developed and agreed upon by the collaborators to delineate the responsibilities and accountabilities of experts, clinicians, lead researchers, funders/sponsors/research managers, and the like (*see section on Elements of Research Ethics and Responsibilities of Foreign Researchers*)

9. Each study shall have separate terms of reference regarding funding support based on scientific merit and ethical soundness.

10. Deficiencies in the performance of agreed-upon responsibilities shall be addressed to ensure the attainment of objectives.

11. Responsibilities shall be set proportionately based on capacities in relation to the overall research agenda.

12. 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

13. Research is a continuing search for knowledge. Each member of the research team is benefited from their 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

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

Sharing Data and Networks

15. 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.

16. Transfer of materials and data, including confidential information, shall be covered by a memorandum of agreement and shall comply with existing Philippine laws and regulations (e.g., Intellectual Property Code [RA 8293], Indigenous People's Rights Act [RA 8371], Data Privacy Act [RA 10173]).

17. Sensitive and personal information that will be transmitted outside the country shall be done in accordance with the Data Privacy Act of 2012 (*see section on Elements of Research Ethics*).

18. Despite an agreement on the transfer of participant data and biological samples, ownership of data and biological samples remains with the Filipino collaborators, and further use of remaining samples shall be subject to Philippine approval by a PHREB-accredited REC.

Dissemination of Results

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

Pooling Profit and Recognition

20. Basic agreements among the collaborators shall be forged at the beginning of the collaboration, describing how profits and recognitions shall be enjoyed and shared, including intellectual property ownership.

Applying Results

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

22. Any product or intervention developed or knowledge generated shall be reasonably available or accessible to benefit the study participants and or their community.

Securing Outcomes

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

Further Use of Clinical Data and Biological Materials

24. 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 an author should, at the very least, ensure 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 the 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 allowed 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
2.4. Involvement in the technical writing and editing

3. Authors shall obtain the informed consent of research participants as a condition for publishing 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 the order of authorship shall be transparent and may follow any of, but not limited to, the following norms depending on prior agreements, provided all authors meet all the four criteria for authorship:

    5.1. Alphabetical order by last name;
    5.2. Relative contribution to the manuscript such that the first author should have the most substantial contribution, followed by the rest of the authors in descending order of contribution); or
    5.3. Commonly acceptable practices such as positioning the senior author last while the author with the most contribution remains the first author.

6. A student shall be listed as the principal author of a publication that substantially derives from the student's dissertation or thesis, provided that the student meets authorship criteria.

7. In collaborative groups, the important consideration shall be identifying the responsible individual for the integrity of the work and the corresponding author.

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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 PNHRS 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 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 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 28th 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
Memorandum Of Understanding: PHREB, NCIP, NCCA, NM on National Research Ethical Guidelines (March 18, 2019)

KNOW ALL MEN BY THESE PRESENTS:

This Memorandum of Understanding (MOU) is made and entered into by and among:

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**,

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

The **NATIONAL COMMISSION FOR CULTURE AND THE ARTS (NCCA)** represented by its Chair, **VIRGILIO S. ALMARIO,** with principal office at 633 General Luna Street, Intramuros 1002Manila, hereinafter referred to as **NCCA** and,

The **NATIONAL MUSEUM OF THE PHILIPPINES (NM)** represented by its Director, **JEREMY R. BARNS,** with principal office at 1000 Padre Burgos Ave., Ermita, Manila, hereinafter referred to as **NM,**
HEREIN referred to as the Parties in this Memorandum of Understanding;

WITNESSETH:

WHEREAS, there are challenges in ensuring compliance with the national research ethical guidelines and related regulations by concerned sectors;

WHEREAS, the **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 Indigenous Cultural

Communities (ICCs) Indigenous Peoples (IPs) with due regard to their ancestral domains and lands, self-governance and empowerment, social justice and human rights, and cultural integrity;

WHEREAS, the **NCCA** is the overall policy making body, coordinating, and grants-giving agency for the preservation, development and promotion of the Philippine arts and culture; and as such, encourages and supports the study, recognition and preservation of endangered human cultural resources such as weavers, chanters, dancers, and other craftsmen as well as the conservation and development of such artistic, linguistic and occupational skill as are threatened with extinction; likewise, encourages and supports scholarly research into and documentation of Philippine cultural traditions, arts and personalities especially in the literary, visual and performing arts and in mass media, as well as the various aspects of Filipino culture per RA No. 7356;

WHEREAS, the **NM** leads in the study and preservation of the nation's rich artistic, historical and cultural heritage through dissemination of scientific and technical knowledge in a more understandable and practical forms conduct of basic research programs combining integrated laboratory and field work in anthropology and archeology, botany, geology and zoology, and maintenance of reference collections on these disciplines and promotion of scientific development in the Philippines;
WHEREAS, **PHREB** is the national policy making body on health research ethics, created under Department of Science and Technology (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 human participants to ensure compliance with ethical guidelines.

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

1. That an Inter-Agency Committee on Inter-Agency Committee on Ethics in Research involving Culture and the Indigenous Cultural Communities/Indigenous Peoples (ICCs/IPs) is hereby formally organized to function as a steering group in joint activities of the parties on research ethics. In this regard, the Inter-Agency Committee shall have the following specific functions:
    a. To build capacities of member-agencies on the establishment of research ethics committees and conduct of ethics review, develop appropriate strategies and measures to ensure that research studies conducted on ICCs/IPs comply with the R.A. 8371, or the Indigenous Peoples Rights Act (IPRA) of 1997 and other related laws; and
    b. To coordinate and cooperate with the appropriate government agencies, non–governmental organizations, and Higher Education Institutions (HEIs) on information dissemination campaign on ethics in research on Philippine culture and arts, specifically those concerning the ICCs/IPs.

2. The Parties shall officially designate their respective permanent and alternate representative/s to the said Inter-Agency Committee. Consequently, it shall be the responsibility of the representative/s to:
    a. Represent his/her agency and act as point person of the Inter-Agency in committee activities;
    b. Regularly update his/her/their respective agencies regarding specific programs and projects of the Inter-Agency;
    c. Attend quarterly meetings with PHREB as Chair/convener and Secretariat. The hosting of meetings may be on rotational basis among the parties; and
    d. Assist in coordinative/collaborative activities of the parties.
3. A strategic planning activity shall be conducted as soon as the agencies agree to the formalization of the Inter-Agency Committee. Initial activities will be for capacity-building in research ethics review.

4. The Parties will promote exchange of information about their respective processes in the review of research projects involving ICCs/IPs.
5. 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 respective guidelines of the Parties.
6. The Parties, may formalize specific partnerships or initiatives through specific Agreement, separate from this Memorandum of Understanding, each clarifying the scope of work and responsibilities of the parties' specific to the Understandings.

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 Understanding of the parties for termination/cancellation of this Understanding.

AND WITNESS WHEREOF the duly authorized signatories of the Parties signed this Memorandum of Understanding in _____ on _____ in four originals.

/s/
LEONARDO D. DE CASTRO, PHD
Chair
Philippine Health Research Ethics Board

/s/
ATTY. LEONOR T. ORALDE-QUINTAYO
Chairperson
National Commission on Indigenous Peoples

/s/
PROF. VIRGILIO S. ALMARIO
National Artist and Chairman,
National Commission for Culture and the Arts

/s/
JEREMY R. BARNS, CESO III
Director IV, National Museum

WITNESSES

/s/
DR. CARLOS P. BUASEN, JR.
Member, National Commission on Indigenous Peoples

/s/
ATTY. MICHAEL M. MAMUKID
Member, National Commission on Indigenous Peoples

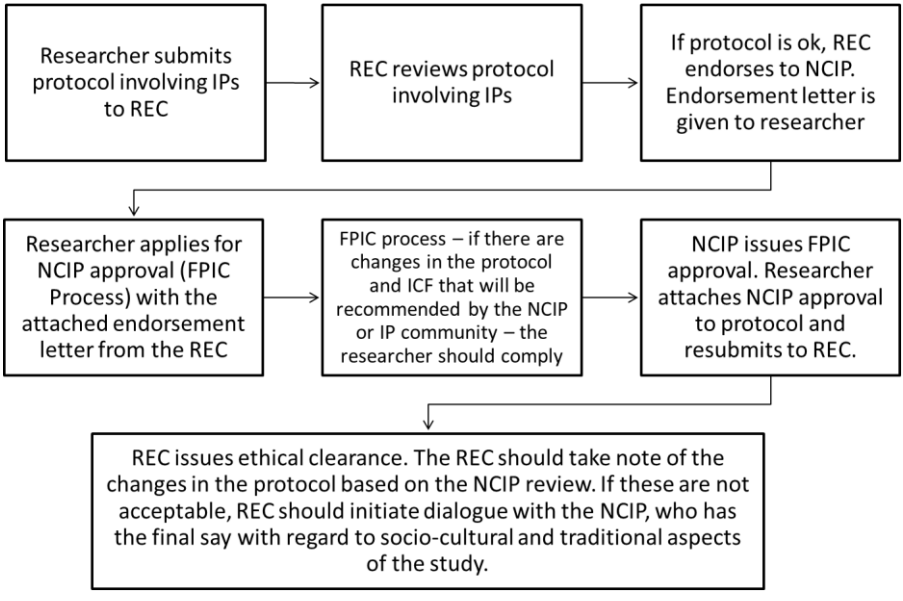
/s/
DR. ANGELICA M. CALIBA-CACHOLA
Alternate Member, National Commission on Indigenous Peoples

/s/
RENEE C. TALAVERA
Member, National Commission for Culture and the Arts

/s/
DR. MARY JANE LOUISE BOLUNIA
Member, National Museum

/s/
DR. MARITA V.T. REYES
Member, National Ethics Committee

Appendix F
Workflow for REC-NCIP Review of Protocols involving IPs



Appendix G
PHREB Policies and Requirements for Accreditation of Research Ethics Committees

(As of 2020)

I. RATIONALE

Section 12 of the Philippine National Health Research System (PNHRS) Act of 2013 on the constitution of the Philippine Health Research Ethics Board (PHREB) states that "The PHREB, shall ensure adherence to the universal principles for the protection of human participants in research. To promote and establish an effective health research protection system, the PHREB, among other things, shall:

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

To fulfill the above functions, PHREB has set requirements to guide in the conduct of quality ethical review of health and health-related research. To this end, PHREB accreditation is a requirement for all RECs.

A Research Ethics Committee (REC) is a body that makes independent decisions regarding the review, approval, and implementation of research protocols/proposals, to ensure the protection of the rights, safety, and well-being of human participants and promotes integrity of research data. It shall be constituted by a duly recognized authority and shall adhere to national and international research ethics guidelines.

II. COVERAGE

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

1. Academic Institution RECs

   These are RECs of 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 RECs

   These are RECs of a hospital. A H-REC that functions independently of others under a hospital must apply for PHREB accreditation separately.

   In the case of specialty clinics/departments, additional and specific requirements shall be fulfilled as described in Section VIII.

3. Government RECs

   These are RECs of 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.

   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.

4. Cluster 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.

5. Research Site RECs

These RECs operate within and for research sites including specialty clinics. An R-REC shall apply for PHREB accreditation as a whole unit regardless of the number of sites or facilities the research will engage.

III. GENERAL POLICIES

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.

In regions with functional Research Ethics Monitoring Boards (REMBs), accreditation of levels 1 and 2 shall be conducted by the respective boards.

The following policies shall be applicable:

1. All health and health-related research protocols/proposals involving human participants shall be reviewed by a Research Ethics Committee (REC).

2. 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). In case NCIP can establish its own REC, ethical clearance shall be issued by the same depending on feasibility.

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

4. Protocols with biosafety issues or pose hazards to the environment including those involving animals and plants need review and approval by the institutional or National Committee on Biosafety of the Philippines (NCBP).

   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.

5. All RECs shall undergo accreditation based on standards set by PHREB (Section IV: Accreditation Criteria).

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

   5.2. Members of the PHREB Accreditation Team shall be selected from the list of qualified accreditors who meet the criteria set by PHREB Committee on Standards and Accreditation (PHREB CSA).

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

6. RECs whose accreditation have expired

   6.1 The list of RECs whose accreditation have expired shall be submitted to concerned institutions like the Food and Drug Administration (FDA), Commission on Higher

Education (CHED), Department of Science and Technology (DOST), Department of Health (DOH), National Commission on Indigenous Peoples (NCIP), Commission on Human Rights (CHR), National Museum and other agency members of the ethics network.

6.2 The RECs whose level 3 accreditation has expired are not authorized to review new applications of clinical trials intended for FDA registration.

6.3. The RECs with expired accreditation shall continue to monitor previously approved protocols.

IV. ACCREDITATION STANDARDS

The PHREB CSA shall evaluate adherence of RECs to international and national research ethics guidelines according to six (6) standards using indicators listed below:

1. Functionality of structure and composition
   - 1.1 Integration within the institutional structure
   - 1.2 Independence
   - 1.3 Multi-disciplinarity
   - 1.4 Gender representation
   - 1.5 Age representation
   - 1.6 Ethics training
   - 1.7 Related expertise to protocols commonly reviewed
   - 1.8 Management of Conflict of Interest

2. Adequacy of standard operating procedures and consistency of implementation
   - 2.1 The REC SOP shall include 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.

2.2 Minimum SOPs:

- 2.2.1 Selection and appointment of members (regular and alternate), officers and independent consultants
- 2.2.2 Management of Initial Submissions
- 2.2.3 Management of Re-submissions
- 2.2.4 Management of Post Approval Submissions
  - 2.2.4.1 Review of Progress Reports
  - 2.2.4.2 Review of Amendments
  - 2.2.4.3 Review of Protocol Deviations
  - 2.2.4.4 Review of Safety Reports
  - 2.2.4.5 Review of Final Reports
  - 2.2.4.6 Review of Early Termination Reports
  - 2.2.4.7 Management of Applications for Continuing Review
- 2.2.5 Exemption from Review
- 2.2.6 Expedited Review
- 2.2.7 Full Review
- 2.2.8 Management of Appeals
- 2.2.9 Preparation for a Meeting including the Meeting Agenda
- 2.2.10 Conduct of Meeting
- 2.2.11 Documentation of REC Actions
- 2.2.12 Management of Active Files
- 2.2.13 Archiving of Files
- 2.2.14 Site Visits
- 2.2.15 Management of Queries/Complaints
- 2.2.16 Writing and Revising SOPs

2.3 Each SOP shall include the use of the appropriate REC forms e.g., appointment letters of REC members, forms, templates of REC communications, relevant institutional/hospital circular policies and memoranda, glossary, history of the SOP and the list of references, approval date, and approving authority.

2.4 Consistency of implementation:

- 2.4.1 Time frame

2.4.2 Decision points and process

3. Completeness of review process
   - 3.1 Assignment of appropriate reviewers
   - 3.2 Complete accomplishment, consistent and meaningful use of the protocol and ICF assessment forms
   - 3.3 Comprehensive discussion (e.g., technical and ethical issues, and ICF) during the REC Meeting

4. Adequacy of post-approval procedures
   - 4.1 REC requirement for submission of reports
   - 4.2 Inclusion of reports in the meeting agenda
   - 4.3 Assessment of the reports

5. Efficiency of the recording and archiving system
   - 5.1 Appropriate protocol coding system
   - 5.2 Use of physical or electronic logbooks that has real time and tamper-proof record of submissions
   - 5.3 Completeness of protocol folders
   - 5.4 Availability of updated databases (e.g., protocol, SAE)
   - 5.5 Systematic filing of administrative and protocol-related documents (e.g., active files and archives)

6. Adequacy of administrative support
   - 6.1 Availability of a designated support staff
   - 6.2 Provision of an office and equipment (e.g., provision of security of files)
   - 6.3 Approved annual budget for REC operations

V. 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. The formal awarding of the certificate shall be held either in March or in August of the year. The REC shall be included in the list of accredited RECs in the PHREB website.

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

1. **Level 1 Accreditation**
   Level 1 accreditation is a provisional accreditation given to new REC applicants. Provisional accreditation allows new RECs to acquire experience in review of research and to give opportunity to comply with the recommendations of the CSA.

   Level 1 accredited REC reviews all types of research except clinical trials required for FDA registration of new drugs within the provisional one (1) year accreditation.

   The REC shall submit required documents according to Section VI.1.4 of the PHREB Policies and Requirements for Accreditation of Research Ethics Committees (RECs) within the first six months.

   Failure to comply with the six-month reporting requirement shall mean termination of the accreditation process and REC delisting from the list of PHREB-accredited RECs.

   Within the year, the PHREB-CSA/REMB-CSA may recommend either submission of application for Level 2 or extension of Level 1 provisional accreditation and require further training and submission of additional evidence of compliance.

2. **Level 2 Accreditation**
   Level 2 accredited REC reviews all types of research except clinical trials required for FDA registration of new drugs.

   RECs who have demonstrated satisfactory performance as a Level 1 REC (i.e., functional structure and composition, adequate SOPs, adequate administrative support, effective management of files and archiving) may apply for Level 2.

   RECs who have not been accredited but have been operating for more than six months can apply for Level 2 accreditation provided they can submit all the necessary requirements.

Level 2 accreditation may be granted for one or three years depending on the degree of satisfactory compliance with the CSA recommendations regarding quality and documentation of review.

3. Level 3 Accreditation

Level 3 Accredited REC reviews all types of research including studies required in applications for marketing authorization of food, drugs, and devices by a regulatory agency (i.e., FDA).

Level 3 accreditation may be granted for one or three years depending on the degree of satisfactory compliance with ICH-GCP standards and CSA recommendations regarding the quality and documentation of review.

VI. REQUIREMENTS AND PROCEDURES FOR ACCREDITATION

1. Level 1 Accreditation

The REC shall have a functional membership structure and composition, appropriate SOPs, adequate administrative support and effective management of files and archiving.

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/s on the following:

a. statement that all research involving human participants shall undergo ethics review by the REC
b. constitution, functions, and responsibilities of the REC
c. Terms of Reference (TOR) of REC Members
d. statement on the independence of the REC in decision-making
e. commitment to support the operations of the REC.

1.1.3 Institutional organogram showing the location of the REC and its relation to the other units

1.1.4 Standard Operating Procedures for REC activities (refer to Section IV. Item No. 3)
1.1.5 Accomplished PHREB Form No. 1.1: Application for Accreditation
1.1.6 Updated CVs (including present official position in the institution) and training records of members (signed and dated)
1.1.7 Research Ethics training plan for members
1.1.8 Accomplished PHREB Form No. 1.4: Self-Assessment for Level 1 or 2 Application for Accreditation

1.2 A provisional Level 1 accreditation shall be issued by PHREB for one (1) year after evaluation of the submitted documents.

1.3 The REC shall be included in the list of accredited RECs in the PHREB website.

1.4 During the provisional year of accreditation, the REC shall be assessed:

1.4.1 After the first six (6) months by submission of PHREB Form 1.3. *Protocol Summary* that includes REC decisions, minutes of the meeting and three protocol files.
1.4.2 Within the provisional year, the REC shall be re-assessed for possible Level 2 accreditation by submission of the following:
1.4.2.1. PHREB Form No. 1.1 Accreditation Application
1.4.2.2. PHREB Form No. 1.4: Self-Assessment for Level 1 or 2 Application for Accreditation
1.4.2.3. Resubmission of institutional policies relevant to the operations of the REC
1.4.2.4. PHREB Form No. 1.2: Annual Report

1.4.2.5. CVs and ethics training records of members (signed and dated) if there are changes in membership

1.4.2.6. Institutional organogram showing the location of REC and its relation to the institution

1.4.2.7. PHREB Form No. 1.3: Protocol Summary

1.4.2.8. Three (3) Protocol Files (at least one (1) full review) where each file shall contain: a) initial protocol; b) revised protocol, if any; c) initial informed consent; d) revised informed consent, if any; e) excerpt of minutes of the meetings where the protocol was discussed; f) decision letters; g) approval letter; h) assessment forms; and, i) reports (e.g. progress, final, and deviation)

1.4.2.9. Copy of the minutes of the three (3) most recent REC meetings

1.4.2.10. Other documents that may be required by PHREB based on its assessment after the first six (6) months

1.4.2.11. Resubmission of photographs of the office space, furniture, equipment, filing cabinets, screenshot of database, picture of the page of the logbook with the last entries

1.5. A REC who fails to achieve level 2 accreditation within three years shall be delisted.

2. **Level 2 Accreditation**

RECs who have been operational for more than 6 months can apply for Level 2 accreditation.

2.1 A Level 2 REC shall comply with the six (6) accreditation standards, Section IV. *Accreditation Standards*. REC applicants for Level 2 accreditation shall submit the following documents:

2.1.1 Cover Letter of application

2.1.2 Accomplished PHREB Form No. 1.1: Application for Accreditation

2.1.3 Accomplished PHREB Form No. 1.4: Self-Assessment for Level 1 or 2 Application for Accreditation

2.1.4 Copy of the institutional issuance on the constitution and terms of reference (TOR) of REC, including a statement of administrative support for the operations of the REC

2.1.5 Copy of an institutional policy statement that all researches involving human participants shall undergo ethics review

2.1.6 Institutional organogram locating the REC and showing its relationship with the other units

2.1.7 Standard Operating Procedures (refer to Section IV: Item No. 3)

2.1.8 Flow chart of REC procedures including timelines from initial submission to approval

2.1.9 Protocol summary for the past two years including the current year based on PHREB Form No. 1.3: *Protocol Summary*

2.1.10 Files of three (3) research protocols that have been reviewed and approved by the REC. The protocol file should include:

2.1.10.1 Copy of the initial and revised protocols, initial and revised informed consent forms, accomplished assessment forms (technical/scientific and informed consent review);

2.1.10.2 Minutes of the meeting when the research protocol was discussed

(initial and subsequent continuing reviews);

2.1.10.3 Letters/communications with the researchers (decision and approval letters); and

2.1.10.4 Progress/final reports and corresponding assessments.

2.1.11 Copies of the agenda and minutes of the most recent three (3) REC meetings.

2.1.12 Photograph of the office showing the equipment, furniture, screenshot of the database, page of the logbook with last entries and storage system

2.2 The REC applicant shall comply with the following:

2.2.1 Inclusion of members with expertise necessary for the type of research protocols being reviewed, at least one (1) non-affiliated member and one (1) non-scientist or lay/community member.

2.2.2 Members shall have training that includes topics on the elements of research ethics based on the national and international ethical guidelines and local regulations, and ethics review of protocols using a combination of didactics and small group discussions. The Chair, the Member-Secretary and Staff Secretary shall have training on SOP Writing and Revision. Members shall be oriented in the REC SOPs.

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.

Level 2 accreditation may be granted for one (1) or three (3) years depending on the degree of satisfactory compliance with the CSA recommendations with regard to quality and documentation of review.

3. **Level 3 Accreditation**

A Level 3 REC shall comply with the six (6) accreditation standards, Section IV. *Accreditation Standards* and must be GCP compliant.

A Level 2 accredited REC may apply for Level 3 Accreditation, with the submission of appropriate requirements (see Section VI, 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.

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

- 3.1.1 Cover letter of application
- 3.1.2 Accomplished PHREB Form No. 1.1 *Application for Accreditation*
- 3.1.3 CVs and research ethics training certificates (signed and dated)
- 3.1.4 Accomplished PHREB Form No.1.3 *Protocol Summary*, in the last three years, including the current year
- 3.1.5 Accomplished PHREB Form No. 1.6 *Self-Assessment for Level 3*
- 3.1.6 Standard Operating Procedures (refer to Section IV *Item No. 3*)

3.2 The REC applicant shall comply with the following:

- 3.2.1 All members shall have research ethics training.
- 3.2.2 The Chair and majority of the members shall have GCP training within the past three (3) years.
- 3.2.3 The Chair, the Member-Secretary and Staff Secretary shall have training on SOP Writing and Revision. Members shall have a documented orientation on SOPs of their REC.
- 3.2.4 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 involves 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. standard operating procedures, membership files, selected protocol files, SAE files, file of agenda and minutes of meetings, communications file, log book of incoming and outgoing communication, and databases).

3.4 Post-visit activities

3.4.1 PHREB-CSA sends the Accreditation Report to the REC within 30 calendar days after the visit;

3.4.2 REC submits an action plan and evidence of compliance to CSA within 30 calendar days after receipt of the CSA Report;

3.4.3 A revisit may be scheduled by the CSA to determine compliance with the action plan and recommend the appropriate accreditation of the REC;

3.4.4 The CSA communicates the final evaluation/decision regarding the accreditation within 30 days after receipt of the evidence of compliance;

3.4.5 PHREB awards a certificate of accreditation with a specified period of validity.

VII. ACCREDITATION OF ACADEMIC (UNIVERSITY) RECs

The following policies shall be applicable to Academic (University) RECs:

1. In universities where the REC consists of panels, only one set of SOPs shall be used by the different panels.
2. In universities where a college or unit sets up its own REC, its accreditation application shall be justified and approved by the institutional authority.
3. The level of independence in decision-making of each panel shall be clearly described and justified in the administrative order constituting the REC and in the SOP of the REC.
4. The Academic (University) applicant RECs shall comply with the following membership requirements:

    4.1 All members of the university REC panels shall be appointed by the institutional appointing authority with the terms of reference, including responsibilities as officers, as members, as non-scientist and non-affiliated. All appointees shall sign the conforme.

    4.2 Faculty/staff who have retired for at least one (1) year from the university may be appointed as non-affiliated members of the REC.

    4.3 All members of the university REC, college REC or panel members shall be listed and identified separately in the PHREB No. 1.1 *Application Form.*

    4.4 All required membership documents, i.e., letter of appointment and conforme, CV, training record and training certificates, shall be included in the application package of the institution.

5. The description of management of submissions shall be clearly described in the SOP, e.g., centralized secretariat, database, coding system, filing of documents

VIII. ACCREDITATION OF RECs IN SPECIALTY CLINICS/HOSPITAL DEPARTMENTS

Introduction:

The level of accreditation of specialty clinics needs special attention because of concerns in the provision of 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/ 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.

These policies also cover RECs established in specific hospital departments.

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 Research Ethics Committee (number of members with at least one non-affiliated medical member in the same specialty, one (1) affiliated medical/scientific member, officers, specialty, affiliation, scientist/non-scientist, gender, age representation and record of research ethics training)
    - 1.6 Affiliation with geographic access (within 5 km radius) to a health facility with general medical services.
    - 1.7 Copy of Specialty Board Policy on Research Misconduct

1.8 Other relevant documents as may be required by the PHREB CSA

2. Application for Level 1 shall be processed according to the 2020 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 1:10) of active consultant members of the research ethics committee to potential researchers (i.e., if there is less than 10 then all REC members should be non-affiliated with the center) and the accessibility of a health facility that offers general medical services to research participants, if needed.

IX. RESPONSIBILITIES OF AN ACCREDITED REC

1. Posting of PHREB Accreditation Certificate

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

2. Submission of Annual Report
   - 2.1 PHREB Form No. 1.2 *Annual Report* on or before 31 March
   - 2.2 Submission of PHREB Form 1.3 *Protocol Summary* version 3 or protocol database that includes protocol title and code, name of researcher, type of review and action, date of approval and status

3. Reporting of any controversial or important ethical issues in the course of its work

   Annual report and other reports should be addressed to the PHREB Chair:

   Mailing address: PCHRD, Executive Lounge, Department of Science and Technology, General Santos Avenue, Bicutan, Taguig City 1631
   Telephone: (02) 8-837-75-37 loc. 403 TeleFax: (02) 8-837-29-24
   Email address: ethics.secretariat@pchrd.dost.gov.ph

X. RENEWAL OF ACCREDITATION CERTIFICATE

Within six (6) months before the expiry of its accreditation, a REC shall apply for renewal by complying with the requirements/responsibilities of accredited RECs (Section VI: Procedures and Requirements for PHREB Accreditation).

XI. BASES FOR SUSPENSION OF ACCREDITATION

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

1. Non-Compliance with PHREB Reportorial/Other Requirements

   An REC that fails to submit an annual report for two (2) consecutive years shall have its certification suspended 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 may or may not have resulted in harm to participants.

XII. FEES

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

The accreditation fee shall include but not limited to the following: (1) accreditor's honorarium; (2) accreditor's accommodation, and airfare/transportation as needed; and (3) travel and health insurance for the duration of the accreditation visit.

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).

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/).

Appendix H
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. For RECs participating in single joint reviews (e.g., DOH SJREB) additional steps related to the REC's participation shall be included in the SOP.

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

1.1. Review of Progress, Final, and Early Termination Reports, and Protocol Amendments
1.2. Review of SAE and SUSAR Reports
1.3. Review of RNE Reports
1.4. Review of Protocol Deviations and Violations
1.5. Review of Applications for Continuing Review

SOP 4: Review Procedures

1.1. Expedited Review
1.2. 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

1.1. Managing the Meeting Minutes
1.2. Communicating REC Decisions

SOP 7: Management and Archiving of Files

1.1. Managing REC Incoming/Outgoing Communications

1.2. Managing Active Files (Administrative and Study Files)
1.3. Archiving of Terminated, Inactive, and Completed Files
1.4. Managing Access to Confidential Files

SOP 8: Management of Appeals

SOP 9: Site Visits

SOP 10: Management of Queries/Complaints

SOP 11: Writing and Revising SOPs

Appendix I
The PHREB Standard Operating Procedure Template

Standard Operating Procedures (SOPs) are the step-by-step description of the different procedures done to accomplish the objective of an activity. SOPs guide Research Ethics Committees (RECs) in ensuring consistency, transparency, and quality in ethical review. The latest version of the SOP PHREB Workbook may be viewed in this link: https://ethics.healthresearch.ph/index.php/phoca-downloads/category/19-2020-phreb-sop-workbook?download=106:2020-phreb-sop-workbook-pdf

The PHREB SOP Workbook may be adopted by the REC in a manner reflective of the specific context and actual practice of the committee.

The SOP should have a **HEADER** which consists of the name and logo of the Institution, name of the REC, 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 assignment of the SOP number and version number. The version number is the latest edition of the SOP. The suggested format is as follows:

<table>
<tr><td rowspan="4">Logo and name of Institution</td><td colspan="2">Name of the REC (e.g., Research Ethics Committee, Ethics Review Committee, Institutional Ethics Review Committee, Institutional Review Board)</td></tr>
<tr><td rowspan="3">SOP No. ___
SOP TITLE</td><td>Version No:</td></tr>
<tr><td>Date of Approval:</td></tr>
<tr><td>Effectivity Date:</td></tr>
</table>

Section 1. The **Policy Statement** consists 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.

Section 2. The **Objective** refers to the purpose of the activity (e.g. for SOP **Preparing for a Meeting**, the objective may be stated as "Preparing for a

meeting aims to ensure that all meeting documents and necessary logistics are available during the meeting.").

Section 3. The **Scope** is based on the Workflow (Section 5) and includes the initial and final steps involved in the activity.

Section 4. The **Workflow** section is a diagram or a matrix briefly showing the different steps involved in the activity and the responsible persons. It may 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. Usually, verb-nouns like "receipt of", "submission of", "conduct of "distribution of", "filing of", "approval of" are used.

Section 5. Detailed Description of Procedures describes the performance of each step in the Workflow. The person/s responsible and the forms to be used are mentioned and cited. The active forms of verbs are used. It is important to ensure that the number of steps in the Workflow (Section 4) is the same number of steps described in Section 5.

Section 6. The **Glossary** is a list of terms, including acronyms and abbreviations used in the SOP that need to be defined or explained. (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).

Section 7. The **Forms** section lists the specific forms (and corresponding codes) used in the activity (e.g., application form, checklist, review guide, communication templates).

Section 8. The **History** section is a tabulation of the version dates and number, authors, and the enumeration of major changes that the SOP has undergone. For example, the history section of **SOP Designation of REC Officers** may be represented as follows:

Version Number	**Date**	**Authors**	**Change/s**

1	2012 June 12	ABC	Initial version
2	2014 December 10	DEF	Added the determination of type of review as a responsibility of the member secretary
3	2018 December 5	GHI	Included a co-chair as an officer.

Section 9. The **References** section is a list of current guidelines, other institutional SOPs, manuals used in the development of the SOP.

Appendix J
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).*

<table>
<tr><th colspan="4">I. GENERAL INFORMATION</th></tr>
<tr><td>TITLE
OF STUDY</td><td colspan="3"></td></tr>
<tr><td>REC CODE
(To be provided by REC)</td><td></td><td>STUDY SITE</td><td></td></tr>
<tr><td rowspan="2">NAME
OF RESEARCHER</td><td rowspan="2"></td><td rowspan="4">CONTACT INFORMATION</td><td>TEL NO:</td></tr>
<tr><td>MOBILE NO:</td></tr>
<tr><td rowspan="2">CO-RESEARCHER/S
(if any)</td><td rowspan="2"></td><td>FAX NO:</td></tr>
<tr><td>EMAIL:</td></tr>
<tr><td>NAME OF INSTITUTION</td><td colspan="3"></td></tr>
<tr><td>INSTITUTION ADDRESS</td><td colspan="3"></td></tr>
<tr><td>TYPE OF STUDY</td><td colspan="2">□ Clinical Trial (Sponsored)
□ Clinical Trials (Researcher-Initiated)
□ Health Operations Research (Health Programs and Policies)
□ Social or Behavioral Research
□ Public Health or</td><td>□ Biomedical research (Retrospective, Prospective and Diagnostic Studies)
□ Stem Cell Research
□ Genetic Research
□ Internet Research
□ Others:
_____</td></tr>
</table>

	Epidemiologic		
	□ Multicenter *(International)*	□ Multicenter *(National)*	□ Single Site
SOURCE OF FUNDING	□ Self-Funded □ Government-Funded □ Scholarship/Research Grant □ Institution-Funded	□ Sponsored by Pharmaceutical Company Specify: _____ □ Others: _____	
DURATION OF THE STUDY	**START DATE**:	**NUMBER OF STUDY PARTICIPANTS**	
	END DATE:		
HAS THE RESEARCH UNDERGONE TECHNICAL REVIEW?	□ **YES** *(please attach technical review results)*	□ **NO**	
HAS THE RESEARCH BEEN SUBMITTED TO ANOTHER RESEARCH ETHICS COMMITTEE?	□ **YES**	□ **NO**	

II. BRIEF DESCRIPTION OF THE STUDY *(use additional sheet if necessary)*
III. CHECKLIST OF DOCUMENTS FOR SUBMISSION

BASIC REQUIREMENTS: □ Letter request for review □ Endorsement/Referral Letter □ Foreign Institutional Ethics Review Approval (if applicable) □ Full Proposal/Study Protocol □ Technical Review Approval □ Curriculum Vitae of Researcher □ Informed Consent Form □ English version □ Filipino version □ Others _____ □ Assent Form *(if applicable)* □ English version □ Filipino version □ Others _____	**SUPPLEMENTARY DOCUMENTS** *(if applicable)*: □ Questionnaire □ Data Collection Forms □ Product Brochure □ Philippine FDA Marketing Authorization or Import License □ Permit(s) for special populations _____ _____ □ Others _____ _____
ACCOMPLISHED BY: _____ *(Signature over printed name)*	**DATE SUBMITTED:**

---------- TO BE FILLED OUT BY THE REC SECRETARIAT ----------

COMPLETENESS OF DOCUMENT	□ Complete □ Incomplete	(place stamp here)
REMARKS		
DATE RECEIVED:		
RECEIVED BY:		

Appendix K
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 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, their designation or title in their agency, field of specialization and their mailing address, telephone, and fax numbers. Percentage time to be devoted to their 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 literature 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 a sound information base, addresses current country health priorities, and will contribute something new to health 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 the 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 study, case-control, cohort)

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 (e.g., instrumentation or data collection tools, special equipment)

Case Report Form (CRF). The 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. These include dependent/outcome and independent variables.

(15). ADDITIONAL SECTION FOR INTERNET RESEARCH

If the protocol involves internet research, details of data collection should be described in the protocol including the following items:

a. Description on how the PI will authenticate the qualification and or identification of the respondents (e.g., use of personal identification number given to participants)
b. Identification and description of the source of online data that will be used in the research

    Blogs, collaborative (e.g., Wikipedia), e-mails, chats, fora, social media platforms (e.g., Facebook, Twitter, Viber), Websites, Video blogs (e.g., Youtube), Others

c. Identification and description of the data to be collected
   Audio, correspondence (e.g., emails), film/video, photos, presentations (e.g., downloaded powerpoint presentations), metadata (e.g. profile, geographic location), text or content, others
d. Listing all URLs to be used
e. Identification of method/s of obtaining the informed consent
   Written consent, email with name, audio-recorded consent, electronic information sheet with 'tick box' for consent or non-consent, consent implied through submission of information, others
f. Description of how participants will get a copy of the ICF
g. Description of how participants will withdraw from the study if they wish to withdraw

(Data protection plan should be included in the section on DATA AND PRIVACY MANAGEMENT PLAN)

(16) PLANS FOR DATA PROCESSING AND ANALYSIS

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

(17) WORK PLAN SCHEDULE

This is a 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.

(18) 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).

(19) ETHICAL CONSIDERATIONS

This section identifies the ethical issues inherent in the study protocol, in particular: (a) process of getting the informed consent/assent, (b) issues of vulnerability and provision for protection of vulnerable participants/communities, (c) risk-benefit assessment and offering measures to enhance benefit and mitigate risks.

(20) DATA AND PRIVACY MANAGEMENT PLAN

This section addresses privacy and confidentiality concerns in research. It should describe the governance and accountability issues regarding data management and security. This section should indicate the medium in which the research data are stored, including security measures appropriate to the medium of storage. It should describe how data collection and storage will be secured (e.g., use of password, encryption, etc.) and limits of access to the server.

The researcher/investigator should disclose other parties who may access the data. In addition, the researcher/investigator should indicate measures to address breaches of confidentiality.

(21) RESEARCH DISSEMINATION/UTILIZATION

This section should indicate the strategies to be used in disseminating and ensuring utilization of the expected research results. Details should be provided on how results of the research will be shared with the participants/communities being studied. For product-based research, proposal should include the prospective technology user, as well as plans for technology transfer.

(22) 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 during 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.

(23) CURRICULUM VITAE

This portion provides relevant information regarding the proponent's research capability

(24) 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.

(25) 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.

(26) 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***
I. Personal Services (PS) *a. Salaries* *b. Honoraria*			
PS SUB TOTAL			
II. Maintenance and Other Operating Expenses (MOOE) *a. Traveling expenses*			

b. Supplies and materials expenses			
MOOE SUBTOTAL			
III. Capital Outlay			
CAPITAL OUTLAY SUBTOTAL			
GRAND TOTAL			

Appendix L
Sample Worksheet for Protocol Assessment

(Adapted from the NEC with new added items)

TITLE OF THE STUDY				
REC CODE		**TYPE OF REVIEW**		
PROPONENT		**INSTITUTION**		
REVIEWER		**PRIMARY REVIEWER?**	☐ YES	☐ NO
-- GUIDE QUESTIONS FOR REVIEWING THE PROPOSAL OR PROTOCOL --				
1. Is/Are the research question(s) reasonable?		☐ UNABLE TO ASSESS	☐ YES	☐ NO
If NO or UNABLE TO ASSESS, please comment.				
2. Are the study objectives specific, measurable, attainable, and reasonable?		☐ UNABLE TO ASSESS	☐ YES	☐ NO
If NO or UNABLE TO ASSESS, please comment.				
3. Is the research methodology appropriate?		☐ UNABLE TO ASSESS	☐ YES	☐ NO
If NO or UNABLE TO ASSESS, please comment.				
4. Does the research need to be carried out with human participants?		☐ UNABLE TO ASSESS	☐ YES	☐ NO

If NO or UNABLE TO ASSESS, please comment.			
5. Does the protocol present sufficient background information or results of previous studies prior to human experimentation?	☐ UNABLE TO ASSESS	☐ YES	☐ NO
If NO or UNABLE TO ASSESS, please comment.			
6. Does the study involve individuals who are vulnerable?	☐ UNABLE TO ASSESS	☐ YES	☐ NO
If YES or UNABLE TO ASSESS, please comment.			
7. Are appropriate mechanisms in place to protect the vulnerable potential participants?	☐ UNABLE TO ASSESS	☐ YES	☐ NONE
If NONE or UNABLE TO ASSESS, please comment.			
8. Are there probable risks to the human participants in the study?	☐ UNABLE TO ASSESS	☐ YES	☐ NONE
If NONE or UNABLE TO ASSESS, please comment.			
9. What are the risks? Are these identified in the protocol? _____	☐ UNABLE TO ASSESS	☐ YES	☐ NO
Are the possible benefits identified in the protocol? _____	☐ UNABLE TO ASSESS	☐ YES	☐ NO
10. Does the protocol adequately address the risk/benefit balance?	☐ UNABLE TO ASSESS	☐ YES	☐ NO

If NO or UNABLE TO ASSESS, please comment.			
11. Does the protocol address issues of privacy and confidentiality? Is there a Data Protection Plan?	☐ UNABLE TO ASSESS	☐ YES	☐ NO
If NO or UNABLE TO ASSESS, please comment.			
12. Are toxicological and pharmacological data adequate?	☐ NOT APPLICABLE	☐ YES	☐ NO
If NO, comment.			
13. Is the informed consent procedure/form adequate and culturally appropriate?	☐ NOT APPLICABLE	☐ YES	☐ NO
If NO, comment.			
14. Are the proponents adequately trained and do they have sufficient experience?	☐ UNABLE TO ASSESS	☐ YES	☐ NO
If NO or UNABLE TO ASSESS, please comment.			
15. Does the protocol describe community engagement/consultation prior to and during the conduct of research?	☐ NOT APPLICABLE	☐ YES	☐ NO
If NO, please comment.			
16. Does the protocol include strategies to be used in disseminating/ ensuring utilization of the expected research results?	☐ NOT APPLICABLE	☐ YES	☐ NO

If NO, please comment.			
17. Is the research facility appropriate?	☐ UNABLE TO ASSESS	☐ YES	☐ NO
If NO or UNABLE TO ASSESS, please comment.			
18. Do you have any other concerns?			

Recommendation:

☐ Exempt from Review
☐ Approved
☐ Minor Revisions Required
_____
_____
☐ Major Revisions Required
_____
_____
☐ Disapproved
Reasons for disapproval:
_____
_____

Signature over Printed Name of Reviewer

Review Date

Appendix M
Reviewer's Worksheet Template for Social Research

Title of the Study			
Type of Review			
Researcher		**Institution**	
Reviewer		**Primary Reviewer**	__Yes __No
First review __Yes __No		**Second Review** __Yes __No	
Guide questions for reviewing the proposal/protocol.			
1. Scientific soundness			
Are the proposal's scientific question(s) reasonable and the research design sound? __Unable to Assess __Yes __No If NO or UNABLE TO ASSESS, please explain.			
2. (Non-)Involvement of human participants			
Does the research need to be carried out with human participants? __Unable to Assess __Yes __No If NO or UNABLE TO ASSESS, please explain.			
3. (Non-)Involvement of vulnerable peoples			

3.1 Does the study involve individuals who belong to vulnerable individuals and/or groups?
__Unable to Assess __Yes __No

If NO or UNABLE TO ASSESS, please explain.

3.2 Can the study be accomplished without the participation of vulnerable individuals and/or groups?
__Unable to Assess __Yes __No

If NO, are appropriate mechanisms in place to protect vulnerable participants?

3.3 For studies involving IPs, does the protocol strictly comply with IPRA, NCIP and PHREB protocols and the need to engage the IPs in genuine dialogue?
__Unable to Assess __Yes __No

If NO, are appropriate mechanisms in place to protect vulnerable participants?

4. Risks, Harms, & Benefits

4.1 Are there probable risks and harms to human participants in the study?
__Unable to Assess __Yes __No

If NO or UNABLE TO ASSESS, please explain.

If YES, are there adequate provisions for mitigating strategies, particularly if it involves a sensitive topic?

Risks/Harms	**Mitigating Strategies**

4.2 Determining Risks and Mitigating Strategies	**Yes**	**No**
4.2.1 Are the participants involved in determining and weighing of risks?		
4.2.2 Is there an adequate provision for the maintenance of the confidentiality of all information?		
4.2.3 Is there an adequate reparation strategy?		
4.3 Does the protocol adequately address the risk/benefit balance? If NO or UNABLE TO ASSESS, please explain.		
4.4 Will the participants and/or their communities benefit from the study?		
4.5 Will the participants be informed of the results of the study in an appropriate manner?		
5. Informed Consent	**Yes**	**No**
5.1 Is the informed consent procedure and form adequate and culturally appropriate?		
5.2 Informed consent procedure		
5.2.1 Is there a palpable care and concern for the welfare and rights of participants in the protocol?		
5.2.1 Does the researcher provide adequate information about the nature of the study and what it expects of participants?		

5.2.2 Does the researcher provide the necessary mechanisms for her or him to determine the prospective participant's understanding of the protocol (e.g., the provision of time and opportunity to read, think, ask questions and make suggestions about the protocol)?		
5.2.3 Does the protocol state that participation in the study is voluntary?		
5.2.4 Does that protocol state that the participant has the right to withdraw at any time from study without penalty?		
5.3 Are the following present in the informed consent form (ICF):		
5.3.1 Purpose and objectives of the study		
5.3.2 Statement that participation is voluntary		
5.3.3 Statement that one can withdraw at anytime from the study without penalty		
5.3.4 Statement that one can refuse to answer a question (or questions) in the course of a study		
5.3.5 Explanation of the research intervention that will be performed		
5.3.6 The projected duration and the time needed for one's participation		
5.3.7 Risks of the study		
5.3.8 Benefits of the study		
5.3.9 Assurance of confidentiality of all information		
5.3.10 Reimbursements and/or just compensation for one's participation		
5.3.11 Sharing of the results of the study		
5.3.12 Persons to contact in case there are concerns/emergency situations		

5.3.13 Certificate of consent with the provision for the name of the participants, her or his signature, and date of signing of ICF		
5.3.14 An alternative manner of giving of consent		
5.3.15 A referral system for appropriate interventions in place in case the need arises		
6. Justice	**Yes**	**No**
6.1 Does the research have social value?		
6.2 Are the participants selected fairly?		
6.3 Does the protocol adequately consider the rights of all stakeholders?		
6.4 If there is a conflict of interest on the part of the researcher, is it managed properly?		
6.5 Is there a provision for just compensation?		
6.6 If there is no compensation, is the explanation reasonable?		
6.7 If the research can be potentially used for unethical ends, are adequate strategies in place to respond to them?		
6.8 If third parties will be potentially adversely impacted by the research, are there strategies that minimize the unintended consequences on those parties?		
6.9 Is there due acknowledgement of the indispensable contribution of participants in the study?		
6.10 Does the research promote inclusivity and justice between the researcher and the participants and their communities as well as the society in general?		

6.11 For studies involving IPs, does the protocol strictly comply with IPRA, NCIP and PHREB protocols and the need to engage the IPs in genuine dialogue?		
7. The Researcher(s)		
Is/are the (principal) researcher(s) adequately educated, trained and/or experienced for the proposed study? __Unable to assess __Yes __No		
8. Other Concerns		
Do you have other concerns about the protocol and/or researcher(s)?		

Recommendation:

☐ Exempt from Review
☐ Approved
☐ Minor Revisions Required
_____
_____
☐ Major Revisions Required
_____
_____
☐ Disapproved
Reasons for disapproval:
_____
_____

_____ Signature over Printed Name of Reviewer		_____ Review Date

Appendix N
Informed Consent Form Template for Clinical Studies

Adapted from the WHO Informed Consent Template (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. New items have been added to ensure compliance with the Data Privacy Act of 2012)

[INSTITUTIONAL LETTERHEAD]

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 Principal 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 the 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. For research protocols using internet/online platforms the risk of breach of privacy and confidentiality should be explained. In addition, describe how the breach of privacy and confidentiality will be managed.

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. For research using internet/online platforms it is good practice to include a statement similar to this – "Confidentiality will be maintained to the degree permitted by the technology used. Your participation in this online survey involves risks similar to a person's everyday use of the Internet."

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.
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 O
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/)

(This template is for research interventions that use questionnaires, in-depth interviews or focus group discussions.)

[INSTITUTIONAL LETTERHEAD]

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 Principal 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 they can take time to reflect on whether they want to participate or not. Assure the participant that they do not understand some of the words or concepts, that these will be explained and that they 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 they 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 they do not have to share any knowledge that they are not comfortable sharing. It is also important for the participant to know that they can still opt out of the study even after the FGD by requesting that their participation not be cited as 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 they do 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 they 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 they may answer the questionnaire personally, or it can be read to them; answered aloud and written down by a member of the research team. Assure the participant that if they do not wish to answer any of the questions, this may be skipped, and they can proceed to the next question. The information recorded is confidential, name is not included on the forms, only a number will identify them, and no one else except [name of persons 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) or confidential in nature, then there is a risk of embarrassment, discomfort or fear. Assure the participant that they do

not have to answer any question or take part in the discussion, interview, or survey if they feel the questions are too personal or if talking about them makes them 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 because 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 because 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 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 that 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 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 P
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/)

(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 Principal 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, they will be attended to promptly. Include the importance of complying with the scheduled visits 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 they get 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. They can think about it and decide later. It will also be ok to say “yes” now and change their 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 they 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.

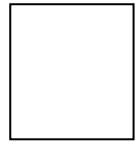
I agree to take part in the research.

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 them 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 _____ (initialed by researcher/assistant)

Parent/Guardian has signed an informed consent
___Yes ___No _____ (initialed by researcher/assistant)

Appendix Q
Sample Informed Consent Assessment Checklist

(Adapted from the NEC with additional items)

TITLE OF STUDY				
REC CODE		**TYPE OF REVIEW**		
PRINCIPAL INVESTIGATOR		**INSTITUTION**		
REVIEWER		**PRIMARY REVIEWER?**	☐ **YES**	☐ **NO**
-- GUIDE QUESTIONS FOR REVIEWING THE INFORMED CONSENT PROCESS AND FORM --				
1. **IS IT NECESSARY TO SEEK THE INFORMED CONSENT OF THE PARTICIPANTS?**				
☐ UNABLE TO ASSESS	☐ YES	☐ NO		
IF NO, please explain				
If YES, are the participants provided with sufficient information about the following items?				
● Purpose of the study?			☐ YES	☐ NO
● Expected duration of participation?			☐ YES	☐ NO
● Procedures to be carried out?			☐ YES	☐ NO
● Discomforts and inconveniences?			☐ YES	☐ NO

● Risks (including possible discrimination)?	☐ YES	☐ NO
● Random assignment to the trial treatments? *(if applicable)*	☐ YES	☐ NO
● Benefits to the participants?	☐ YES	☐ NO
● Alternative treatments/procedures? *(if applicable)*	☐ YES	☐ NO
● Compensation and/or medical treatments in case of injury?	☐ YES	☐ NO
● Who to contact for pertinent questions and/or for assistance in a research- related injury?	☐ YES	☐ NO
● Refusal to participate or discontinuance at any time will involve penalty or loss of benefits to which the subject is entitled?	☐ YES	☐ NO
● Extent of confidentiality? If informed consent is taken through online/electronic means, Is there a statement that says, "Confidentiality will be maintained to the degree permitted by the technology used. Your participation in this online survey involves risks similar to a person's everyday use of the Internet."	☐ YES	☐ NO
● Is there an adequate and clear description of the data protection plan and details about how data will be stored (including who has access to the data)?	☐ YES	☐ NO
● For online/internet-based research and/or if the informed consent is taken electronically:: ○ Is the instruction of providing informed consent through online or electronic means clear and easy to follow?		

○ Does the online consent process provide a mechanism for the participant to ask questions? ○ Is there a clear description of how the participant can withdraw from the study if the participant wishes to withdraw or withdraw their information? ○ Is there a description of how the participant will obtain a copy of their consent form (i.e., if a hard copy or an online copy will be provided and how)? ○ If compensation will be provided, is there a description of how the compensation will be given/delivered to the participant?		
2. **IS THE INFORMED CONSENT WRITTEN OR PRESENTED IN NON-TECHNICAL LANGUAGE THAT PARTICIPANTS CAN UNDERSTAND?**	☐ YES	☐ NO
3. **DOES THE PROTOCOL INCLUDE AN ADEQUATE PROCESS FOR ENSURING THAT CONSENT IS VOLUNTARY?**	☐ YES	☐ NO
4. **DO YOU HAVE ANY OTHER CONCERNS?**		

Recommendation:

☐ Exempt from Review
☐ Approved
☐ Minor Revisions Required

_____
_____
_____

☐ Major Revisions Required

_____
_____

_____

☐ Disapproved

Reasons for disapproval:

_____

_____

_____

Signature over Printed Name of Reviewer		Review Date

Appendix R
CARE Checklist (2016): Information for Writing a Case Report

(www.care-statement.org)

Topic	Item		Page #	Reviewer's Comments
Title	1	The words "case report" should be in the title along with the area of focus		
Key Words	2	Four to seven key words—include "case report" as one of the key words		
Abstract	3a	Background: What does this case report add to the medical literature?		
	3b	Case summary: chief complaints, diagnosis, interventions, outcomes		
	3c	Conclusion: What is the main "take-away" lesson from this case?		
Introduction	4	The current standard of care and contributions of this case—with references (1-2 paragraphs)		
Timeline	5	Information from this case report organized into a timeline (table or figure)		
Patient information	6a	De-identified demographic and other patient or client specific information		
	6b	Chief complaint—what prompted this visit?		

	6c	Relevant history including past interventions and outcomes		
Physical Exam	7	Relevant physical examination findings		
Diagnostic Assessment	8a	Evaluations such as surveys, laboratory testing, imaging, etc.		
	8b	Diagnostic reasoning including other diagnoses considered and challenges		
	8c	Consider tables or figures linking assessment, diagnoses and interventions		
	8d	Prognostic characteristics where applicable		
Interventions	9a	Types such as life-style recommendations, treatments, medications, surgery		
	9b	Intervention administration such as dosage, frequency and duration		
	9c	Note changes in intervention with explanation		
	9d	Other concurrent interventions		
Follow-up and Outcomes	10a	Clinician assessment (and patient or client assessed outcomes when appropriate)		
	10b	Important follow-up diagnostic evaluations		
	10c	Assessment of intervention adherence and tolerability, including adverse events		
Discussion	11a	Strengths and limitations in your approach to this case		

	11b	Specify how this case report informs practice or Clinical Practice Guidelines (CPG)		
	11c	How does this case report suggest a testable hypothesis?		
	11d	Conclusions and rationale		
Patient perspective	12	When appropriate include the assessment of the patient or client on this episode of care		
Informed Consent	13	Informed consent from the person who is the subject of this case report is required by most journals		
Additional Information	14	Acknowledgement section; Competing Interests; IRB appoval when required		

(adopted *with permission from CARE*)

Appendix S
Checklist for Making Distinctions Between Public Health Practice and Research

To use this Checklist, please answer the key Assumptions [As] and Questions [Qs] in Steps 1-4 below, proceeding in accordance with your responses, to reach the Conclusions in Step 5. In some cases, this process will not require addressing all of the steps; in other cases, each of the steps may contribute to clarifying the distinction.

Steps and Related Assumptions and Questions	Yes	No	Next Action	
			If Yes, then	If No, then
Step 1: Check Key Assumptions				
Assumption 1.A: Are you a governmental public health official, agent, agency, or entity at the federal, tribal, state, or local level (or an authorized partner conducting public health activities via contract or other agreement)?			Go to **A 1.B**	**Stop**. This checklist does not apply
Assumption 1.B: does your activity involve the acquisition, use, or disclosure of identifiable health data (i.e., individually-identifiable data that relate to a person's past, present, or future physical or mental health or condition or provision or payment of health care, or identifiable bodily tissues or biological samples)?			Go to **Step 2**.	**Stop**. This checklist does not apply
Step 2: Assess the Foundations of Public Health Practice				
Assumption 2.A: In general, does your activity involve the collection and analysis of identifiable health data for the purpose of protecting the health of a particular community, where the benefits and risks are primarily designed to accrue to the participating community?			Go to **Q 2.A.**	Go to **Step 3.**
Question 2.A: Is there a *specific* legal authorization (via statute, administrative regulation, or other law) and corresponding governmental duty to use identifiable			**Stop**. This activity is practice.	Go to **Q 2.B.**

health data for a public health purpose that underlie the activity?				
Question 2.B: does your activity involve direct performance or oversight by a governmental public health authority (or its authorized partner) and accountability to the public for its performance?			Go to **Q 2.C.**	Go to **Step 3.**
Question 2.C: Does your activity legitimately involve persons who must participate in the activity or did not specifically volunteer to participate (i.e., they did not provide informed consent absent a waiver under the Common Rule?)			**Stop**. This activity is practice.	Go to **Step 3.**
Step 3: Assess the foundations of Human Subjects Research				
Assumption 3.A: In general, does your activity involve the collection and analysis of identifiable health data for the purpose of generating knowledge that will benefit those beyond the community of persons who bear the risks of participation?			Go to **Q 3.A.**	The activity is likely practice. Go to **Step 4.**
Question 3.A: Does your activity involve living individuals?			Go to **Q 3.B.**	**Stop**. This is not human subjects research.
Question 3.B: Does your activity involve, in part, private information as defined in the Common Rule?			Go to **Q 3.C.**	**Stop**. This is not human subjects research.
Question 3.C: Does your activity involve persons who voluntarily participate via informed consent or consent of their guardian, absent a waiver of informed consent under the Common Rule?			Go to **Step 4.**	**Stop**. This activity is practice.
Step 4: Consider Enhanced Guidance				
Question 4.A: *General Legal Authority*: Is there *general* legal authorization (via			The activity is	Go to **Q 4.B. 1-2.**

statue, administrative regulation, or other law) and a corresponding governmental duty supporting the use of identifiable health data for a legitimate public health purpose?			likely practice. Go to **Q 4.B. 1-2**	
Question 4.B.1: Specific Intent: is there any intent underlying the activity to test a hypothesis and seek to generalize the findings or acquired knowledge beyond the activity's participants?			The activity is likely research. Go to **Q 4.C.**	Go to Q4.B.2.
Question 4.B.2: Specific Intent: Is the primary intent underlying the activity to assure the conditions in which people can be healthy through public health efforts that are primarily aimed at preventing known or suspected injuries, diseases, or other conditions, or promoting the health of a particular community?			The activity is likely practice. Go to **Q 4.C.**	Go to **Q 4.C.**
Question 4.C: Responsibility: Is responsibility for the health, safety, or welfare of the participants vested or assigned to an identified person, like a principal investigator?			The activity is likely research. Go to **Q 4.D 1-2**	Go to **Q 4.D.1.**
Question 4.D.1: Participant Benefits: Is the activity designed to provide some benefit to the participants to their population as a whole?			The activity is likely practice. **Go to Q 4.E.**	Go to **Q 4.D.2.**
Question 4.D.2: Participant Benefits: Does the activity involve additional risks imposed on participants in order to make the results generalizable beyond the participants themselves?			The activity is likely research. **Go to Q 4.E.**	Go to **Q 4.E.**
Question 4.E: Is the activity designed to introduce non-standard or experimental elements or methods to the research subjects or the analysis of their identifiable health data?			The activity is likely research.	Go to **Q 4.F.**

			Go to Q 4.F.	
Question 4.F: Subject Selection: Are the participants in the activity selected randomly so that the results of the activity can be generalized to a larger population?			**Stop**. The activity is likely research.	**Stop**. The activity is likely practice.
Step 5: Conclusions				
Conclusion 5. A: ***Public Health Practice***. I f your responses affirm that your activity (or some part thereof) is or is likely public health practice, the activity is not subject to the Common Rule. However, it must still be conducted consistent with principles of law and ethics designed to protect individuals and their privacy while furthering the public's health. In addition, while the HIPAA Privacy Act allows sharing of identifiable health data without written authorization for public health purposes, note that the Rule does not require data sharing. Authorization for disclosures from covered entities under the Rule derive from other public health laws or policies. For helpful guidance on the impact of the HIPAA Privacy Rule on public health practice, please see HIPAA Privacy Rule and Public Health: Guidance from CDC and DHHS. available at: http://www.cdc.gov/privacvrule/Guidance/Content.htm.				
Conclusion 5.B: ***Human Subject Research***. If your responses affirm that your activity (or some part thereof) is or is likely human subjects research, the Common Rule may apply, subject to an exemption. In addition, the activity may be entitled to expedited review under the Common Rule. For additional guidance and a helpful flowchart, please see the Guidelines for the Conduct of Research published by the Office for Human Subjects Research at NIH , available at: http://wvvw.nihtraining.coni/ohsrsite/guidelines/graybook.html				

From "Public Health Practice vs. Research; A Report for Public Health Practitioners Including Cases and Guidance for Making Distinctions," by Hodge, J.G. and Gostin, L.O., 2004, p. 53
https://idph.iowa.gov/Portals/1/userfiles/144/Public%20Health%20Practice%20vs%20%20Research.pdf. Reprinted with permission.

Appendix T
Composition of the Philippine Health Research Ethics Board

(As of January 2022)

LEONARDO D. DE CASTRO, PhD
Philosophy
Chair

SONIA E. BONGALA, 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

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PTR. ALDRIN M. PEÑAMORA
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Ex officio Member

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Philippine Council for Health Research and Development
Ex officio Member

Appendix U
Composition of the National Ethics Committee

(As Of December 2021)

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Molecular Biology
Chair

RICARDO M. MANALASTAS, JR., MD
Clinical Research
Co-Chair

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Art History and Anthropology

LEONARDO D. DE CASTRO, PhD
Philosophy and Bioethics

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Appendix V
The Ad Hoc Committee for Updating the National Ethical Guidelines

THE AD HOC COMMITTEE FOR THE UPDATING OF THE 2017 NATIONAL ETHICAL GUIDELINES FOR HEALTH AND HEALTH RELATED RESEARCH patiently and carefully reviewed and revised the old guidelines and formulated new ones 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:

Core Members	
MARIA SALOME N. VIOS, MD (Chair)	Member, PHREB Committee on Standards and Accreditation (CSA)
RICARDO M. MANALASTAS, JR., MD (Vice-Chair)	Chair, PHREB Committee on Information Dissemination, Training, and Advocacy (CIDTA)
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Technical Consultants	
LEONARDO D. DE CASTRO, PhD	Chair, PHREB

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Appendix X
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APPENDIX Y
Bill of Rights in Health Research, Studies, and Clinical Trials

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); a response to a marketed medicinal product that is noxious and unintended, and which occurs at doses normally used in human for prophylaxis, diagnosis, or therapy of diseases or modification of physiological function (ICH-GCP). 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. *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 a 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** clinical manifestations in the advanced stages of HIV infection characterized by the breakdown of the immune system

Alternative Medicine or Alternative Healthcare Modalities other forms of non-allopathic, occasionally non-indigenous or imported healing methods, though not necessarily practiced for centuries nor handed down from one generation to another; may include reflexology, acupressure, chiropractic, nutritional therapy, and other similar methods (TAMA, 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 45).

Archival Research study involving the examination of records or documents

Artificial Intelligence ability of a digital computer or computer-controlled robot to perform tasks commonly associated with intelligent beings. The term is frequently applied to the project of developing systems endowed with the intellectual processes characteristic of humans, such as the ability to reason, discover meaning, generalize, or learn from experience. (Copeland, 2020)

Assent authorization for one's participation in research given by a minor or another participant who cannot give informed consent; a requirement for research, in addition to the 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 to establish 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)

Augmented reality technology that superimposes a computer-generated image on a user's view of the real world, thus, providing a composite view (GVIS - Visualization Devices, n.d.)

Autonomy 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 they are 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, 2018). *See also Double Blinding*

Clinical Equipoise a state or condition, based on available data, of genuine uncertainty on the part of the researcher 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) to discover or verify the effects of or identify any adverse reactions to investigational products, or to study the absorption, distribution, metabolism, and excretion of the products with the object of ascertaining their efficacy and safety (ICH-GCP, 2018). *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 trial (ICH-GCP, 2018).

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 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.

Complex emergency as defined in Republic Act 10121 (Philippine Disaster Risk Reduction and Management Act of 2010), "a form of human-induced emergency in which the cause of the emergency as well as the assistance to the afflicted is complicated by intense level of political considerations."

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) (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, 2018).

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 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 deciding that they 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)

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 45).

Disaster as defined in Republic Act 10121 (Philippine Disaster Risk Reduction and Management Act of 2010), "a serious disruption of the functioning of a community or a society involving widespread human, material, economic or environmental losses and impacts, which exceeds the ability of the affected community or society to cope using its own resources."

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 cruelness 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.

Emergency as defined in Republic Act 10121 (Philippine Disaster Risk Reduction and Management Act of 2010), "unforeseen or sudden occurrence, especially danger, demanding immediate action."

Epidemic/outbreak as defined in Republic Act No. 11332 (Mandatory Reporting of Notifiable Diseases and Health Events of Public Health Concern Act), "an occurrence of more cases of disease than normally expected within a specific place or group of people over a given period of time."

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 or 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 on behalf of another person. *See also Legally Authorized Representative*

Health - a state of optimal physical, mental, and social well-being and the ability to function at the individual level (PNHRS Act).

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.

Impartial Witness A person, who is independent of the trial, who cannot be unfairly influenced by people involved with the trial, who attends the informed consent process if the subject or the subject's legally acceptable representative cannot read, and who reads the informed consent form and any other written information supplied to the subject (ICH-GCP)

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 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-ascription 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 one's 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 15*) 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.

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*

Juridical person a non-human legal entity that is not a single natural person but an organization or an organic unit resulting from a group of persons or mass to which the state grants or recognizes personality and capacity to hold patrimonial rights independent of those component members, e.g. the State and its political subdivisions, corporations, institutions and entities for public or for private interests (Civil Code of the Philippines: Juridical Persons, Arts. 44, 45 ,46).

Justice - the ethical obligation to treat each person in accordance with what is morally right and proper, to give each person what is due them; 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). *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 on 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 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/IIa 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 normality 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.

Public Health Emergency an occurrence or imminent threat of an illness or health condition that meets the criteria stipulated in Section 3(l) of Republic Act No. 11332 (Mandatory Reporting of Notifiable Diseases and Health Events of Public Health Concern Act)

Quality of Life state or condition wherein an individual is able to live as how one normal person wants to live their 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 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) 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 development of knowledge with the aim of understanding health challenges and mounting an improved response to them. This covers the full spectrum of research in five (5) generic areas of activity: (1) measuring the problem; (2) understanding its cause(s); (3) elaborating solutions; (4)

translating the solutions or evidence into policy, practice, and products; and (5) evaluating the effectiveness of solutions (PNHRS Act).

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 that takes responsibility for initiating, managing, and financing 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.

State of Calamity as defined in Republic Act 10121 (Philippine Disaster Risk Reduction and Management Act of 2010), "a condition involving mass casualty and/or major damages to property, disruption of means of livelihoods, roads and normal way of life of people in the affected areas as a result of the occurrence of natural or human-induced hazard."

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.

Toxidrome the constellations of signs associated with a class of poisons

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 their personal data, including the risks and safeguards involved, the identity of personal information controller, their 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.

Virtual Reality is the use of computer technology to create the effect of an interactive three-dimensional world in which the objects have a sense of spatial presence. (The Virtual Windtunnel, n.d.)

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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