MAKATI MEDICAL CENTER

Hospital Policies and Procedures Manual

Governance, Leadership and Direction (GLD)		Document Code: MMC-HPP-GLD-014	Rev. Code : 00
Conduct of Research Involving Patients and Hospital Staff as Research Subjects		Effective Date: June 28, 2021	Page 1 of 18
Issued by: **Institutional Review Board**	New ☑	Supersedes: Policy on Hospital Staff as a Research Subject MMC-HPP-PFR-001 Rev. 00, Policy on Conduct of Research Involving Patients MMC-HPP-PFR-023 Rev. 01 and Policy on Participation in Clinical Research, Clinical Investigations, and Clinical Trials MMC-HPP-GLD-007 Rev. 03	
Approved by: *(original document signed)* **Saturnino P. Javier, MD** Medical Director	Date Signed (MMM/DD/YYYY)	*(original document signed)* **Atty. Pilar Nenuca P. Almira** President and CEO	Date Signed (MMM/DD/YYYY)

Objective:

A. To provide guidelines in conducting clinical research involving patients and hospital staff of Makati Medical Center;
B. To identify the circumstances in which a member of the hospital staff can serve as a research subject;
C. To establish and implement safeguards to protect the safety, rights and well-being of hospital staff involved in research studies conducted at Makati Medical Center; and
D. To establish a process wherein patients and their families can access clinical research and clinical trials in compliance with the regulatory laws.

Scope:

This policy applies to all consultants, fellows, residents, medical interns, pharmaceutical companies, healthcare professionals and other (affiliated) investigators who plan to conduct clinical researches involving the patients, hospital staff and students (e.g., medical, nursing, medical technologists, etc.) of Makati Medical Center (MMC) and/or outside MMC by an affiliated investigator and/or studies involving human subjects for publication.

Definition of Terms:

Vulnerable Subjects - Individuals who are incapable of protecting their own interests.
Hospital Staff - Employees, interns, residents, fellows, consultants, nurses and other personnel of Makati Medical Center who provide care, treatment and services in the institution and receive pay.
Privacy - The state of keeping and protecting patient information from the public.

Confidentiality	-	Non-disclosure of any personal data of the patient during the conduct of a research.
Clinical Trial	-	Study of investigational products (IP) on human subjects to discovers its pharmacological/ pharmacodynamic effects including the absorption, distribution, metabolism and excretion of the IP, safety and efficacy and possible adverse reactions.

Policy:

All researches involving human subjects will undergo review and approval by the Makati Medical Center Institutional Review Board (MMC-IRB). Makati Medical Center (MMC) safeguards the safety, well-being and rights of MMC patients and hospital staff as research subjects.

Makati Medical Center shall inform, when applicable, patients and their families of the latest in clinical research and trials which have undergone ethics review by the MMC-Institutional Review Board (IRB). The latest information on the same shall form part of the communication from attending physician(s) in the course of patient care. That information includes the following:

a. Expected benefits;
b. Potential discomforts and risks;
c. Alternatives that might help them; and
d. Procedures that must be followed.

All MMC-IRB approved researches undergo Research Compliance Review (MMC-HPP-GLD-012), including but not limited to the validation of data by the Clinical Research Center.

Careful consideration is required for all studies involving vulnerable subjects specifically junior or subordinate members of a hierarchal group. Inclusion of such subjects should not be subjected to undue influence, coercion or fear of disapproval if the subject refuses.

**For full details regarding the review of research involving human subjects (e.g., patients, medical staff, employees, etc.), please refer to the Makati Medical Center Institutional Review Board Operating Procedures Chapters 1, 2 and 3.*

Guidelines:

I. In having a research reviewed and approved by the MMC IRB and in conducting the research, the following International Council for Harmonisation – Good Clinical Practice (ICH GCP) principles are considered:

A. Research studies are conducted based on ethical principles of the Declaration of Helsinki, Good Clinical Practice and other regulatory requirements.
B. Prior to the initiation of the study, the anticipated benefits are weighed against the foreseeable risks whereas the benefits justify the risks.
C. The rights, safety and well-being of the study participants are prioritized throughout the trial.
D. There is sufficient clinical and non-clinical information on the investigational product or procedure to support the study protocol.
E. The research study is ethically and scientifically sound. This is presented in a detailed protocol. For the contents of the protocol, refer to the Makati Medical Center Institutional Review Board Standard Operating Procedures (MMC IRB SOP).
F. The conducted research is compliant with the protocol reviewed and approved by the MMC IRB.
G. Each clinical department regularly apprises members of the medical staff on the latest trend in research and trials which have been reviewed and approved by the MMC IRB.
H. Each department and respective medical staff shall include research and trials as treatment options for the patient and family, as applicable to the patient's medical needs.
I. A qualified physician is responsible for the provided medical care and medical decisions made on behalf of the study participant.
J. The Principal Investigator, Co-investigator(s) and other members of the research team are qualified through education, training, and experience; thus, individual tasks are performed appropriately.
K. The rule on conflict of interest shall be strictly implemented and the attending physician is required to disclose any conflict of interest, as set in the ethical review.
L. Prior to study participation, an informed consent is obtained from the participant.

M. Inquiries from patients and families about research and trials are accorded immediate and competent response. Attending physicians endeavor to communicate such information, as necessary, within a reasonable interval from the time of diagnosis and inquiry.

N. For those study protocols which have undergone ethical review from MMC IRB, full disclosure of potential discomfort, risk, and benefits is done, and other requirements of a valid informed consent are satisfied (refer to Policy on Informed Consent, MMC-HPP-PFR-002). Patients and families are also informed of alternatives that might help them and the procedures that must be followed. They are informed that they can refuse to participate or withdraw from participating in the study at any given time without compromising their access to hospital services (refer to Right to Refuse or Discontinue Treatment, Withhold Resuscitative Services, and Forego or Withdraw Life-Sustaining Treatments, MMC-HPP-PFR-006). The informed consent process is documented in the patient medical record and all necessary documents are signed by the patient or by the patient's legal representative.

O. All study information is documented adequately. Documents are managed and stored appropriately for accurate reporting, interpretation and verification.

P. The participation of patients in research and trials shall be within the bounds of legal and ethical parameters of medical practice.

Q. The privacy and confidentiality of the participants' identity is maintained throughout and after the study in accordance with the Data Privacy Act 2012 and other applicable regulations.

R. All other applicable policies and procedures of MMC-IRB regarding the protection of participants apply.

S. All protocols for clinical research and trials are reviewed and approved by the Institutional Review Board and the Bioethics Committee, as applicable.

T. The manufacture, handle and storage of the investigational products are according to the good manufacturing practice (GMP) and the approved protocol.

U. Assurance of quality of the trial must be implemented.

II. Guidelines for Clinical Trials

Based on the National Ethical Guidelines for Health and Health-Related Research 2017, the protocol should include the following:

A. Cover Sheet
This specifies the revision date and number, title of the research, signatures and dates of the authors, implementing agency, cooperating agency and approval of the primary investigator and contact numbers of the authors and cooperating agency.

B. Table of Contents

C. Introduction
To understand the rationale study, this provides a brief summary of the background in relation to the research design methodology

D. Title of the Study

E. Program or Project Leader
This specifies information about the Program or Project Leader:
1. Name
2. Designation or Title in his/her agency
3. Field of specialization
4. Email address
5. Telephone
6. Fax Numbers
7. Percentage time to be devoted to the research

F. Implementing Agency
This is the agency(ies) that will implement the research.

G. Cooperating Agency
This is the agency(ies) that will contribute to the research.

H. Significance of the Proposal
This explains the purpose/ rationale of the research.

I. Literature Review
This is the discussion of literature related to the study. This is used to prove that the research proposal is sound information based, addresses current health priorities of the country and contributes something new.

J. Objectives
This is the enumeration of the goals of the research. The general objective(s) is separated from the specific objectives. These are Specific, Measurable, Attainable, Relevant and Time-Bound.

K. Expected Outcome(s)
A specific statement of the primary and secondary endpoints, if any, to be measured during the trial.

L. End-Users or Target Beneficiaries
This specifies the end-users or expected beneficiaries of the research.

M. Duration of Program or Project
Time period when the study is conducted (i.e., start, completion and duration in months).

N. Methodology
1. Research Design
This specifies how the study objectives will be obtained. A description of the type of trial to be conducted (e.g. double- blind, placebo-controlled, parallel design) and a schematic diagram of trial design, procedures and stages.

2. Research Population
This describes the study participants required. This includes the number of study subjects that will be accrued to complete the study.
   a. Inclusion Criteria
   To be included in the study, this section describes the criteria the subjects must meet (e.g., age, gender, race, diagnosis/condition, etc.).
   b. Exclusion Criteria
   This section specifies the criteria to determine if the subject is not eligible to participate in the study.

c. Subject withdrawal criteria (i.e., terminating trial/ investigational product treatment and procedures specifying:
   1) When and how to withdraw subjects from the trial/ investigational product treatment
   2) Type and timing of the data to be collected for withdrawn subjects
   3) Whether and how subjects are to be replaced
   4) Follow up of subjects withdrawn from trial/ investigational product treatment.

d. Sample Size Computation
   This describes the process of computing the sample size (including the assumptions used) and the type of sampling design.

3. Research Site
   This is the location where the research will be conducted.

4. Research Plan
   This is a detailed discussion of the procedures and methods that will be used during the study. This includes the tests, interviews, data collection that will be performed. This includes the assessment of efficacy and safety:
   a. Specification of the efficacy parameters
   b. Methods and timing for assessing, recording and analyzing of efficacy parameters
   c. Specification of safety parameters
   d. The methods and timing for assessing, recording, and analyzing safety parameters.
   e. Procedures for eliciting reports of, and for recording and reporting adverse events and intercurrent illnesses.
   f. Provision for managing adverse reactions
   g. The type and duration of the follow up of subjects after adverse events.

5. Case Report Form
   Printed copy of this form is attached to the study protocol. The Case Report Form is a record used to document information gathered related to the study protocol.

6. Variables to be Investigated
   These are the dependent/ outcome and independent variables

O. Plans for Data Processing and Analysis
This includes the computer facilities to be used, software packages, statistical tools/ tests to be used and dummy tables.

P. Work Plan Schedule
This is the chronological order of study activities. Through the use of a Gantt Chart, the time frame and schedule of the research activities is presented.

Q. Ethical Clearance
Researches that involve human subjects require approval by the Institutional Review Board prior initiation.

R. Research Utilization
This explains how the expected research results will be disseminated and utilized.

S. Estimated Budgetary Requirements
This discusses the annual budget for the proposal wherein the major expenses for the first year is specified. There is a detailed breakdown of financial assistance based on the New Government Accounting System (NGAS) and reflection of the financial requirements and other source of funds.

T. Curriculum Vitae
This presents the proponent's qualifications and capabilities to conduct the research.

U. Endorsement from the Agency Head
This describes the support of the implementing agency in terms of assistance in the conduct including facilities and equipment.

V. Bibliography
This lists the references used for the research.

W. Line Time Budget
This is the table that will present the sources of funds and the amount provided by implementing/ sponsoring agencies.

X. Informed Consent

The rights and welfare of human participants in medical research shall be adequately protected by a legally effective informed consent. For details on the contents of the Informed Consent Form, refer to the Makati Medical Center Institutional Review Board Standard Operating Procedures Appendix on Guidelines on Submitting an Informed Consent Form (FM-MMC-IRB-039).

III. Guidelines in Obtaining Informed Consent

A. Informed consent is obtained from all human research participants or from his/her authorized guardian/representative before the participation. Informed consent is obtained from prospective research participants.

1. For the mentally-ill, the guardian or the court (in the absence of a guardian) can give the informed consent.
2. Children and their parents/guardian are given full explanation of the aims, possible hazards, inconveniences, and benefits as research participants. Their consent is obtained in addition to the consent of both parents or legal guardian. Moreover, among street children with no parent or guardian, informed consent is obtained from an appropriate government agency.
3. For institutionalized children (orphanage, reform schools, etc.), their consent, as well as that of the nearest kin, are obtained.
4. Research on pregnant and lactating mothers is conducted only without risk to the well-being of the fetus or the healthy development of the nursing infant. Consent must be obtained from both the mother and father. An explanation must be provided in case the father is not available to give consent.
5. The individual who seeks to obtain the consent of members in the hierarchically-structured group is not from the direct supervisor of the potential participants but from the individual himself. Further, the consent is obtained without duress or promise of promotion or reward.
6. Community-based research, e.g., experimental treatment of water supplies, trials of new insecticides, prophylactic agents, nutritional adjuvant or substitutes, etc., may dispense with individual consent.
7. A separate consent is obtained if body tissues/fluids of patients are stored or intended for use in other future research.
8. If informed consent is deemed unnecessary, the reason is clearly stated in the protocol.

B. In obtaining consent, no element of force, fraud, deceit, duress of any form of constraint or coercion shall be employed.

C. A written consent is signed and dated by the study participant or by the authorized guardian or representative of the subject. The study participant is provided with a copy of the signed informed consent.

IV. Guidelines on Hospital Staff as a Research Subject

1. Benefits expected are related to the field of work of the subject.
2. Staff must be informed about the study process, benefits and risks, alternative treatments and procedures prior to study participation.
3. The staff can only participate in a study that has been reviewed by the Makati Medical Center Institutional Review Board (MMC IRB).
4. The participant's identity and other personal data must be kept private and confidential at all times during and after the conduct of the study. The investigator can only disclose the information upon the consent of the participant.
5. Subjects are free to refuse or withdraw from the study anytime. Such refusal or withdrawal does not result in any sanction/ penalty or any compromise in the care and access to hospital services. This should not affect their employment or performance evaluation.
6. As much as possible, supervisors are not informed of employees who participate in studies.
7. For recruitment purposes, research subjects must not directly interact with employees who directly report to any of the investigators.

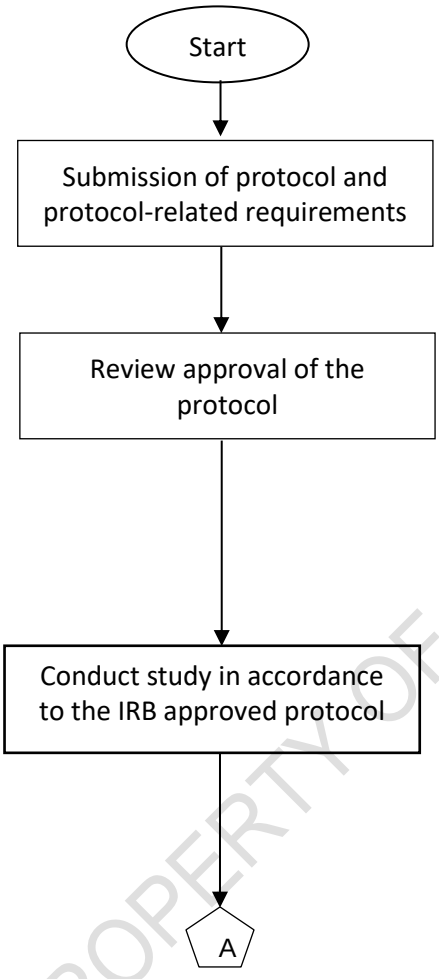
V. Criteria for Approval of Research Proposals

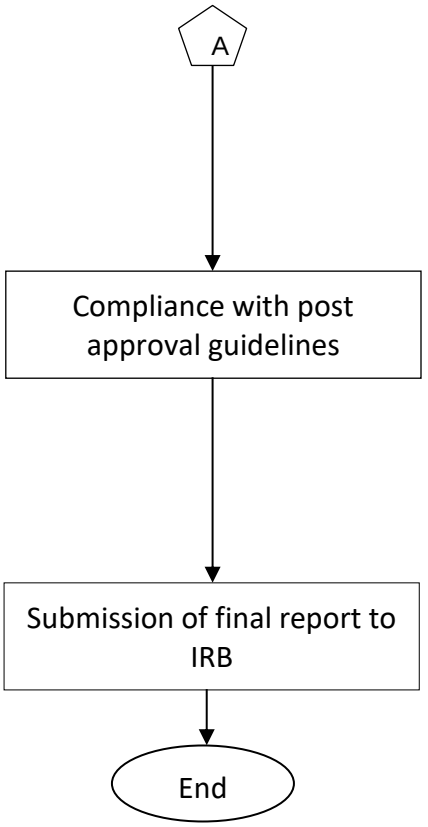
All research proposals involving human subjects must be approved by the IRB. No study proposals using unapproved or unregistered drug by FDA can be conducted at the center. Protocol approval is based on the following criteria:

A. Nature and gravity of the risk to the human subjects
B. Adequacy of safeguards and protection against risks
C. Magnitude of potential benefits vis-à-vis harm to the individual or community
D. Validity of the informed consent
E. Ecological impact
F. Clarification of potential conflicts of interest

This should include statement on ability to compensate patients for injury as stated on "Characteristics of Informed Consent"

Procedure

Process Flow Map	Person Responsible	Details of the step
	Principal Investigator	The principal investigator complies with all the IRB requirements for the submission of a protocol for review by MMC IRB.
	IRB	The IRB reviews the complete protocol documents and recommends approval of the study protocol according to the defined criteria in the MMC IRB SOP.
	Principal Investigator	The principal investigator implements the approved study protocol while protecting and ensuring the participant's rights and safety.



Principal Investigator	Informed consent is obtained prior to study participation of the patient.
	The principal investigator submits the necessary reports during the conduct of the study.
Principal Investigator	A final report is submitted to IRB to review the result of the study.

Responsibility:

The Department Chairs, Section Chiefs, Training Officers and Research Proponents (Principal and Co-Investigators) ensure compliance to this policy.

A. Investigator
The responsibilities of the Principal Investigator are specified in the Makati Medical Center Institutional Review Board Post Approval Guidelines (Appendix 1).

B. Sponsor
1. Safety Information
   a. The sponsor is responsible for the ongoing safety evaluation of the investigational product.

b. The sponsor promptly notifies all concerned investigators/ institutions and the regulatory authority of findings that could affect adversely the safety of subjects, or alter the IRB's approval/ favorable opinion to continue the trial.

2. Adverse Drug Reaction Reporting
   The sponsor expedites the reporting of all adverse drug reactions (ADRs) that are both serious and unexpected, to all concerned investigators/ institutions, to the IRB, and to the regulatory authority where required.

   Such expedited reports comply with the applicable regulatory requirements and with the International Conference on Harmonization – Good Clinical Practices Guideline for Clinical Safety Data Management: Definitions and Standards for Expedited Reporting.

   The sponsor submits to the regulatory authority all safety updates and periodic report, as required by applicable regulatory requirements.

3. Compensation to Subjects and Investigators
   If required by the applicable regulatory requirements, the sponsor provides insurance or indemnifies (legal and financial coverage) the investigator/ institution against claims arising from the trial, except for claims that arise from malpractice and/or negligence. The sponsor's policies and procedures address the costs of treatment of trial subjects in the event of trial-related injuries in accordance with the applicable regulatory requirements. When trial subjects receive compensation, the method and manner of compensation complies with the applicable regulatory requirements.

Required Education:

Good Clinical Practice (renewed every three years).

Attachment:

1. Appendix 1: Post-Approval Guidelines
2. Appendix 2: Guidelines on Submitting an Informed Consent Form

Review: The IRB Chair or designate reviews this policy every three (3) years or earlier as indicated.

Reference/s:

1. Philippine Health Research Ethics Board Ad Hoc Committee for Updating the National Ethical Guidelines. *National Ethical Guidelines for Health and Health-Related Research 2017.* Philippines: Department of Science and Technology – Philippine Council for Health Research and Development, 2017.

2. Joint Commission National. *Joint Commission International Accreditation Standards for Hospitals including Standards for Academic Medical Center Hospitals 7th Edition.* USA: Joint Commission International, 2020.

3. International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH). (2016). ICH Harmonised Guideline Integrated Addendum to ICH E6 (R1): Guideline for Good Clinical Practice E6(R2). Retrieved from https://www.ich.org/fileadmin/Public_Web_Site/ICH_Products/Guidelines/Efficacy/E6/E6_R2__Step_4_2016_1109.pdf

Signatories:

Author (s) *(original document signed)*
D. Darwin A. Dasig, M.D.
Institutional Review Board/Office of the Medical Director

Reviewed by:

1. Jose Paulo P. Lorenzo, MD — Director, Division of Medical Education and Research
2. Teresita R. Sanchez, MD — Chair, Legal Medicine

Appendix 1: Post-Approval Guidelines

MAKATI MEDICAL CENTER

INSTITUTIONAL REVIEW BOARD

POST-APPROVAL GUIDELINES

1. The Principal Investigator and the Study Team are urged to:
   a. Comply with all relevant international and national guidelines and regulations.
   b. Abide by the principles of Good Clinical Practice and ethical research.
   c. Comply with Makati Medical Center's policy on Medication Management and Use: Management of Investigational Drugs.
   d. Comply with all post-approval provisions of MMC-IRB

2. All approved Informed Consent Forms and other recruitment materials (e.g., posters, etc.) should bear the MMC IRB Stamp of Approval before these documents are used.

3. The following must be reported:
   a. All on-site Serious Adverse Events (IRB SAE Form 3.1A) within seven (7) days. Please forward two (2) copies of this form to the IRB office after encoding. Events from other sites must be reported along with progress report. SAEs are submitted online via the link below: https://docs.google.com/forms/d/1NpL_xfOcGuXIIFvrWQcP-eX-zHkWkkGL_lPgxoRK0H_Y/viewform?c=0&w=1&usp=mail_form_link
   b. Any scientific update, interim report, advisory or development related to the study drug, procedure, technology or device (particularly those that will adversely affect study participants)
   c. Any claims for damages or compensation instituted by any subject or patient.
   d. All protocol deviations /violations (Form 3.5)

4. In special instances, the Investigator may be requested to come and enlighten the Board when necessary on any matter related to the study.

5. Changes in the protocol should not be implemented without prior written IRB Approval. Please submit the following for Amendments:
   a. Five (5) Copies of the amendment with letter of intent.
   b. Summary of the amended components (Form 3.2). (Please highlight and flag the page where the amendment is located.)

6. An end-of-trial report (Form 3.4) or an annual report (Form 3.3), whichever comes first, must be submitted. A Progress report should be submitted one (1) month before the expiration of the approval. Final reports are required after the completion of protocol procedures at the study site.

   For trainees (interns, residents and fellows), submission of the Final Report is necessary for clearance purposes from MMC-IRB before issuance of certificate from Medical Education and Training Division.

   The FINAL REPORT should provide the following information among other things:
   a. Number of subjects enrolled
      i. Target Population for the entire study (for multicenter studies)
      ii. Target Population for the Makati Medical Center site
   b. Number of withdrawals (dropout rate) and the reason(s) for withdrawals
   c. Adverse events during conduct of study (e.g., nature of adverse events, etc.)
   d. Date the study was initiated and completed
   e. Date the study was terminated/ and reason for termination
   f. Results and conclusions of the study

Kindly extend full cooperation to the IRB Staff who will regularly track all protocol-related matters. For any questions regarding IRB, please contact any of the following:
   a. John David S. Agustin (IRB Staff) local 3972
   b. Kristine D. Mercado (IRB Staff) local 7166
   c. D. Darwin A. Dasig, MD (MMC-IRB Chair) loc. 3971

FM-MMC-IRB-042 REV 07 OCT 2019

Appendix 2: Guidelines on the Submission of an Informed Consent

MAKATI MEDICAL CENTER

INSTITUTIONAL REVIEW BOARD

GUIDELINES ON SUBMITTING AN INFORMED CONSENT FORM

The informed consent is defined as a process by which a subject voluntarily confirms his or her willingness to participate in a particular trial, after having been informed of all aspects of the trial that are relevant to the subject's decision to participate.

Both the discussion and the written informed consent provided to the subjects should include explanations of the following:

1. That the trial involves research.
2. The purpose of the trial.
3. The trial treatment(s) and the probability for random assignment to each treatment.
4. The trial procedures to be followed, including all invasive procedures.
5. The subject's responsibilities.
6. Those aspects of the trial that are experimental.
7. The reasonably foreseeable risks or inconveniences to the subject and, when applicable, to an embryo, fetus or nursing infant.
8. The reasonably expected benefits. When there is no intended clinical benefit to the subject, the subject should be made aware of this.
9. The alternative procedure(s) or course(s) of treatment that may be available to the subject, and their important potential benefits and risks.
10. The compensation and/or treatment available to the subject in the event of trial-related injury.
11. The anticipated prorated payment, if any, to the subject for participating in the trial.
12. The anticipated expenses, if any, to the subject for participating in the trial.
13. That the subject's participation in the trial is voluntary and that the subject may refuse to participate or withdraw from the trial, at any time, without penalty or loss of benefits to which the subject is otherwise entitled.
14. That the monitor(s), the auditor(s), the Institutional Review Board (IRB), and the regulatory authority (ies) will be granted direct access to the subject's original medical records for verification of clinical trial procedures and/or data, without violating the confidentiality of the subject, to the extent permitted by the applicable laws and regulations and that, by signing a written informed consent form, the subject or the subject's legally acceptable representative is authorizing such access.
15. That the records identifying the subject will be kept confidential and, to the extent permitted by the applicable laws and/or regulations, will not be made publicly available. If the results of the trial are published, the subject's identity will remain confidential.
16. That the subject or the subject's legally acceptable representative will be informed in a timely manner if information becomes available that may be relevant to the subject's willingness to continue participation in the trial.

17. The person(s) to contact for further information regarding the trial and the rights of trial subjects, and whom to contact in the event of trial-related injury.
18. The foreseeable circumstances and/or reasons under which the subject's participation in the trial may be terminated.
19. The expected duration of the subject's participation in the trial.
20. The approximate number of subjects involved in the trial.
21. For concerns regarding patient's rights, the participant may contact the following:

- Makati Medical Center Institutional Review Board
  7th Floor, Keyland Center
  143 Dela Rosa cor. Adelantado Sts. Legaspi Village, Makati City
  Tel. No. 8888-999 Loc. 7166, 3972 or 3973
  Fax No. 8888-999 Loc. 7182
  Email address: irbmmc.admin@makatimed.net.ph

References: ICH-GCP 1.28
ICH-GCP 4.8.10