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Hospital Authority (HA) Guide on Research Ethics (for Study Site & Research Ethics Committee)

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1. INTRODUCTION

- 1.1 Clinical trials and clinical research (collectively referred to as “Clinical Research”) are necessary if medicine is to progress. They contribute to the generation of knowledge and development of technology for healthcare advancement. Such objectives, however, do not take precedence over the interests of the research subjects (“Research Subjects”).
- 1.2 Clinical Research is premised on trust. At times, it places Research Subjects at risk for the good of the community. The community and the Research Subjects therefore have legitimate expectations that a system of protection should be in place. The guideline sets out the system of protection within HA. The requirements have been developed with reference to overseas practice and local experience. HA expects that the requirements set out in this document should apply to all clinical trials conducted in HA to safeguard the safety of trial subjects.
- 1.3 For research oversight on Phase 1 clinical trials, please refer to the following guideline and standard operating procedure for additional requirements for Phase 1 clinical trials:
- (i) Guideline of Ethics Oversight and Scientific Evaluation of Phase 1 Clinical Trials
 - (ii) Standard Operating Procedure of the Joint Scientific Committee for Phase 1 Clinical Trial

2. ETHICAL REQUIREMENTS IN CLINICAL RESEARCH

- 2.1 In Clinical Research, the mandatory ethical requirements are the principles of the Declaration of Helsinki, and whenever applicable, the International Conference on Harmonisation – Good Clinical Practice Guidelines (“ICH-GCP Guidelines”). Legal requirements and local institution policies must also be complied with. Some of the important requirements are:
- (i) Clinical Research methodology must be scientifically valid and adequate in addressing the questions posed.
 - (ii) Clinical Research designed must minimize the potential risks to the Research Subjects, and its anticipated benefits must justify the potential risks.
 - (iii) Equipoise must exist between different arms of a therapeutic trial comprising different interventions or different dosages.
 - (iv) To ensure voluntary participation in Clinical Research, Research Subjects must be adequately informed of the experimental nature of the understanding; the

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nature of the Clinical Research, its risks, burdens and benefits, and their rights to withdraw at any time, which will not affect the care they entitle.

- (v) As each person weighs risks and benefits differently, we must respect other's freedom to decide, based on his/her own value and belief, without coercion and undue influence
- (vi) Selection precautions should be taken to protect vulnerable Research Subjects.
- (vii) Throughout a trial, Research Subjects should be provided with updated information about the Clinical Research (including adverse events) so that they are free to decide whether or not to continue.

3. HA'S OBLIGATIONS AS A RESEARCH INSTITUTION

3.1 As a public healthcare provider, HA has to ensure that:

- (i) services are accorded priority;
- (ii) Research Subjects' rights, safety and welfare are protected;
- (iii) Clinical Research is conducted ethically and lawfully amongst its staff;
- (iv) public confidence is sustained by an environment that upholds scientific and ethical integrity; and
- (v) liabilities to HA be minimized.

3.2 HA established an ethical review and oversight mechanism through the Research Ethics Committee ("REC") structure which is an added layer of protection for Research Subjects.

4. GOVERNANCE STRUCTURES AND FUNCTIONS OF REC

4.1 REC is organized on two levels: HA Head Office ("HAHO") and the Clusters

4.2 HAHO Steering Committee on Research Ethics ("HA REC")

4.2.1 HA REC is accountable to HA:

- (i) To steer the development of research governance in HA
- (ii) To align research ethics standards and practices within HA and with affiliating academia
- (iii) To monitor and audit research governance in HA
- (iv) To handle appeals against Cluster REC review procedures

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4.3 Cluster REC

4.3.1 The Cluster REC is responsible for conducting ethics review and overseeing the execution of study duties within the Cluster.

4.3.2 There are four Cluster RECs under the governance structure of Cluster Management, as follows:

- (i) Hong Kong East Cluster Research Ethics Committee (HKE CREC)
- (ii) Kowloon Central / Kowloon East Cluster Research Ethics Committee (KC/KE CREC)
- (iii) Kowloon West Cluster Research Ethics Committee (KW CREC)
- (iv) New Territories West Cluster Research Ethics Committee (NTW CREC)

4.3.3 For the two Clusters with the teaching hospitals, the Cluster RECs are under the joint governance of Cluster Management and the affiliating University, as follows:

- (i) Institutional Review Board of The University of Hong Kong / Hospital Authority Hong Kong West Cluster (HKU/HA HKW IRB)
- (ii) Joint Chinese University of Hong Kong – New Territories East Clinical Research Ethics Committee (Joint CUHK-NTE CREC)

4.3.4 While the Cluster REC is accountable to the governance represented by the Cluster Chief Executive (“CCE”) or the joint governance represented by CCE and Dean of the Medical Faculty (“Dean”) respectively, it should function as independently as possible according to the Cluster REC’s Standard Operating Procedure.

4.3.5 Besides ethical approval by Cluster REC, Clinical Research on HA patients or within HA facilities must

- (i) Seek approval by Study site management (i.e. the hospital and affiliating academia if applicable) and
- (ii) Comply with regulatory requirements if applicable, (e.g. Clinical Trial Certificate by Department of Health and Personal Data (Privacy) Ordinance).

5. RESPONSIBILITIES OF THE STUDY SITE MANAGEMENT

5.1 At the study site (“Study Site”), all Clinical Research must, first of all, be approved by the Chief of Services (“COS”) of the implicated department(s) before submitting to Cluster REC for ethics approval. The investigator has to submit the required documents (collectively “Application Dossiers”) to the COS. (Please refer to Annex 1 for the details

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of Application Dossiers)

5.2 Administrative approval

- (i) By signing the Research Ethics Application Form, the COS endorses the Clinical Research as both scientifically and ethically sound. S/he also confirms that:
 - (a) Services priority of the department will not be affected;
 - (b) Research team is competent;
 - (c) The investigator has sufficient resources to conduct the Clinical Research safely;
 - (d) Therapeutic intervention(s), if any, can be performed by appropriate personnel proficient in managing conditions that may arise; and
 - (e) The Study Site has sufficient facilities to support the Clinical Research; and
 - (f) If the Clinical Research is sponsored, the CTA has been approved (or under process) by the HAHO Legal Services Section and an approved Letter of Indemnity is in place (or under process).
- (ii) If in doubt, the COS should submit the Application Dossiers to the hospital management. Before approving the Clinical Research, the hospital management has to satisfy itself that:
 - (a) Service priority of the hospital will not be adversely affected by the Clinical Research;
 - (b) The hospital has in place sufficient facilities/resources to conduct the Clinical Research safely and to manage conditions that may arise;
 - (c) If the Clinical Research is sponsored, the CTA has been approved (or under process) by the HAHO Legal Services Section and an approved Letter of Indemnity is in place (or under process); and
 - (d) The Cluster Chief Executive (“CCE”) or his/her designate’s approval is required if the Clinical Research involves testing of an article for unlicensed indications, which exposes the hospital to unknown risks.
- (iii) In negotiating a CTA with the sponsor:
 - (a) The hospital management can approach the Legal Services Section for pre-approved HA CTA template and/or pre-approved drug company CTA templates.
 - (b) Other than where a pre-approved CTA is used, the hospital management has to liaise with sponsors and Legal Services Section for amendments and approval of CTA.
 - (c) If the Clinical Research is a multi-centre trial, the principal investigator’s hospital is responsible for ensuring the approval of CTA and that the Letter of Indemnity is in place for all HA Study Sites. The principal investigator

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should notify the Legal Services Section that s/he is co-ordinating the approval for all HA Study Sites.

5.3 Handling of complaints on clinical research

- (i) Complaints on Clinical Research, whether in respect of incompetence, negligence, misconduct or otherwise, should be investigated promptly at the hospital level.
- (ii) If there is a genuine concern on the safety of Research Subjects, the hospital should suspend the Clinical Research while the complaint is being investigated.
- (iii) Cluster REC and HA REC should be notified of the complaint and the investigation findings.

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ANNEX 1

Application Dossiers:

- (i) A duly completed and signed Application Form*;
- (ii) The research protocol;
- (iii) Investigator's brochure (if available);
- (iv) Consent form and information to be provided to Research Subjects (such as recruitment notice, invitation letter and safety information) in suitable language(s);
- (v) Curriculum vitae and relevant experience of the principal investigator and other investigators;
- (vi) Other relevant documents, such as support from an academia for student projects;
- (vii) For sponsored Clinical Research or where commercial interest is involved (e.g. collecting data, evaluating a device, comparing different drugs, drug dosages or off label use of a licensed drug), the following documents must be submitted:
 - (a) Conflict of interest declaration by the investigator*;
 - (b) Letter of Indemnity* for the standard indemnity agreement and procedure;
 - (c) Draft Clinical Trial Agreement ("CTA")*;
 - (d) A Certification of Clinical Trial or Medicinal Test (to be submitted when available at a later date) or other documents required by law; and
 - (e) The investigator should also state whether in his knowledge, the Clinical Research is to be conducted in other HA hospitals, and if so, the names of those hospitals.

Requirements under sub-paragraphs (vii)(b) and (vii)(c) do not apply to HA initiated Clinical Research.

*Use standard forms approved by the respective Cluster REC.